



Nature vs nurture in Food selection; A debate!

Sidra Khalid

PhD Human Nutrition and Dietetics Lahore Medical Research Center LLP

ARTICLE INFO

How to Cite:

Khalid, S. . (2022). Nature vs nurture in Food selection; A debate!. Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.641>

When it comes to dietary and nutritional preferences, no discussion of human nutrition is validated without addressing the underlying genetic composition. Genetic differences might also shadow someone's food likes and dislikes, enrooted to food preferences in nutritional behavior. Among the food bloggers its always been a point of debate that among the 'Nature versus nurture' which is more powerful. Recent literature states that scientist are still tracing this ancient concept touching temperament to exercise and from tendencies to eat. Numerous factors play an important role in our food selection and affect what we eat, however current literature have displayed that possibly the DNA plays a bigger role in a person's diet and food choices than we expect.

'Our DNA affects what we eat'. The genetic code can play a significant role in the alteration of tendencies towards food, involving gluten sensibility, taste choices, and lactose intolerance, among others. Additionally, multiple notable scientists and researchers have associated specific genetic pointers with specific characteristics. Such as recent studies linked a variant of a genes for bitter sense of taste stimuli; responsible for either one enjoy drinking coffee or not. The individual encompassing this kind of a genetic marker observe an increased bitter flavor while showcasing a greater propensity to drink more coffee. Among the factors that impact food preferences and selections, the surrounding society and the availability of specific type of foods play a major part in choosing a certain food material. Upon determination of numerous associated genetic markers, the role of heredity in particular eating patterns of human beings has been disclosed. In the Central Nervous System (CNS), the genetic disparity can potentially have an impact in the degree of satiety, observation of taste, and numerous other elements that have frequent effect on food intake. In the present day, no such authenticated data or information is available for human beings in this particular range. Similarly, the nutrient absorption in human beings could also be varied or impacted. For instance, there is an elevated level of iron absorption in hemochromatosis with genetically associated mitigation of gastric intrinsic factor, eventually resulting in pernicious anemia and faulty and imperfect vitamin B12 absorption. Moreover, the innate variances in the functionality of enzymes and multiple different active proteins add to differences in nutritional specifications and preferences, leading to variable relation of specific nutrients with genetically dependent biochemical and metabolic facets. Whereas, this innate variation is relatively altered from epigenetic possibilities in numerous life stages pertaining to growth, old age, and gestation.

In all the aspects of food selection, scientists have also taken into consideration, the role of cultural and ethnical elements. The families or relatives linked to a similar ancestor are more likely to show a bit identical genetic makeup. Ultimately, an ethnic group can be described as a comprehensive family having somewhat similar reflections. Subsequently, the uniformities of genetically dependent behaviors and disorders will be displaying a difference among different races, even among various ethnic groups of similar race. In consideration of the possibility of a racial group present in a distinct environment doesn't really demonstrate the role of multiple genes in the ethnic or racial difference of certain traits. Furthermore, the distinction among various genetic and environmental factors can be made a lot stronger if the presence of the genes can be validated.



Breast Cancer Screening and Diagnostic Advancements

Sana Hasan¹

¹Standards Development & Dissemination, Directorate of Clinical Governance & Organizational Standard, Punjab Health Care Commission, Lahore, Pakistan

*sana.hasan@phc.org.pk

ARTICLE INFO

How to Cite:

Hassan, S. (2022). Breast Cancer Screening and Diagnostic Advancements. Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.599>

The best tool to detect breast cancer (BC) is 'screening'. Earlier screening improves prognosis and better treatment outcomes. Screening is basically looking for different signs before the appearance of actual symptoms. The process of screening specifically used for BC is known as mammography.

Mammography is an explicit kind of imaging system that uses X-Rays (low dose) to ascertain cancer in breasts. This diagnostic procedure is in practice since the past 30 years but in the past 15 years, there is an improved set of techniques being introduced resulting in better results. Recently, three major diagnostic procedures for breast cancer which are in vogue include digital mammography, computer-aided testing and tomosynthesis. Out of these 3 diagnostic tools, tomosynthesis, furthermore branded as three-dimensional (3-D) mammography and digital tomosynthesis, is the supreme and innovative system of breast imaging where numerous pictures of the breast from diverse angles are taken and remodeled ("synthesized") resulting in formation of a three-dimensional group of images. That is why, 3-D imaging technique is alike computed tomography imaging system in which a sequences of thin "slices" are gathered to formulate a 3-D reformation of the body.

Even though the strength of radiation for few tomosynthesis systems is higher to some extent as compared to power of the dosage used in typical mammography, but as long as it is in the predefined radiation limit approved by FDA it's not harmful. Some of the systems have doses comparable to conventional mammography. Some previous studies on large populations have proved that breast screening with tomosynthesis have resulted in enhanced the rate of detection of breast cancer detection rates and it has also decreased the chances of recalls, especially at occasions where females are called back for screening for added testing because of a possibly uncharacteristic finding.

Tomosynthesis has an edge on other diagnostic procedures as it may help in prior recognition of cancerous lesions that may be not be revealed on a conventional mammogram, it also eradicates the need for small number of preventable biopsies or supplementary testing and increases the probability of detection of several breast tumors. It also provides stronger imagining of irregularities within condensed breast tissue and greater precision in pinpointing the location, size and shape of breast anomalies.

Women should at least get a standard mammogram once a year beginning at age 40. The major risk factors for BC development are old age, inactivity, reproductive history, genetic mutations, family history of ovarian or BC, being overweight or obese after menopause, history of administration of hormones. Also, if someone, have had radiation treatment to the chest in the past, it's highly recommended that such women should have annual mammograms at a younger age (often beginning around age 30).



Review Article

Prediabetes; Prevention and Management: A Review Article

Asad Ali Mughal¹, Syed Taha Abbas¹, Huma Asad¹, Muhammed Zubair¹, Nasir Ali Khan¹, Shehla Naseem², Muhammad Zaman Shaikh³

¹Department of Endocrinology, College of Family Medicine, Karachi, Pakistan

²Department of Academic and Research, College Of Family Medicine, Karachi, Pakistan

³Department of Medicine, Sir Syed College Of Medical Sciences for Girls, Karachi, Pakistan

ARTICLE INFO

Key Words:

Impaired glucose tolerance, Impaired fasting glucose, Metformin, Diabetes, Prediabetes.

How to Cite:

Ali Mughal, A., Taha Abbas, S. ., Asad, H. ., Zubair, M. ., Ali Khan, N. ., Naseem, S. ., & Zaman Shaikh, M. . (2022). Prediabetes; Prevention and Management: Prediabetes; Prevention and Management. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.527>

***Corresponding Author:**

Asad Ali Mughal
 Department of Endocrinology, College of Family Medicine, Karachi, Pakistan
dr.mughal@yahoo.com

Received Date: 8th June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Pre-diabetes is the state of hyperglycemia at an intermediate stage in which parameters of blood glucose are above standard value but less than the threshold of diabetes. Diabetes mellitus is measured as a risk factor with a high probability of its development. Although the analytic measures for pre-diabetes are not the same in different international professional organizations, the danger of diabetes development is still in height, with conversion rates ranging from 5% to 10% per year. Databased studies propose a relationship between diabetic complications and pre-diabetes like early kidney disease, early retinopathy, small fiber neuropathy and the danger of macrovascular disease. Numerous analyses have revealed the effectiveness of daily routine interpositions in preventing diabetes, with a comparative danger decrease of 40% to 70% in prediabetic adults. Though there is cumulative indication that drug therapy is effective in preventing diabetes in prediabetic adults, drug options for treatment rather than metformin are related with side effects that bound their usage in prediabetics. There are no studies of systematic assessment of the healthiness consequences associated with prediabetes among Children. The effect of pharmacology treatment of pre-diabetes on development and growth in children during adolescence is unidentified. Secondary involvement with metformin pharmacology treatment is recommended for speculative persons, but the standards for assessing the advantage of such primary interference, the longstanding cost-effectiveness of such treatment is still uncertain. Pharmacological treatment should be cast-off with care in prediabetic children. Although pre-diabetes is usually asymptomatic, pre-diabetes always occurs before diabetes develops. The high blood sugar level persists and therefore pre-diabetes cannot be considered completely mild. Conclusions: The purpose of this review is to define the difficulties related with the analysis of pre-diabetes, the potential adverse outcomes of pre-diabetes, and the treatment opportunities and validation of its practice in the context of pre-diabetes.

INTRODUCTION

Diagnosis of Prediabetes: Various organizations have defined pre-diabetes using non-uniform criteria. The WHO has demarcated pre-diabetes as a condition of moderate hyperglycaemia by means of 2 precise constraints: Impaired fasting glucose is definite as fasting glucose between 6.1 mmol / L to 6.9 mmol / L or FBS 110-125 mg / dl and impaired glucose tolerance definite as a glucose concentration in plasma of 7.7-11.0 mmol / L (140-200 mg / dL) for 2 hours afterwards taking oral glucose load (75 g or double of it) based on 2 hours OGTT [1-2]. The ADA has the

same threshold (140-200 mg / dL) for IGT but a lesser threshold (100-125 mg / dL) for IFG and has HbA1c grounded criteria (5.7% to 6.4%) for the definition of pre-diabetes A1c (HbA1c) [3-4]. Numerous analyses have revealed a weak association between IFG, IGT and HbA1c [5]. The helpfulness of diagnosing diabetes or pre-diabetes with IGT and IFG is questioned because these glycaemic cut-offs do not take into account the pathology associated with diabetes and the likelihood of progressing towards diabetes in the future [6]. These cut-offs point also lose

their reliability due to reduced sensitivity of these tests in children and adults. While HbA1c is supposed to signify mean blood levels of sugar and ideally must more accurately reflect hyperglycaemia, it is not completely accurate. HbA1c is largely resolute by hereditary influences not dependent on blood sugar values and can be an inaccurate means for measuring normal sugar levels in blood [7]. Though there is reasonable concern about the analytical principles for pre-diabetes, pre-diabetes is less reproducible (about 52%) than diabetes (about 73%). Grounded on the accessible suggestion, it seems that pre-diabetes, definite by several substitute criteria, comprises of a lapping group of people at one or more time blood glucose irregularities [8-9]. It is probable that the existence of IGT and IFG may identify patients with various pathological anomalies in metabolism of glucose, and the incidence of both indicates a further deterioration in general homeostasis of glucose metabolism.

Prediabetes Prevalence: There have been studies of an expanded frequency of mean diabetes and FPG in both industrialized and under developing states [10]. The National Diabetes Statistics Description by the Centers for Disease Control and Prevention proposes that somewhere in the range of 2009 and 2012, 37% of American grown-ups beyond 20 years old and 51% of those beyond 65 years old had prediabetes, as estimated by glucose levels on void stomach or HbA1c [11]. Worldwide IGT frequency was assessed at 343 million (7.8%) in 2010, arriving at 5.8% in Southeast Asia and 11.4% in the nations of the North America and the Caribbean area. The IDF assesses that by 2035, the pervasiveness of pre-diabetes overall will increment to 471 million [12].

Health Risks Associated With Prediabetes Progression to diabetes: The proportion of transition from pre-diabetes to diabetes varies depending on the features of the people and the standards applied to define pre-diabetes. In meta-analysis held in 2007 about the prediabetes progression to diabetes, the yearly prevalence was 6-9% for isolated IGF, 4-6% for lonely IGT and 15% for isolated IGF and IGT [13-14]. The studies available earlier to 2004 were included in this meta-analysis. The yearly frequency of transition from pre-diabetes to DM were comparable in the large studies described below. In the Study of Diabetes Prevention Program, the diabetes incidence in the control group was 11% [15]. In the USA, International Atherosclerosis analysis, the yearly prevalence of DM in the group of IFG was just over 4.2%. In Health Management Center study of Toranomom Hospital, the frequency of DM was 7.7% to 6.4% in the HbA1c group and 8.9% in the group of IFG. The collective 20-year diabetes mellitus incidence in people with IGT definite by relapse of OGTT in the control group was over 90% testified by the China Da Qing Diabetes Prevention

Study (CDQDPS) [16]. It has been shown that the usage of ADA criteria versus criteria of WHO to describe pre-diabetes correspondingly affects the diabetes mellitus incidence, with less morbidity in those definite by criteria of ADA in comparison to the WHO diabetes criteria. A diabetes risk assessment grounded on a more available factors such as gender, age, fasting glucose, ethnicity, HDL cholesterol, systolic blood pressure, diabetes history and BMI has been shown to be better predictive of diabetes [17-18].

Variable	Studies	Sample size	Positive cases	Prevalence, % (95% CI)	I ²	95%, Prediction interval	p-Heterogeneity	p Egger	P-Difference
Prediabetes	9	88702	6443	11.62 (7.17-16.97)	0.998	(0.29-35.23)	< 0.001	0.1209	0.8978
Male prediabetes	7	39241	2796	10.98 (6.95-15.79)	0.994	(0.58-31.47)	< 0.001		
Female prediabetes	8	49201	3565	11.40 (6.55-17.40)	0.997	(0.01-37.55)	< 0.001		
Diabetes	15	103063	15429	14.39 (12.51-16.38)	0.984	(7.37-23.23)	< 0.001	0.7296	
Undiagnosed	8	91526	6798	8.60 (6.48-10.99)	0.992	(2.25-18.48)	< 0.001	0.2363	
By Gender								0.7555	0.6063
Male	12	45580	6697	13.80 (11.94-15.77)	0.961	(7.53-21.56)	< 0.001		
Female	13	55678	7992	14.54 (12.50-16.70)	0.973	(7.49-23.40)	< 0.001		
By Setting								0.8733	0.0594
Rural	11	37307	5060	12.72 (10.63-14.97)	0.966	(5.84-21.73)	< 0.001		
Urban	7	61561	9285	15.89 (13.59-18.34)	0.984	(8.23-25.48)	< 0.001		
By Age								0.3720	0.0001
20 to 29	5	2078	110	3.16 (3.62-6.94)	0.493	(1.35-11.05)	0.0915		
30 to 45	4	5935	815	13.71 (12.85-14.60)	0.000	(11.84-15.69)	< 0.001		
46 to 59	4	11165	2517	25.66 (20.60-31.07)	0.966	(5.70-53.57)	< 0.001		
60+	6	10191	3489	33.45 (28.45-38.64)	0.955	(17.14-52.08)	< 0.001		
Time period								0.7296	0.0210
1995-2010	5	42949	5250	11.82 (9.44-14.43)	0.951	(4.56-21.81)	< 0.001		
2011-2020	10	64615	11003	15.77 (13.75-17.89)	0.974	(8.98-24.00)	< 0.001		
Ethnicity								0.1269	<0.0001
Malay	10	56435	7718	15.25 (11.59-19.29)	0.993	(3.70-32.67)	0.0001		
Chinese	9	18057	1949	12.87 (9.73-16.37)	0.974	(3.29-27.38)	0.0233		
Indian	9	7909	1724	25.10 (20.19-30.35)	0.959	(9.14-45.65)	0.0001		
Bumiputeras	9	9699	704	8.62 (5.41-12.47)	0.968	(0.37-25.27)	0.3535		
Others	6	1710	122	6.91 (5.71-8.19)	0.000	(5.25-8.76)	0.8290		

Table 1: Summary of overall and subgroup meta-analyses.

The kidney disease and Nephropathy

Various researches have publicized an increased risk of CKD and an association between early kidney disease and pre-diabetes [19]. The contributory nature of this association is still indistinct as it is because of the higher prevalence of DM in this group or to additional aspects related to both hyperglycaemia and renal disease, relative to the effect of pre-diabetes [20]. **Neuropathies:** Pre-diabetes has been found to be associated with autonomic cardiac dysfunction, as manifested by decreased heart rate variability, reduced heart modulation by parasympathetic system, and an augmented incidence of erectile dysfunction in pre-diabetic men. Non-invasive assessment of nerve dysfunction in people with IGT showed suggestively more anomalies, more frequent hyperalgesia and hypoesthesia, and higher heat sensing thresholds perceived by 4 out of 5 cardiovascular response assessments[21-22]. In addition, there is growing evidence suggesting high prevalence of painful sensory neuropathy, idiopathic polyneuropathy, and small fiber neuropathy in pre-diabetic people with Impaired glucose tolerance test. These results recommend that pre-diabetes involves small nerve fibers in unmyelinated form that transmit temperature, pain and control autonomic functions preceding to the progression of DM[23].

Retinopathy: The DPP study found that approximately 8 percent of participants with pre-diabetes had diabetic retinopathy. Although it is related with an amplified jeopardy of diabetic retinopathy in few researches, these results vary with screening method[24].

Macrovascular disease: Pre-diabetes is related with an amplified danger of evolving macrovascular disease, although it is uncertain that this increased risk is because of the progression to diabetes or prediabetes alone [25]. Although cross-sectional researches have publicised a higher incidence of CAD in people who are pre-diabetic, this association can be confused with the communal causing influences between pre-diabetes and cardiovascular disease.

TREATMENT OPTIONS FOR PREDIABETES

Lifestyle Interventions: The overarching refrain of lifestyle interference plans is changing adjustable risk factors for pre-diabetes and DM by focusing on obesity through increased dietary changes and exercise. The 2 major studies on prevention of diabetes, Finnish diabetes prevention study (DPS) and US DPP study, found valuable impacts of daily routine interferences. In the study of DPP, later to 3 years of follow-up, severe lifestyle modification led to reduce risk about 58%. ILS included changes in exercise and diet to help to lose weight[26]. The loss of

weight was institute to be the sturdiest forecaster of risk reduction. The study found that for each one-kg loss of weight, the jeopardy of progressing DM in the future is condensed by sixteen percent [27]. The DPS found that the aids depended on the achievement by the participant achieving the intended goals of the involvement. These aims were weight loss >5%, consumption of saturated fat < 10% of energy intake, <30% total fat intake of energy intake, consumption of 15 g or more of fiber per 1000 kcal [28]. Although these two studies were conducted primarily among Caucasians, similar benefits were found in the Asian population studies.

Pharmacotherapy: In the context of pre-diabetes, various antidiabetic drugs groups such as thiazolidinediones, biguanides, GLP-1 analogues, α -glucosidase inhibitors and non-diabetic therapies and drugs such as bariatric surgery and anti-obesity drugs have been considered. For eras, diabetes continued to be treated with Metformin and supposed to show to produce supplementary positive results like better cholesterol profile and lower body mass index (BMI) [29]. The communal suggestion from inter-individual studies with IGT showed a 45% decrease in the jeopardy of progression of type-II diabetes mellitus. Metformin was supposed to be much valuable for those with advanced FPG and BMI. Several scientists have also analysed metformin in children who are obese. The combined data suggested a minimum advantage in terms of reduction in BMI compared to routine life modifications, but the advantage was statistically important and the greatest benefit was only short-term with no difference at 6 and 12 months. Glitazones are synthetic ligands for the peroxisome proliferator-activated γ receptor [30]. They upsurge uptake of glucose and reduce hepatic gluconeogenesis and consumption in peripheral organs, thus decreasing resistance of insulin. In a placebo-controlled and double-blinded diabetes reducing trial with rosiglitazone and ramipril, former was operative in reducing the danger of developing DM by sixty percent after three years, but was related with substantial adverse events with raised frequency of HF (0.6% vs 0.2%) and general cardiovascular issues (2.8% vs 2.2%) in the interventional group in comparison to the group of control [31]. The ACT NOW study showed that pioglitazone reduced the diabetes risk by > 70% in IGT and obese patients. Some of the additional profits were lower diastolic blood pressure, a lower intimal-to-middle carotid thickness ratio, and a higher rise in HDL cholesterol, but these were related with greater gain in weight (about three kg extra than placebo) and edema (13% vs 6% in the control group). In the 3-year prospective, placebo-controlled and double-blinded study of IDPP-2, no variance in the diabetes mellitus incidence between placebo and those who

received lifestyle intervention and pioglitazone [32]. In a recent Canadian normoglycemic study, a low-dose grouping of metformin and rosiglitazone was verified contrary to placebo to inspect that this combination therapy of low-dose could reduce the type 2 diabetes mellitus incidence with fewer side effect or not. Significantly fewer cases of diabetes occurred in the active therapy group (15%) in comparison to the group of placebos (40%) [33]. The comparative reduction of risk was 67% and the absolute reduction of risk was 27%; 80% of patients in the group given treatment returned to normoglycaemia in comparison to 54% of patients in the group of control, but there were more reports of diarrhea in patients in the active treatment group (17% vs. 7% in the control group). Generally, there are concerns of safety with thiazolidinediones that limit their use in the treatment of pre-diabetes, including liver toxicity, weight gain, possible link to bladder cancer and increased cardiovascular risk. The Glucosidase inhibitors like voglibose and acarbose protract the total time of carbohydrates digestion and reduce the proportion of absorption of glucose, thus reducing the postprandial increase in glucose. The study of STOP-NIDDM showed that acarbose reduced the diabetes relative risk by 26% over 3.3 years of follow-up in IGT patients. The drug was related with a numeral of GIT side effects counting diarrhea and flatulences. A study in Japan showed a reduction of 40% in the risk of developing DM in risky people with IGT with voglibose in 48-week time. It has same like acarbose side effects, but 7% only patients withdrawn from the drug because of side effects. The anti-obesity drug Orlistat also analysed in the context of pre-diabetes. Orlistat is a lipase inhibitor in gastrointestinal tract cast-off in the management of obesity that works by preventing the dietary absorption of fat about 30%. Studies have shown that after 1.5 years of follow-up, the usage of Orlistat in combination with a low-energy diet is related with high loss of weight (3.8 kg vs 3.9 kg). The XENDOS study also showed a similar finding concerning the effectiveness of Orlistat, with 38% comparative decrease in the risk of developing DM after treatment for four-years [34].

IDPP (80)	Lifestyle intervention or metformin	3 years	NNT of 6.4 with lifestyle intervention and 6.9 with metformin
DPP (79)	Lifestyle (7% weight loss and 150 minutes of moderate exercise/week) or metformin	5 years	Reduction in diabetes incidence of 58% with lifestyle modification and 31% with metformin
ACT NOW (82)	Pioglitazone	2.5 years	72% reduction in diabetes incidence
STOP-NIDDM (81)	Acarbose	3.3 years	25% reduction in diabetes incidence
CANOE (84)	Rosiglitazone and metformin	3.9 years	66% relative risk reduction in diabetes incidence and NNT of 4
DREAM (83)	Rosiglitazone	3 years	60% reduction in diabetes incidence
Bariatric surgery (86)	Laparoscopic adjustable gastric banding	4 years	75% reduction in diabetes incidence
Dapagliflozin once-daily and exenatide once weekly dual therapy: a 24-week randomized, placebo-controlled, phase II study (85)	Dapagliflozin and exenatide	24 weeks	50% reversal to normal glucose tolerance

Table 2: Clinical Trials Showing the Effectiveness of Antidiabetic Drugs to manage Prediabetes

Bariatric surgery: Bariatric surgical procedure involves various methods intended at inducing a restrictive state, malabsorption state, or a mixture of these two to restrict consumption of calories. Commonly used methods comprise laparoscopic gastric banding, Roux-en-Y gastric bypass, duodenal biliary pancreatic resection and sleeve gastrectomy [35]. In an obese Swedish patient, bariatric surgery led to loss of weight (24.2% after two years and 15.9% after ten years) and comparative decline in the risk of DM by 75% in comparison to the control group. Bariatric surgery has also been connected with a reduced incidence of cardiovascular disease, type-II diabetes mellitus, and cardiovascular death in obese adults aged 2 and 10 years [36]. A previous study found that 78% of people with pre-existing diabetes and 98% of people with IGT returned to normal blood sugar levels after gastric bypass surgery.

CONCLUSION

In conclusion, a systematic assessment of the healthiness consequences of pre-diabetes and the reimbursements of early treatment, if any, is needed. Choosing the right results for such a study is crucial. In addition, the standards cast-off to describe pre-diabetes need to be polished based on longstanding medical outcomes. Though these researches may appear necessary, the time required to investigate adverse outcomes in pre-diabetes and the low incidence of these findings may be a restrictive factor for such analysis. There is currently no tangible indication to support clinical strategies for the management of prediabetes. Lifestyle modifications continue to be an important fragment of treating pre-diabetic patients. The usage of pharmacological therapy must be based on distinct approach. When pharmacological therapy is used to manage pre-diabetes, the plan of treatment must be started with aims and endpoints established in advance by the medical doctor. A careful method to the use of pharmacotherapy in children and adolescents is warranted.

REFERENCES

- [1] Kandula NR, Moran MR, Tang JW, O'Brien MJ. Preventing diabetes in primary care: providers' perspectives about diagnosing and treating prediabetes. *Clinical Diabetes*. 2018 Jan; 36(1):59-66. doi:10.2337/cd17-0049
- [2] Keck JW, Thomas AR, Hieronymus L, Roper KL. Prediabetes knowledge, attitudes, and practices at an academic family medicine practice. *The Journal of the American Board of Family Medicine*. 2019 Jul; 32(4):505-12. doi:10.3122/jabfm.2019.04.180375
- [3] López-Jaramillo P, Nieto-Martínez RE, Aure-Fariñez G, Mendivil CO, Lahsen RA, Silva-Filho RL et al. Identification and management of prediabetes: results of the Latin America Strategic Prediabetes Meeting. *Revista Panamericana de Salud Pública*. 2018 May; 41:e172. doi:10.26633/RPSP.2017.172
- [4] Vos MB, Abrams SH, Barlow SE, Caprio S, Daniels SR, Kohli R, et al. NASPGHAN clinical practice guideline for the diagnosis and treatment of nonalcoholic fatty liver disease in children: recommendations from the Expert Committee on NAFLD (ECON) and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN). *Journal of pediatric gastroenterology and nutrition*. 2017 Feb; 64(2):319. doi:10.1097/MPG.0000000000001482
- [5] Giustina A, Barkan A, Beckers A, Biermasz N, Biller BM, Boguszewski C, et al. A consensus on the diagnosis and treatment of acromegaly comorbidities: an update. *The Journal of Clinical Endocrinology & Metabolism*. 2020 Apr; 105(4):e937-46. doi:10.1210/clinem/dgz096
- [6] Selby NM, Taal MW. An updated overview of diabetic nephropathy: Diagnosis, prognosis, treatment goals and latest guidelines. *Diabetes, Obesity and Metabolism*. 2020 Apr; 22:3-15. doi:10.1111/dom.14007
- [7] Azmi S, Petropoulos IN, Ferdousi M, Ponirakis G, Alam U, Malik RA et al. An update on the diagnosis and

- treatment of diabetic somatic and autonomic neuropathy. *F1000Research*. 2019; 8. doi.10.12688/f1000research.17118.1
- [8] Ibáñez L, Oberfield SE, Witchel S, Auchus RJ, Chang RJ, Codner E et al. An international consortium update: pathophysiology, diagnosis, and treatment of polycystic ovarian syndrome in adolescence. *Hormone research in paediatrics*. 2017; 88:371-95. doi.10.1159/000479371
- [9] Malla MA, Dubey A, Kumar A, Yadav S, Hashem A, Abd-Allah EF et al. Exploring the human microbiome: the potential future role of next-generation sequencing in disease diagnosis and treatment. *Frontiers in Immunology*. 2019 Jan; 9: 2868. doi.10.3389/fimmu.2018.02868
- [10] Farhad K. Current diagnosis and treatment of painful small fiber neuropathy. *Current Neurology and Neuroscience Reports*. 2019 Dec; 19(12):1-8. doi.10.1007/s11910-019-1020-1
- [11] Martins B, Amorim M, Reis F, Ambrósio AF, Fernandes R. Extracellular vesicles and MicroRNA: putative role in diagnosis and treatment of diabetic retinopathy. *Antioxidants*. 2020 Aug; 9(8):705. doi.10.3390/antiox9080705
- [12] Zito G, Della Corte L, Giampaolino P, Terzic M, Terzic S, Di Guardo F et al. Gestational diabetes mellitus: Prevention, diagnosis and treatment. A fresh look to a busy corner. *Journal of Neonatal-Perinatal Medicine*. 2020 Jan; 13(4):529-41. doi.10.3233/NPM-190305
- [13] Yorek M, Malik RA, Calcutt NA, Vinik A, Yagihashi S. Diabetic neuropathy: new insights to early diagnosis and treatments. *Journal of Diabetes Research*. 2018 Dec; 2018. doi.10.1155/2018/5378439
- [14] Serhiyenko VA, Serhiyenko AA. Cardiac autonomic neuropathy: risk factors, diagnosis and treatment. *World journal of diabetes*. 2018 Jan; 9(1):1. doi.10.4239/wjd.v9.i1.1
- [15] Berry C, Lal M, Binukumar BK. Crosstalk between the unfolded protein response, MicroRNAs, and insulin signaling pathways: in search of biomarkers for the diagnosis and treatment of type 2 diabetes. *Frontiers in Endocrinology*. 2018 May; 9:210. doi.10.3389/fendo.2018.00210
- [16] Yi DY, Kim SC, Lee JH, Lee EH, Kim JY, Kim YJ et al. Clinical practice guideline for the diagnosis and treatment of pediatric obesity: recommendations from the Committee on Pediatric Obesity of the Korean Society of Pediatric Gastroenterology Hepatology and Nutrition. *Pediatric gastroenterology, hepatology & nutrition*. 2019 Jan; 22(1):1-27. doi.10.5223/pghn.2019.22.1.1
- [17] Basantsova NY, Starshinova AA, Dori A, Zinchenko YS, Yablonskiy PK, Shoenfeld Y et al. Small-fiber neuropathy definition, diagnosis, and treatment. *Neurological Sciences*. 2019 Jul; 40(7):1343-50. doi.10.1007/s10072-019-03871-x
- [18] Lee HY, Shin J, Kim GH, Park S, Ihm SH, Kim HC et al. 2018 Korean Society of Hypertension Guidelines for the management of hypertension: part II-diagnosis and treatment of hypertension. *Clinical hypertension*. 2019 Dec; 25(1):124. doi.10.1186/s40885-019-0124-x
- [19] Wang M, Tan Y, Shi Y, Wang X, Liao Z, Wei P. Diabetes and sarcopenic obesity: pathogenesis, diagnosis, and treatments. *Frontiers in endocrinology*. 2020:568. doi.10.3389/fendo.2020.00568
- [20] Tehrani FR, Amiri M. Polycystic ovary syndrome in adolescents: challenges in diagnosis and treatment. *International journal of endocrinology and metabolism*. 2019 Jul; 17(3). doi.10.5812/ijem.91554
- [21] Hermida RC, Smolensky MH, Mojon A, Crespo JJ, Rios MT, Dominguez-Sardina M, et al. New perspectives on the definition, diagnosis, and treatment of true arterial hypertension. *Expert Opinion on Pharmacotherapy*. 2020 Jul; 21(10):1167-78. doi.10.1080/14656566.2020.1746274
- [22] Zand A, Ibrahim K, Patham B. Prediabetes: why should we care? *Methodist DeBakey cardiovascular journal*. 2018 Oct; 14(4):289. doi.10.14797/mdcj-14-4-289
- [23] Alves C, Della-Manna T, Albuquerque CT. Cystic fibrosis-related diabetes: an update on pathophysiology, diagnosis, and treatment. *Journal of Pediatric Endocrinology and Metabolism*. 2020 Jul; 33(7):835-43. doi.10.1515/jpem-2019-0484
- [24] Khan RM, Chua ZJ, Tan JC, Yang Y, Liao Z, Zhao Y et al. From pre-diabetes to diabetes: diagnosis, treatments and translational research. *Medicina*. 2019 Sep; 55(9):546. doi.10.3390/medicina55090546
- [25] He B, Shu KI, Zhang H. Machine learning and data mining in diabetes diagnosis and treatment. *In IOP Conference Series: Materials Science and Engineering 2019 Apr*; 490(4): 42049. IOP Publishing. doi.10.1088/1757-899X/490/4/042049
- [26] Somerville M, Burch E, Ball L, Williams LT. 'I could have made those changes years earlier': experiences and characteristics associated with receiving a prediabetes diagnosis among individuals recently diagnosed with type 2 diabetes. *Family Practice*. 2020 Jun; 37(3):382-9. doi.10.1093/fampra/cmz081
- [27] Kleinherenbrink W, Osei E, den Hertog HM, Zandbergen AA. Prediabetes and macrovascular disease: Review of the association, influence on outcome and effect of treatment. *European Journal*

- of Internal Medicine. 2018 Sep; 55:6-11. doi.10.1016/j.ejim.2018.07.001
- [28] Burch P, Blakeman T, Bower P, Sanders C. Understanding the diagnosis of pre-diabetes in patients aged over 85 in English primary care: a qualitative study. BMC family practice. 2019 Dec; 20(1):1-0. doi.10.1186/s12875-019-0981-0
- [29] Evert AB, Dennison M, Gardner CD, Garvey WT, Lau KH, MacLeod J, Mitri J et al. Nutrition therapy for adults with diabetes or prediabetes: a consensus report. Diabetes care. 2019 May; 42(5):731-54. doi.10.2337/dci19-0014
- [30] Khramilin VN, Zavyalov AN, Demidova IY. Diagnosis and treatment of the early stages of diabetic polyneuropathy. Journal: Meditsinskiy sovet= Medical Council. 2020(7):56-65. doi.10.21518/2079-701X-2020-7-56-65
- [31] Yang X, Fang T, Li Y, Guo L, Li F, Huang F, Li L. Pre-diabetes diagnosis based on ATR-FTIR spectroscopy combined with CART and XGBoots. Optik. 2019 Feb; 180:189-98. doi.10.1016/j.ijleo.2018.11.059
- [32] Rhee TG, Capistrant BD, Schommer JC, Hadsall RS, Uden DL. Effects of depression screening on diagnosing and treating mood disorders among older adults in office-based primary care outpatient settings: An instrumental variable analysis. Preventive medicine. 2017 Jul; 100:101-11. doi.10.1016/j.ypmed.2017.04.015
- [33] Eyasu K, Jimma W, Tadesse T. Developing a Prototype Knowledge-Based System for Diagnosis and Treatment of Diabetes Using Data Mining Techniques. Ethiopian journal of health sciences. 2020 Jan; 30(1). doi.10.4314/ejhs.v30i1.15
- [34] Kim CH, Moon JS, Chung SM, Kong EJ, Park CH, Yoon WS et al. The changes of trends in the diagnosis and treatment of diabetic foot ulcer over a 10-year period: single center study. Diabetes & metabolism journal. 2018 Aug; 42(4):308-19. doi.10.4093/dmj.2017.0076
- [35] Connell JM, Manson SM. Understanding the economic costs of diabetes and prediabetes and what we may learn about reducing the health and economic burden of these conditions. Diabetes Care. 2019 Sep 1;42(9):1609-11. doi.org/10.2337/dci19-0017
- [36] Khetan AK, Rajagopalan S. Prediabetes. Canadian Journal of Cardiology. 2018 May; 34(5):615-23. doi.10.1016/j.cjca.2017.12.030



Review Article

Incidence and Management of Complications Associated With Myocardial Infarction

 Muhammad Ahsan Waqar¹, Tehseen Riaz^{1*}, Imtiaz Majeed¹, Mustafa Khurram¹, Faiza Waseem², Tooba Mehboob¹, Naila Tabassam¹, Rabia Aslam¹ and Irfan Bashir¹
¹Faculty of Pharmacy, University of Central Punjab, Lahore (UCP), Lahore, Pakistan

²Lahore College for Women University, Lahore, Pakistan

ARTICLE INFO

Key Words:

Congestive Heart Failure, Myocardial Infarction, Acute Myocardial Dead Tissue, Coronary Artery Disease, Pericarditis, Cardiogenic Shock

How to Cite:
 Ahsan Waqar, M. ., Riaz, T., Majeed, I. ., Khurram, M. ., Waseem, F. ., Mehboob, T. ., Tabassam, N. ., Aslam, R. ., & Bashir, I. . (2022). Incidence And Management of Complications Associated with Myocardial Infarction: Incidence and Management of Complications Associated With Myocardial Infarction. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.555>
***Corresponding Author:**
 Tehseen Riaz
 Department of Pharmacology, University of Central Punjab, Lahore, Pakistan
tehseen.riaz@ucp.edu.pk
Received Date: 12th June, 2022Acceptance Date: 27th June, 2022Published Date: 30th June, 2022

ABSTRACT

Coronary heart disease (CHD) is a major cause of morbidity and mortality all around the world. Incidence of the complications of myocardial infarction (MI) had decreased to less than 1% since invention of the percutaneous coronary intervention, although the mortality results from myocardial infarction had decreased in recent years, however the burden of this disease have not ceased. Modern treatment of MI is basically built on any of the clinical evidences that are based on many of the studies that have been studied from previous thirty years. Clinical practice's evolution had significantly decreased morbidity or mortality linked by this disorder. Severe complications of the myocardial infarction include cardiogenic shock, inferior myocardial infarction, pericarditis and noteworthy right ventricular infarction. These complications are very rare; however, their reputation is neglected for the possible failure to manage early diagnosis and appropriate treatment. Inferior wall myocardial infarction accounts for 40- 50% of all the myocardial infarctions and are mostly seen as having a more promising diagnosis than the anterior wall infarctions. Pericarditis is the common disorder and a complication that arises after the myocardial infarction and has multiple causes. This is present in many secondary care and primary care settings. Frequently pericarditis has been often self-restricted, and the non-steroidal anti-inflammatory agents (NSAIDs) remains treatment of first line in the simple cases. Pharmacological management of complications includes beta blockers, Angiotensin Converting Enzyme Inhibitors, Antiplatelet Agents, and Non-Steroidal Anti-Inflammatory Drugs.

INTRODUCTION

Myocardial infarction (MI) has been the major reason of disability and death around the globe. Myocardial infarction (MI) could be the first indicator of chronic coronary artery disease (CAD), or it could have occurred frequently in the patients with already conventional illness. From the view of epidemiologically, the cause of myocardial infarction in the population could be used as for the prevalence of mainly coronary artery disease in that specified population area [1]. Physiologically myocardial infarction is defined as myocardial death of the cells, because of long term ischemia. Cell death is identified physiologically as

coagulation or contraction band necrosis, which had usually evolved mainly through the oncosis, but could results in a lesser degree from apoptosis. Careful analysis of the histological sections by the experienced observer is essential to identify the entities [2]. Neurotically, cell demise is characterized mainly as coagulation and also by further compression band deterioration that typically forms by the process of oncosis, however it could result less by apoptosis. Myocardial infarction could likewise be identified as a sudden ischemic death of the myocardial tissue. Mostly in clinical settings, myocardial infarction is

Myocardial infarction (MI) has been the major reason of disability and death around the globe. Myocardial infarction (MI) could be the first indicator of chronic coronary artery disease (CAD), or it could have occurred frequently in the patients with already conventional illness. From the view of epidemiologically, the cause of myocardial infarction in the population could be used as for the prevalence of mainly coronary artery disease in that specified population area [1]. Physiologically myocardial infarction is defined as myocardial death of the cells, because of long term ischemia. Cell death is identified physiologically as coagulation or contraction band necrosis, which had usually evolved mainly through the oncosis, but could results in a lesser degree from apoptosis. Careful analysis of the histological sections by the experienced observer is essential to identify the entities [2]. Neurotically, cell demise is characterized mainly as coagulation and also by further compression band deterioration that typically forms by the process of oncosis, however it could result less by apoptosis. Myocardial infarction could likewise be identified as a sudden ischemic death of the myocardial tissue. Mostly in clinical settings, myocardial infarction is due to the thrombotic impairment of the coronary vessel that brings about by rupture of the weak plaque. Ischemia instigates noteworthy metabolic or ionic annoyances in inclined myocardium or causes the rapid depression of the systolic function [3]. Myocardial infarction has been classified into 5 sorts and was presented in 2007 as a significant segment of the all-inclusive description. Rather than the plaque burst associated with the type 1 myocardial infarction, type 2 myocardial infarction is viewed as an irregularity among the supply and demand of oxygen in the myocardium [4]. At the point when confronted with patient having intense chest ache, clinicians should recognize myocardial infarction (MI) from any remaining reasons for intense chest pain. On the off chance that MI is suspected, ongoing therapeutic treatment incorporates concluding in terms of regulating thrombolysis and essential percutaneous transluminal coronary angioplasty and to allow patients to move to CCU (coronary care unit) [5].

Mortality and Morbidity: Current management of the intense myocardial infarction (MI) is based on some clinically proof base strained from numerous investigations embraced in the course of recent many years. Advancement in the clinical practices have generously diminished mortality and morbidity related with this disorder [6]. Patients with diabetes mellitus, creating intense myocardial infarction, is the group with especially high danger of death and reinfarction [7]. Half year mortality in inferior MI was 7.8% contrasted with anterior MI recorded as 13.2%. Patients suffering from inferior myocardial infarction, arrhythmias are altogether more

normal in patients with RV myocardial inclusion which likewise has the pattern towards larger mortality, failure of the pump and many mechanical complications [8]. Overall danger for all reason of deaths and CVS results (cardiovascular deaths, repetitive MI) was as a minimum of 30% larger than those in the overall reference population of both from 1–3 years and from 3–5 years subsequently after the MI attack. Danger features prompting more regrettable results after MI included comorbid diabetes, hypertension and peripheral artery disease, older age, reduced renal function, and history of stroke [9].

Incidence Of Complications Associated With Myocardial Infarction In Developing And Developed Countries: In Europe, many of about 55% female deaths are being brought about by the cardiovascular diseases, particularly CHD, contrasted and 44% of every single male demise. The morbidity of CHD would increment by 146% in ladies and 174% in men in Middle East nations. In Jordan, Middle Eastern agricultural nation, as indicated by the most recent WHO report, chronic heart disease deaths came to almost 19% of all out deaths. Deaths rate per 100,000 because of CHD is 131 of all the population, finishing to make Jordan to be positioned number 46 on the planet. Estimated at every 25 seconds regular intervals an American will have a CVD event. Acute myocardial dead tissue (AMI) is the essential result of CHD. AMI is a main source of death in Jordan [10]. Occurrence of cardiogenic shock in the community has rapidly increased over time. Cardiogenic shock (CS) remains the major chief cause of death for patients that are admitted with myocardial infarction (MI). While, shock had often developed early after the MI onset, it is mainly not been detected on the hospital presentation [11]. The evolutionary clinical practices have substantially reduced the mortality and morbidity associated with this disorder [12]. All the developing countries contribute a significant offer to the worldwide burden of cardiovascular disease. Acute myocardial infarction (AMI) specifically stays one of the main sources of death in the developing world [13].

Complications Associated With Myocardial Infarction: Complications of myocardial infarction incorporate ventricular septal rupture with acute ventricular septal defect, papillary muscle rupture with severe mitral regurgitation, acute and subacute free-wall rupture, and hemodynamically substantial right ventricular infarction. Such of the complications have been inconsistent, their significance is emphasized due to the possible capacity to address them with the early determination and for the suitable treatment. These complications are not common, their importance is neglected because they are not detected during the early diagnosis and proper treatment couldn't be provided [14]. Significant complications of the acute myocardial infarction are right ventricular

myocardial infarction, rupture of the free wall and pseudo aneurysm, rupture of the ventricular septum, cardiogenic shock, infarct expansion or extension, acute mitral regurgitation, pericarditis, peri-infarction hypertension, bradyarrhythmias and tachyarrhythmia. For every one of the diseases, rules for the diagnosis and for the treatment is advertised [15].

Cardiogenic Shock: Cardiogenic shock (CS) is a basic disorder of the end organ hypoperfusion brought about by essential heart illness, with up to 80% brought about by intense myocardial infarction (AMI). Notwithstanding standard treatments for AMI-CS including reperfusion and vasoactive aids, mechanical circulatory support (MCS) gadgets are frequently utilized to diminish the myocardial oxygen demand, lessen left ventricular divider stress, and consequently help in myocardial recuperation [16]. In patients with the cardiogenic shock, crisis revascularization didn't essentially lessen generally mortality at 30 days. Nonetheless, following a half year there was a serious existence benefit. Early revascularization ought to be unequivocally measured for the patients with myocardial infarction confounded via cardiogenic shock (CS) [17]. Patients in whom cardiogenic shock created had an essentially more serious danger of death on during hospitalization (71.7 %) than the individuals who didn't have cardiogenic shock. The frequency of cardiogenic shock continued generally stable after some time, averaging 7.1 percent among the patients with myocardial infarction [18].

Hollenberg, is shown in black. The influence of the inflammatory response syndrome initiated by a large MI is illustrated in red. LVEDP indicates left ventricular end-diastolic pressure.

Inferior Wall Myocardial Infarction: Inferior myocardial infarctions represent 40-50% of all intense myocardial infarctions and are for the most part seen as having a more good visualization than foremost divider areas of dead tissue [20]. According to a study, around 40- 50% of all myocardial infarctions are inferior wall myocardial infarction and are usually considered as to be more promising prognosis than anterior wall infarctions [21]. Inferior infarction is viewed as less broad than front and normally of short emergency clinic stay, great visualization and not many in-medical clinic difficulties. Be that as it may, a significant number of significant difficulties when occurred during intense mediocre dead tissue like total heart block, tricuspid or mitral worth ineptitude and ventricular septal imperfections may entangle this less broad nature of localized necrosis and delay medical clinic stay, increment in-medical clinic complexities and mortality to about twice higher when contrasting and sub-par dead tissue who didn't have these intricacies at the hour of their introduction or a short time later during CCU stay.

Right Ventricular Infarction: Patients suffering from inferior MI who had right ventricular (RV) myocardial inclusion seem +to having a more terrible prognosis than the individuals who don't had RV contribution. Be that as it may, past investigations have been restricted by little patient numbers. Right ventricular infarction arises 14% in patients suffering from myocardial infarction. This mainly occurs exclusively as a complication of posterior left ventricular infarction [22]. The chief reason for right ventricular infarction includes the atherosclerotic posterior obstruction in the right coronary artery. Posterior impediment of the artery prompts electrocardiographically recognizable of the right heart ischemia or an expanded danger of severe damage within sight of the acute inferior infarction. Hemodynamic impacts in the right ventricular damage might incorporate dysfunction in right ventricle to siphon enough blood in the aspiratory circuit to one side ventricle, with ensuing systemic hypotension. Treatment mainly includes the concerns towards, volume loading, reperfusion, rhythm and rate control, and mainly inotropic support [23]

Free Wall Myocardial Rupture : In patients with the myocardial infarction, left ventricular free wall rupture has been an infrequent complexity (2-4%) however it is related with a large mortality from the pericardial tamponade [24]. Ventricular free-wall rupture stays one of the main sources of death after myocardial infarction (MI). With expanded capacities for conclusion and revival procedures, careful

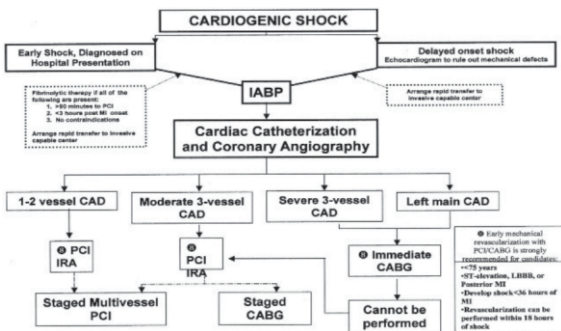


Figure 1 : Recommendations for initial reperfusion therapy when CS complicates Acute MI

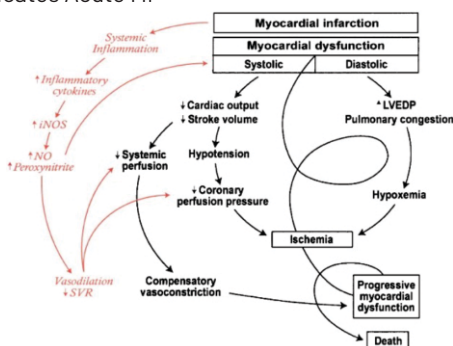


Figure 2: Classic shock paradigm, as illustrated by S.

adjustment of free-wall myocardial imperfections coming about because of ischemia and rot may turn into a basic methodology of treatment, bringing about progress of the endurance rate [25]. There are various danger pointers that are related with cardiac rupture, for example, female sexual orientation, mature age, hypertension, and first MI. Common indications of heart crack are repetitive or constant chest pain, syncope, and distension of jugular veins. Electrocardiographic signs may incorporate sinus tachycardia, new Q-waves in at least 2 leads, tenacious or intermittent ST section height, deviation of expected developmental T-wave design, and electromechanical separation in end-stage cases [26].

Pericarditis: Acute pericarditis, irritation of the pericardium, is found in around 5% of patients admitted to department of emergency for chest torment somewhat unrelated to the acute myocardial infarction. It happens frequently in men 20 to 50 years old. Patients with intense pericarditis regularly present with intense, sharp, retrosternal chest torment that is eased by sitting or inclining forward. Glucocorticoids are customarily saved for extreme or stubborn cases, or in situations when the reason for pericarditis is likely connective tissue infection, autoreactivity, or uremia. Cardiology discussion is suggested for patients with extreme illness, those with pericarditis recalcitrant to empiric treatment, and those with indistinct etiologies [27]. Pericarditis is mainly a communal disorder and a complication that arises after the myocardial infarction and has multiple causes. This is present in various secondary care and primary care cases. Pericarditis has been frequently often self-restraining, and non-steroidal anti-inflammatory agents (NSAIDs) remain the treatment of first line for simple cases [28]. Patients with the acute pericarditis ought to be dealt with exactly with nonsteroidal mitigating drugs. Colchicine might be utilized as monotherapy or in blend with a nonsteroidal mitigating drug for the primary scene of intense pericarditis [29].

PHARMACOLOGICAL MANAGEMENT

Although complications of myocardial infarction are not properly treatable, but are manageable by the help of following agents.

Beta Blockers: Beta-blockers address an exceptional progression in pharmacotherapy. Beta-blockers are quite possibly the most broadly utilized class of medications in cardiovascular medication for patients with coronary illness, arrhythmias, heart failure (HF), and hypertension [30]. The early utilization of beta-blockers is related with diminished rate of CR, recommending some advantageous impacts of beta-blockers on infarct mending after the acute MI [31].

Angiotensin Converting Enzyme Inhibitors: At the point

when initially presented, Angiotensin-converting enzyme (ACE) inhibitors in 1981 were shown uniquely for the treatment of the refractory high blood pressure. From that point forward, these mainly have been appeared to lessen the mortality or morbidity in congestive heart failure, myocardial infarction, chronic renal insufficiency, diabetes mellitus, and atherosclerotic cardiovascular disease [32]. Angiotensin-converting enzyme inhibitors have acquired the place alongside aspirin, β -blockers, and thrombolytic agents as clinical treatments demonstrated to decrease death rates in intense myocardial infarction [33].

Antiplatelet Agents: Antiplatelet agents are recommended generally for essential and secondary prevention of the cardiovascular illness in Western nations to diminish the frequency of intense cerebro- and cardiovascular occasions. These occasions are firmly connected to the shakiness of atheromatous plaques and to the thrombogenicity of blood. For instance, more than 66% of the unexpected heart occasions (intense coronary condition or abrupt cardiovascular demise) and half of the postoperative myocardial infarctions (MIs) are because of the interruption and thrombosis of an unstable plaque [34]. Antiplatelet treatment diminishes genuine vascular events and vascular demise in patients with Peripheral vascular infection. There is likewise proof to help the utilization of the antiplatelet drugs other than aspirin for the counteraction of vascular occasions in those with PVD [35].

Non-Steroidal Anti-Inflammatory Drugs: Utilization of some nonsteroidal anti-inflammatory drugs (NSAIDs) is related with expanded cardiovascular risk in a few of the patient groups, however whether this abundance hazard exists in evidently solid people has not been explained [36]. An expanded danger of cardiovascular occasions among all and new current clients of rofecoxib, valdecoxib, and indomethacin in patients with no set of history of the CVD [37].

Non-Pharmacological Management: Poor diet quality, including overabundance of the caloric ingestion and some unnatural food decisions, decreased physical acts and psychological pressure, are some of the major adjustable way of life factors that are likely to cause the disease transmission of HF [38]. Cell transplantation, LV restriction gadgets, and tissue designing methodologies have arisen as potential options in contrast to heart transplantation for the treatment of ruptured myocardium. Later methodologies incorporate the utilization of in vitro designed tissue, which is refined in vitro and afterward embedded in vivo, and in situ designed tissue, which is infused directly into the myocardium. Polymer networks have additionally been used to forestall LV expansion [39]. The frequency of MI in different parts of the world is being

influenced by demographic qualities and way of life of the people. It should be a hazardous sickness by patients and they property it to their way of life. Conduct hazard factors are frequently related and closer adherence to a better way of life may lessen the danger of coronary illness. A few examinations show that way of life change forestalls as well as controls the advancement of heart illnesses and decreases the event of cardiovascular occasions in the patients with cardiovascular infections. Way of life alteration to forestall the occurrence of coronary vascular issues is among the fundamental projects of WHO. Picking a sound way of life alongside a decent eating regimen lessen the pace of MI and the need to a medical procedure and angioplasty. Despite the accessibility of boundless examinations with respect to the significance of improving the danger factors and changing the way of life after MI, about portion of the patients experience a few difficulties like further MI three years after it on the grounds that changing the way of life is troublesome. One of the issues of patients with intense MI is making change in their way of life during a brief timeframe [40].

CONCLUSIONS

Above literature shows that the medications provided to the patients with the complications are mostly manageable and are not treatable completely. These complications could arise in the patients after the MI attack. There have been many of the consistent and advanced developments in the materialistic movements for the enduring survivals and many cardiovascular consequences afterward MI attack. Many MI survivor remains at the larger hazards than general population, especially for the population with all the additional advanced hazard features such as hypertension, diabetes, or older age. However, there are some interventions that could be done to minimize the complications that are associated with myocardial infarction.

REFERENCES

- [1] Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). *European heart journal*. 2019 Jan 14; 40(3):23769. doi.10.1093/eurheartj/ehy462
- [2] Thygesen K, Alpert JS, White HD, Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. *Journal of the American College of Cardiology*. 2007 Nov; 50(22):2173-95. doi.10.1161/CIRCULATIONAHA.107.187397
- [3] Frangogiannis N G, Pathophysiology of Myocardial Infarction. *Compr Physiol*, 2015. 5(4): p. 1841-75. doi.10.1002/cphy.c150006
- [4] Saaby L, Poulsen TS, Hosbond S, Larsen TB, Diederichsen AC, Hallas J, Thygesen K, Mickley H. Classification of myocardial infarction: frequency and features of type 2 myocardial infarction. *The American journal of medicine*. 2013 Sep; 126(9):789-97. doi.10.1016/j.amjmed.2013.02.029
- [5] Panju AA, Hemmelgarn BR, Guyatt GH, Simel DL. Is this patient having a myocardial infarction?. *Jama*. 1998 Oct; 280(14):125663. doi.10.1001/jama.280.14.1256
- [6] White HD, Chew DP. Acute myocardial infarction. *The Lancet*. 2008 Aug; 372(9638):57084. doi.10.1016/S0140-6736(08)61237-4
- [7] Herlitz J, Malmberg K, KARLSON BW, RYDÉN L, HJALMARSON Å. Mortality and morbidity during a five-year follow-up of diabetics with myocardial infarction. *Acta Medica Scandinavica*. 1988 Jan 12; 224(1):31-8. doi.10.1111/j.0954-6820.1988.tb16735.
- [8] Athanasuleas CL, Stanley AW, Buckberg GD, Dor V, DiDonato M, Blackstone EH, et al. Surgical anterior ventricular endocardial restoration (SAVER) in the dilated remodeled ventricle after anterior myocardial infarction. *Journal of the American College of Cardiology*. 2001 Apr; 37(5):1199-209. doi.10.1016/S0735-1097(00)01089-5
- [9] Johansson S, Rosengren A, Young K, Jennings E. Mortality and morbidity trends after the first year in survivors of acute myocardial infarction: a systematic review. *BMC Cardiovascular Disorders*. 2017 Dec; 17(1):1-8. doi.10.1186/s12872-017-0482-9
- [10] AbuRuz ME, Al-Dweik G. Depressive symptoms and complications early after acute myocardial infarction: gender differences. *The Open Nursing Journal*. 2018; 12:205. doi.10.2174/1874434601812010205
- [11] Menon V and J S Hochman, Management of cardiogenic shock complicating acute myocardial infarction. *Heart*. 2002 Nov; 88(5):531-7. doi.10.1136/heart.88.5.531
- [12] Anderson J L and D A Morrow, Acute myocardial infarction. *New England Journal of Medicine*. 2017 May 25; 376(21):2053-64. doi.10.1056/NEJMra1606915
- [13] Abdallah MH, Arnaout S, Karrowni W, Dakik HA. The management of acute myocardial infarction in developing countries. *International journal of cardiology*. 2006 Aug 10; 111(2):189-94. doi.10.1016/j.ijcard.2005.11.003
- [14] Reeder GS. Identification and treatment of complications of myocardial infarction. In *Mayo Clinic Proceedings*. Elsevier. 1995 Sep; 70(9): 880-4. doi.10.1016/S0025-6196(11)63946-3
- [15] Lavie C J and B J Gersh. Mechanical and electrical

- complications of acute myocardial infarction. in Mayo Clinic Proceedings. Elsevier. 1990 May; 65(5):709-730). doi.10.1016/S0025-6196(12)65133-7
- [16] Vallabhajosyula S, Subramaniam AV, Murphree Jr DH, Patlolla SH, Ya'Qoub L, Kumar V, et al. Complications from percutaneous-left ventricular assist devices versus intra-aortic balloon pump in acute myocardial infarction-cardiogenic shock. PloS one. 2020 Aug; 15(8):e0238046. doi.10.1371/journal.pone.0238046
- [17] Hochman JS, Sleeper LA, Webb JG, Sanborn TA, White HD, Talley JD, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. New England Journal of Medicine. 1999 Aug; 341(9):625-34. doi.10.1056/NEJM199908263410901
- [18] Goldberg RJ, Samad NA, Yarzebski J, Gurwitz J, Bigelow C, Gore JM. Temporal trends in cardiogenic shock complicating acute myocardial infarction. New England Journal of Medicine. 1999 Apr; 340(15):1162-8. doi.10.1056/NEJM199904153401504
- [19] Tehrani BN, Truesdell AG, Psotka MA, Rosner C, Singh R, Sinha S et al. A standardized and comprehensive approach to the management of cardiogenic shock. Heart Failure. 2020 Nov; 8(11):879-91. doi.10.1016/j.jchf.2020.09.005
- [20] Berger PB, Ryan TJ. Inferior myocardial infarction. High-risk subgroups. Circulation. 1990 Feb; 81(2):401-11. doi.10.1161/01.CIR.81.2.401
- [21] Mehta LS, Beckie TM, DeVon HA, Grines CL, Krumholz HM, Johnson MN, Lindley KJ, Vaccarino V, Wang TY, Watson KE, Wenger NK. Acute myocardial infarction in women: a scientific statement from the American Heart Association. Circulation. 2016 Mar 1;133(9):916-47. doi.org/10.1161/CIR.0000000000000351
- [22] Kinch JW, Ryan TJ. Right ventricular infarction. New England Journal of Medicine. 1994 Apr 28;330(17):12117. doi.10.1056/NEJM199404283301707
- [23] Horan LG, Flowers NC. Right ventricular infarction: specific requirements of management. American Family Physician. 1999 Oct; 60(6):1727.
- [24] Figueras J, Cortadellas J, Soler-Soler J. Left ventricular free wall rupture: clinical presentation and management. Heart. 2000 May; 83(5):499-504. doi.10.1136/heart.83.5.499
- [25] Pappas PJ, Cernaianu AC, Baldino WA, Cilley Jr JH, DelRossi AJ. Ventricular free-wall rupture after myocardial infarction:treatmentandoutcome.Chest. 1991 Apr; 99(4):892-5. doi.10.1378/chest.99.4.892
- [26] Wehrens XH, Doevendans PA. Cardiac rupture complicating myocardial infarction. International journal of cardiology. 2004 Jun; 95(2-3):285-92. doi.10.1016/j.ijcard.2003.06.006
- [27] Snyder MJ, Bepko J, White M. Acute pericarditis: diagnosis and management. American family physician. 2014 Apr; 89(7):553-60.
- [28] Troughton RW, Asher CR, Klein AL. Pericarditis. The Lancet. 2004 Feb; 363(9410):717-27. doi.10.1016/S0140-6736(04)15648-1
- [29] Imazio M, Trincherò R. Triage and management of acute pericarditis. International journal of cardiology. 2007 Jun; 118(3):28694. doi.10.1016/j.ijcard.2006.07.100
- [30] Harari R, Bangalore S. Beta-blockers after acute myocardial infarction: an old drug in urgent need of new evidence!. European Heart Journal. 2020 Oct 1;41(37):3530-2. doi.10.1093/eurheartj/ehaa436
- [31] Gong W, Feng S, Wang X, Fan J, Li A, Nie SP. Beta-blockers reduced the risk of cardiac rupture in patients with acute myocardial infarction: A meta-analysis of randomized control trials. International Journal of Cardiology. 2017 Apr; 232:171-5. doi.10.1016/j.ijcard.2017.01.035
- [32] Bicket DP. Using ACE inhibitors appropriately. American family physician. 2002 Aug 1;66(3):461.
- [33] Pfeffer MA. ACE inhibitors in acute myocardial infarction: patient selection and timing. Circulation. 1998 Jun; 97(22):2192-4. doi.10.1161/01.CIR.97.22.2192
- [34] Chassot PG, Delabays A, Spahn DR. Perioperative antiplatelet therapy: the case for continuing therapy in patients at risk of myocardial infarction. British Journal of Anaesthesia. 2007 Sep; 99(3):316-28. doi.10.1093/bja/aem209
- [35] Robless P, Mikhailidis DP, Stansby G. Systematic review of antiplatelet therapy for the prevention of myocardial infarction, stroke or vascular death in patients with peripheral vascular disease. British Journal of Surgery. 2001 Jun; 88(6):787800. doi.10.1046/j.0007-1323.2001.01774.x
- [36] Fosbøl EL, Gislason GH, Jacobsen S, Folke F, Hansen ML, Schramm TK, et al. Risk of myocardial infarction and death associated with the use of nonsteroidal anti-inflammatory drugs (NSAIDs) among healthy individuals: a nationwide cohort study. Clinical Pharmacology & Therapeutics. 2009 Feb; 85(2):190-7. doi.10.1038/clpt.2008.204
- [37] Roumie CL, Choma NN, Kaltenbach L, Mitchell, Jr EF, Arbogast PG, Griffin MR. Non-aspirin NSAIDs, cyclooxygenase-2 inhibitors and risk for cardiovascular events-stroke, acute myocardial infarction, and death from coronary heart disease. Pharmacoepidemiology and Drug Safety. 2009 Nov; 18(11):1053-63. doi.10.1002/pds.1820
- [38] Aggarwal M, Bozkurt B, Panjra G, Aggarwal B, Ostfeld RJ, Barnard ND, Gaggin H, Freeman AM, Allen

- K, Madan S, Massera D. Lifestyle modifications for preventing and treating heart failure. *Journal of the American College of Cardiology*. 2018 Nov; 72(19):2391-405. doi:10.1016/j.jacc.2018.08.2160
- [39] Christman KL, Lee RJ. Biomaterials for the treatment of myocardial infarction. *Journal of the American College of Cardiology*. 2006 Sep; 48(5):907-13. doi:10.1016/j.jacc.2006.06.005
- [40] Molazem Z, Rezaei S, Mohebbi Z, Ostovan MA, Keshavarzi S. Effect of continuous care model on lifestyle of patients with myocardial infarction. *ARYA atherosclerosis*. 2013 May; 9(3):186.



Review Article

Nutritional and Potential Health Effect of Pumpkin seeds.

Madiha Khan Niazi¹, Farooq Hassan², Syed Zahoor ul Hassan Zaidi³, Azka Afzal sahi¹, Jawad Ashfaq⁴, Faiza Ejaz¹, Zeerak Aamir⁵, Sahar Imran¹.

¹University Institute of Diet and Nutritional Sciences, Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan

²Punjab Healthcare Commission, Lahore, Pakistan.

³Faculty of Eastern Medicine, Hamdard University, Karachi, Pakistan.

⁴Himayat e Islam Tibbia College, Lahore, Pakistan.

⁵Zeerak Matab Herbal and Hijama, Johar Town, Lahore, Pakistan.

ARTICLE INFO

Key Words:

Pumpkin seeds, Medicine, Anticancer, Antioxidant, Nutraceutical

How to Cite:

Niazi, M. Khan, Hassan, F. H., Hassan Zaidi, S. Z. ul., Afzal sahi, A., Ashfaq, J., Ejaz, F., Aamir, Z., & Imran, S. (2022). The Nutritional and Potential Health Effect of Pumpkin seeds: Health Effect of Pumpkin seeds. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.515>

***Corresponding Author:**

Madiha Khan Niazi
 University Institute of Diet and Nutritional Sciences,
 Faculty of Allied Health Sciences, The University of
 Lahore, Lahore, Pakistan
dr.madihaniaz@gmail.com

Received Date: 6th June, 2022

Acceptance Date: 20th June, 2022

Published Date: 30th June, 2022

ABSTRACT

The Cucurbitaceae family's pumpkin seeds are often viewed as industrial waste and discarded. In many regions of the world, seeds are eaten raw, boiled, or roasted, but only for personal consumption. Because they are high in protein, fiber, minerals, and vitamins, they may be considered essential for the food industry. Because the seeds are a byproduct of the pumpkin fruit, they are less expensive, and their inclusion in a variety of foods may result in higher nutritious content at a lower cost. Pumpkin seeds have been found to be beneficial to one's health. More research and study on the transformation of these agro industrial waste products into valuable materials is most likely a huge step in the right direction for worldwide efforts in food sustainability.

INTRODUCTION

Seeds and nuts have garnered increased attention in recent years due to the significant nutraceutical and therapeutic potential of their bioactive components [1]. Pumpkin seeds are not an exception. The Cucurbitaceae family includes pumpkins with oily seeds [2]. Pumpkins are grown for a variety of purposes around the world, ranging from commercial to decorative to agricultural [3]. Researchers have turned their focus to pumpkin because of its popularity in many traditional medicine systems (A.R. Abdel-Aziz). While pumpkin seeds are commonly thought

of as agro-industrial trash [4], they are nutritional powerhouses with intriguing nutraceutical qualities. After being roasted and salted, the seeds are frequently eaten straight as snacks. They're also employed in the baking business as food additives [5]. A large number of research have found a link between food's Natural bioactive components, illness prevention, and health promotion [6]. Functional foods are the foods that qualify this diet-health association. Plants are rich in bioactive chemicals and are frequently employed as functional food additives. Like

other seeds, pumpkin seeds are high in useful components. They include a lot of vitamin E (tocopherols), carotenoids, provitamins [7], pigments, pyrazine, squalene, saponins [8], phytosterols, phenolic compounds triterpenoids, and their derivatives [9], coumarins, unsaturated [10]. In addition, pumpkin seeds are high in potassium, magnesium, and phosphorus, as well as minor minerals [11]. Some of these bioactive and minerals have the potential to confer physiological benefits, promote well-being, and reduce the risk of non-communicable disorders such as tumors, microbial infections [12], hyperglycemia and diabetes [13], oxidative stress-related complications [14], prostate disorders, and urinary bladder complications [15]. Hepatoprotective [16], wound healing and hair-growth promoting, anthelmintic, antioxidant, and chemoprotective qualities are among the other medicinal properties of pumpkin seed extract (PSE) [17].

Components	Nutritional Values	RDA Percentage
Energy	559Kcal	28
Total Fats	49.05g	164
Carbohydrates	10.71 grams	8
Protein	30.23g	54
Cholesterol	0mg	0
Micronutrients (Vitamins)		
B3 (Niacin)	4.8mg	31.0
Vit. E	35.1mg	272
B9 (Folic acid)	58 micro gram	15
B6	0.14mg	11.0
B5	0.75mg	15.0
B1 (Thiamin)	0.272mg	23
Vit. A	16 IU	0.50
Vit. C	0.272mg	3.0
B2	0.15mg	12
Major Minerals		
K+	809.0mg	17.0
Na+	7.0mg	0.5
Mineral Deposits		
Mg	592mg	148
Cu	1.43mg	148.0
Zn	7.8mg	17.0
C+	46.0mg	4 1/2
P	1232mg	175
Fe (Iron)	8.8mg	110.0
Se	9.40 micro gram	17.0
Mn	4.54 mg	195
Phytochemicals		
Beta-Carotenoid	9 micro gram	--
Lutein-Zeaxanthin	74 micro gram	--
Beta-Crypto Xanthin	1 micro gram	--

Table 1: Nutritional Values of Pumpkin seeds per 100g..

Pumpkin seeds have numerous nutritional composition as shown in table 1. The seeds are very helpful for human health against diseases [18].

Potential Health Effects: Many research studies have demonstrated the health benefits and preventive effects of pumpkin as demonstrated in Figure 1.

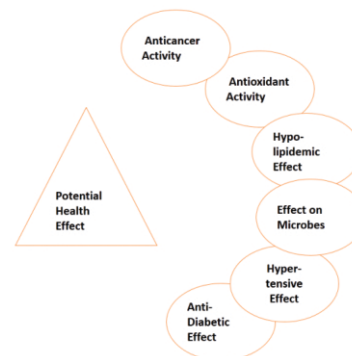


Figure 1: Potential Health Benefits

Anticancer Activity

Pumpkin seeds are a fantastic cancer preventative and/or therapy option. Pumpkin seeds extract has a cytotoxic effect on cancer cells and an increase in estrogen synthesis. This is contrary to the normal behavior of phytoestrogen chemicals, such as genistein and daidzein. In Sprague dawdle rats, pumpkin seed oil inhibited testosterone-induced hyperplasia. After three months of treatment with pumpkin seed oil, the symptoms of benign prostate cancer were minimized. Cucurbitains have been isolated from a number of different pumpkin seed types and have been demonstrated to cause apoptosis in cells [19,20].

Antioxidant Activity

The oil extracted from pumpkin seeds using cold pressure performed better in rat skin than the untreated group in an in-vitro study, according to Bardaa et al. [21-23]. Pumpkin seeds have a high antioxidant impact and protect against genotoxic chemicals, according to Elfiky et al (2012). Pumpkin seed oil was regularly and powerfully proved to be an antioxidant and free radical scavenger. According to Fahim et al., treatment with pumpkin seed oil lowered free radicals and improved arthritic symptoms (1995). Pumpkin seed extract also demonstrated antioxidant and Geno protective effects, according to Yasir et al. (2016). Overall, pumpkin seeds' high quantities of tocopherol could be considered protective against hazardous compounds and free radicals.

Hypolipidemic Effects

In an animal model-based experimental inquiry, Makni and his colleagues evaluated the role of a pumpkin seed and flax seed blend by feeding rats a 1 percent cholesterol diet. After the study was completed, they noted a significant increase. Based on the elevated antioxidant defense system and the level of malondialdehyde, the pumpkin and flex seeds combination had anti-atherogenic benefits

[24]. Pumpkin and flax seeds, as well as pumpkin and purslain seeds were used to study the effects of a 2 percent cholesterol diet are all edible seeds, lower lipid levels, and these seed combinations are regarded to have anti-atherogenic characteristics [25].

Effect on Microbes

Bacteria, parasites, viruses, and fungus are the leading causes of death in many people, despite a sanitary environment and food. Pumpkin seed oil includes antibacterial components that have been extracted from pumpkin seed oil. *Aeromonas veronii*, *Enterococcus faecalis*, *Candida albicans*, *Escherichia coli*, *Typhimurium*, *Salmonella enterica*, and *Staphylococcus aureus* are all inhibited by pumpkin seed oil at a dosage of 2%. [26]. The basic proteins MAP2, MAP11, and MAP4 found in pumpkin seeds have been used to inhibit yeast cell development. MAP11 was shown to have the most inhibitory effects of all the basic proteins [27]. Furthermore, it has been shown that phloem exudates from pumpkin seeds have anti-fungal characteristics and suppress the pathogenic fungus [28]. Park and his colleagues discovered the pr-1 protein from pumpkin seeds, which has antifungal properties and is nontoxic to human erythrocytes. It is a heat stable protein with no growth inhibitory action against *E. coli* and *Staphylococcus* bacteria at 700 degrees Celsius [29].

Hypertensive Effect

Pumpkin seeds aid in the reduction of blood pressure and the relaxation of blood vessels. In rats with high blood pressure caused by a chemical, the role and effects of pumpkin seed oil were investigated. The daily dose of oil for six weeks is between 40 and 100mg/kg. Chemical induction caused raised blood pressure, but consumption of the oil greatly lowered it, and ECG changes returned to normal. The overall result showed pumpkin seed oil's preventive impact against pathological alterations in the aorta and coronary heart. The amino acid L-arginine is used to indicate NO generation. Pumpkin seeds oil's high magnesium (mg) concentration has also been linked to a lower risk of coronary heart attack. The calcium channel blocker, amlodipine, has the same effects on pumpkin seeds as a dietary supplement [30].

Anti-Diabetic Effect

Diabetes is a chronic condition that affects people of all ages. Diabetes mellitus is a metabolic condition in which the body produces insufficient insulin or does not respond effectively to the insulin that is produced. The two most frequent kinds of diabetes are Type I diabetes and Type II diabetes. Pumpkin is often avoided by diabetics due to its high carbohydrate content even though pumpkin eating poses no risk. Pumpkin seeds and flax seeds combined have been shown to provide hypoglycemic and antioxidant benefits in diabetic rats. Histopathological changes

include decreased MDA (malondialdehyde and antioxidant enzyme) increased GSH (growth promoting hormone), CAT (Chloramphenicol acetyltransferase) and SOD (superoxide dismutase) [31].

CONCLUSION

The preceding investigations revealed that pumpkin seeds have nutritional and medicinal capabilities, and that they are also consumed as a delectable food in many parts of the world. The Analysis of the nutritional content of pumpkin seeds revealed that they are extremely nutritious and contain a wide range of necessary components. Pumpkin seeds offer nutritional and therapeutic properties and have been used for medicinal purposes. Pumpkin seeds are high in micronutrients and are utilized in the treatment and control of diabetes, cancer management, hyperlipidemia, hyper tension and heart protection, among other things. Pumpkin seeds are utilized for growing in Pakistan and then discarded as garbage. More research and knowledge about their dietary and therapeutic significance are needed so that people will include them in their regular diet.

REFERENCES

- [1] Yang C, Wang B, Wang J, Xia S, Wu Y. Effect of pyrogallol (1, 2, 3-benzenetriol) polyphenol-protein covalent conjugation reaction degree on structure and antioxidant properties of pumpkin (*Cucurbita* sp.) seed protein isolate. *Lwt.* 2019 Jul 1;109:443-9. doi:10.1016/j.lwt.2019.04.034
- [2] Abou-Zeid SM, AbuBakr HO, Mohamed MA, El-Bahrawy A. Ameliorative effect of pumpkin seed oil against emamectin induced toxicity in mice. *Biomed Pharmacother.* 2018 Feb;98:242-251. doi: 10.1016/j.biopha.2017.12.040.
- [3] Amin MZ, Islam T, Uddin MR, Uddin MJ, Rahman MM, Satter MA. Comparative study on nutrient contents in the different parts of indigenous and hybrid varieties of pumpkin (*Cucurbita maxima* Linn.). *Heliyon.* 2019 Sep 13;5(9):e02462. doi:10.1016/j.heliyon.2019. e02462
- [4] Pham TT, Tran TT, Ton NM, Le VV. Effects of pH and salt concentration on functional properties of pumpkin seed protein fractions. *Journal of food processing and preservation.* 2017 Aug;41(4):e13073. doi/10.1111/jfpp.13073
- [5] Jafari M, Goli SA, Rahimmalek M. The chemical composition of the seeds of Iranian pumpkin cultivars and physicochemical characteristics of the oil extract. *European Journal of Lipid Science and Technology.* 2012 Feb;114(2):1617. doi:10.1002/ejlt. 201100102
- [6] Willhoft EM. Bread staling: I.-Experimental study. *Journal of the Science of Food and Agriculture.* 1971

- Apr; 22(4):176-80..doi.o10.1002/jsfa.2740220406
- [7] Broznić D, Čanadi Jurešić G, Milin Č. Involvement of α -, γ -and δ -tocopherol isomers from pumpkin (*Cucurbita pepo* L.) seed oil or oil mixtures in the biphasic DPPH disappearance kinetics. *Food technology and biotechnology*. 2016 Jun 24;54(2):200-10. doi.10.17113/ftb.54.02.16.4063
- [8] Naziri E, Mitić MN, Tsimidou MZ. Contribution of tocopherols and squalene to the oxidative stability of cold-pressed pumpkin seed oil (*Cucurbita pepo* L.). *European Journal of Lipid Science and Technology*. 2016 Jun;118(6):898-905. doi.10.1002/ejlt.201500261
- [9] Acorda JA, Mangubat IY, Divina BP. Evaluation of the in vivo efficacy of pumpkin (*Cucurbita pepo*) seeds against gastrointestinal helminths of chickens. *Turkish Journal of Veterinary & Animal Sciences*. 2019;43(2):206-11. doi.10.3906/vet-1807-39
- [10] Aghaei S, Nikzad H, Taghizadeh M, Tameh AA, Taherian A, Moravveji A. Protective effect of Pumpkin seed extract on sperm characteristics, biochemical parameters and epididymal histology in adult male rats treated with Cyclophosphamide. *Andrologia*. 2014 Oct;46(8):927-35. doi.10.1111/and.12175
- [11] Koh WY, Uthumporn U, Rosma A, Irfan AR, Park YH. Optimization of a fermented pumpkin-based beverage to improve *Lactobacillus mali* survival and α -glucosidase inhibitory activity: A response surface methodology approach. *Food Science and Human Wellness*. 2018 Mar 1;7(1):57-70. doi.10.1016/j.fshw.2017.11.001
- [12] Brogan DM, Mossialos E. A critical analysis of the review on antimicrobial resistance report and the infectious disease financing facility. *Globalization and health*. 2016 Dec;12(1):1-7. doi.10.1186/s12992-016-0147-y
- [13] Bharti SK, Kumar A, Sharma NK, Prakash O, Jaiswal SK, Krishnan T et al . Tocopherol from seeds of *Cucurbita pepo* against diabetes: Validation by in vivo experiments supported by computational docking. *Journal of the Formosan Medical Association*. 2013 Nov 1;112(11):676-90. doi.10.1016/j.jfma.2013.08.003
- [14] Sun J, Blaskovich MA, Jove R, Livingston SK, Coppola D, Sebt SM. Cucurbitacin Q: a selective STAT3 activation inhibitor with potent antitumor activity. *Oncogene*. 2005;24:323645. doi.10.1038/sj.onc.1208470
- [15] Vonk MM, Diks MA, Wagenaar L, Smit JJ, Pieters RH, Garssen J et al . Improved efficacy of oral immunotherapy using non-digestible oligosaccharides in a murine cow's milk allergy model: a potential role for Foxp3+ regulatory T cells. *Frontiers in immunology*. 2017 Sep 29;8:1230. doi.org/10.1159/000350515
- [16] Plat J, Baumgartner S, Vanmierlo T, Lütjohann D, Calkins KL, Burrin DG et al . Plant-based sterols and stanols in health & disease: "Consequences of human development in a plant-based environment?". *Progress in lipid research*. 2019 Apr 1;74:87-102.
- [17] Zhang L, Fan XR, Xie H, He QH, Nie YS, Zhang M et al . Anti-Inflammatory and antioxidant effects of kelong-capsule on testosterone-induced benign prostatic hyperplasia in rats. *Evidence-Based Complementary and Alternative Medicine*. 2018 Jun 26;2018. doi.10.1155/2018/5290514
- [18] Gohari AA, Farhoosh R, Haddad K. Chemical Composition And Physicochemical Properties Of Pumpkin Seeds (*Cucurbita pepo* Subsp. *pepo* Var. *Styriaca*) grown in Iran.
- [19] Gossell-Williams M, Davis A, O'connor N. Inhibition of testosterone-induced hyperplasia of the prostate of sprague-dawley rats by pumpkin seed oil. *Journal of Medicinal Food*. 2006 Jun 1;9(2):284-6. doi.10.1089/jmf.2006.9.284.
- [20] Hong H, Kim CS, Maeng S. Effects of pumpkin seed oil and saw palmetto oil in Korean men with symptomatic benign prostatic hyperplasia. *Nutrition research and practice*. 2009 Dec 1;3(4):323-7. doi.10.4162/nrp.2009.3.4.323
- [21] Xanthopoulou MN, Nomikos T, Fragopoulou E, Antonopoulou S. Antioxidant and lipoxygenase inhibitory activities of pumpkin seed extracts. *Food Research International*. 2009 Jun 1;42(5-6):641-6. doi.10.1016/j.foodres.2009.02.003
- [22] Lin KL, Lin JJ. Neurocritical care for anti-NMDA receptor encephalitis. *biomedical journal*. 2020 Jun 1;43(3):251-8. doi.10.1016/j.bjbas.2014.08.001
- [23] Hernández-Santos B, Rodríguez-Miranda J, Herman-Lara E, Torruco-Uco JG, Carmona-García R et al . Effect of oil extraction assisted by ultrasound on the physicochemical properties and fatty acid profile of pumpkin seed oil (*Cucurbita pepo*). *Ultrasonics Sonochemistry*. 2016 Jul 1;31:42936. doi.10.1016/j.ultsonch.2016.01.029
- [24] Makni M, Fetoui H, Gargouri NK, Garoui EM, Jaber H, Makni J et al. Hypolipidemic and hepatoprotective effects of flax and pumpkin seed mixture rich in ω -3 and ω -6 fatty acids in hypercholesterolemic rats. *Food and Chemical Toxicology*. 2008 Dec 1;46(12):3714-20. doi.10.1016/j.fct.2008.09.057
- [25] Vetvicka V, Vetvickova J. Immune enhancing effects of WB365, a novel combination of *Ashwagandha* (*Withania somnifera*) and *Maitake* (*Grifola frondosa*) extracts. *North American journal of medical sciences*. 2011 Jul;3(7):320. doi.10.4297/najms.

- 2011.3411
- [26] Hammer KA, Carson CF, Riley TV. Antimicrobial activity of essential oils and other plant extracts. *Journal of applied microbiology*. 1999 Jun;86(6):985-90.
- [27] Cheong NE, Choi YO, Kim WY, Bae IS, Cho MJ, Hwang I et al . Purification and characterization of an antifungal PR-5 protein from pumpkin leaves. *Molecules & Cells (Springer Science & Business MediaBV)*.1997Apr30;7(2).
- [28] Xie JM. Induced polarization effect of pumpkin protein on B16 cell. *Fujian Med Univ Acta*. 2004;38(4):394-5..
- [29] Park SC, Lee JR, Kim JY, Hwang I, Nah JW, Cheong H et al , a novel antifungal protein from pumpkin rinds. *Biotechnology letters*. 2010 Jan;32(1):125-30. doi.10.1007/s10529-009-0126-y
- [30] El-Mosallamy AE, Sleem AA, Abdel-Salam OM, Shaffie N, Kenawy SA. Antihypertensive and cardioprotective effects of pumpkin seed oil. *Journal of Medicinal Food*.2012Feb1;15(2):1809. doi.10.1089/jmf.2010.0299
- [31] Teugwa CM, Boudjeko T, Tchinda BT, Mejiato PC, Zofou D. Anti-hyperglycaemic globulins from selected Cucurbitaceae seeds used as antidiabetic medicinal plants in Africa. *BMC complementary and alternative medicine*. 2013 Dec;13(1):1-8. doi.10.1186/1472-6882-13-63



Review Article

Pharmacological Effects of *Curcuma longa* and Its Bioactive Constitute Curcumin
 Nazia Koser^{1*}, Rida Abbas¹, Bahisht Rizwan¹, Huzaifa Sultan¹, Zeenat Islam¹, Maham Jawad¹, Mahin Jawad¹, Mahnoor Waheed¹ and Shahnai Basharat¹
¹ Faculty of Allied Health Sciences, University Institute of Diet & Nutritional Sciences, University of Lahore, Pakistan

ARTICLE INFO

Key Words:

Curcuma longa, Curcuminoids, Turmeric, Medicinal Properties

How to Cite:

Koser, N. ., Abbas, R. ., Rizwan, B. ., Sultan, H., Islam, Z. ., Jawad, M. ., Jawad, M. ., Waheed, M. ., & Basharat, S. . (2022). Pharmacological Effects of Curcuma Longa and Its Bioactive Constitute Curcumin : Curcuma Longa and Its Bioactive Constitute Curcumin . Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.441>

***Corresponding Author:**

Hafiza Nazia Koser
 University Institute of Diet & Nutritional Sciences,
 Faculty of Allied Health Sciences, The University of
 Lahore, Lahore, Pakistan
hafiza.nazia@dnsc.uol.edu.pk

Received Date: 14th May, 2022

Acceptance Date: 27th May, 2022

Published Date: 30th June, 2022

ABSTRACT

Curcuma longa (Turmeric) belongs to the family Zingiberaceae, commonly used as a spice, pigment and additive also are one of the most important ingredients in the Indian subcontinent. In recent years' research revealed several important functions of it. Among those being investigated is Turmeric. The aim of this review is to summarize the chemistry, referend, formulations of curcuminoids and their biological activities and provides an update mainly on the pharmacological activities of the Turmeric, its extracts and credible medicinal applications of Turmeric, along with their safety evaluation. Its most important active ingredient is curcuminoids. Which are phenolic compounds and volatile oils being also present in turmeric are known for their functional and nutraceutical properties. Various preclinical cell culture and animal studies suggest that curcuminoids have extensive biological activity as antioxidants, neuroprotective, antitumor, anti-inflammatory, anti-acidogenic, radioprotective, and arthritis. Different clinical trials also suggest a potential therapeutic role for curcuminoids in numerous chronic diseases like colon cancer, lung cancer, breast cancer, inflammatory bowel diseases. Nowadays, several drugs have been developed deriving from traditional products, and current drug research is actively investigating the possible therapeutic roles of many Ayurvedic and Traditional Indian medicinal therapies. Health benefits attributed to curcuminoids have resulted in their comprehensive utilization in food and pharmaceutical formulations.

INTRODUCTION

BIOACTIVE COMPONENTS OF TURMERIC

Curcuma longa is known to contain certain beneficial constituents such as flavonoids, curcuminoids, and phenolic acids, which are effective against many diseases [10]. Among the curcuminoids, Curcumin (CUR), demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC) show anti-cancer, inflammation lowering, and free radical scavenging properties [11]. The most abundant curcuminoid is diferulomethane, also known as curcumin, comprising 60-70% of raw *Curcuma*. This compound is significantly known to have therapeutic benefits. Besides these, other little bioactive substances include volatile oils

like zingiberene, atlantone and turmerone, carbohydrates, proteins, and certain gums [12]. Among the nutrients present, macronutrients such as carbohydrates count for 40%, proteins for 17%, fats for 5%, and micronutrients like Mg and Fe constitute just 3% of the *Curcuma* extract. An abundant amount of fiber was also found present in addition to other nutrients [13]. TSO, which is also called Turmeric spent oleoresin, is generally discarded like rubbish in industries. It is made after the removal of curcuminoids from turmeric. Recent research on this industrial refuse shows its excellent therapeutic properties against various diseases. The product mainly

contains polyphenols and other beneficial compounds, which make it a powerful microbe killer, free radical scavenger, and food safety agent. Bisdemethoxycurcumin, ferulic acid, dihydro curcumin, bisabolocurcumin ether, myristicin, furanodiene, cyclocurcumin, terpecurcumin O, curcumin, and 6-methoxy-2-[2-(3-methoxyphenyl) ethyl] are the major chemical substances commonly found in this golden spice [14].

Anti-Obesity Effect of Curcumin

These days' obesity is a worldwide serious global issue according to high statistics obesity data; its prevalence is more common in developing countries because of obesity death rate is increasing day by day and also affecting people's health [15]. It's a serious health factor that causes many ailments and emergency medical conditions like heart attack, high blood pressure, atherosclerosis [16]. According to WHO high amount of fat stored in the body and BMI of more than 25 is known as overweight, and more than 29 is known as obesity [17]. These days, a phytochemical called Curcumin is popular concerning those who are obese and have metabolic issues [18]. Curcumin impacts white adipose tissue to decrease fiery macrophage invasion, control fiery adipokine synthesis, and extend adiponectin generation; it has antioxidant properties [19]. Anti-inflammation results of curcumin and curcuminoids within the obesity type 1 or types two states are delivered by regulating a great range of atomic targets [20]. In fat tissue and many other types of cells and tissues, curcumin synchronizes the DNA-binding and conversion actions of the inflammation factors NF- κ B and AP-1, receptive oxygen species, and inhibits Mitogen-activated protein kinase created by inflammatory provocation [21]. One study stated that Curcumin given in the meal at a dosage of 0.05 percent weight reduced, but bodyweight increased without altering food intake in mice fed a 22 percent high-fat diet for 12 weeks [22]. By Dual-energy X-ray absorptiometry, we can find bone density and body fat mass. Following curcumin therapy in high-fat-diet which is fed to mice, X-Ray absorptiometry shows the results in a reduction in body fat mass and % fat, corroborating earlier research that measured changes in body and organ mass by actual weighing, which yields the total mass but not necessarily the fat content [23]. Curcumin is shown to reduce intracellular cholesterol levels, inhibit fat buildup, and control metabolic activity. Curcumins control the expression of transcription factors involved in adipocyte and lipid synthesis. Curcumin therapy raised phospho-AMPK levels, decreased glycerol-3-phosphate acyltransferase, and enhanced carnitine palmitoyl-transferase 1A expression, resulting in more fat oxidation and far less fatty acid esterification [24].

Anti-diabetic Properties of Curcumin

Diabetes mellitus is one of the common diseases in which insulin is not working, or insulin is insufficient by which blood glucose level increases. It also affects the digestion of carbohydrates and fats due to this body energy becoming low [25]. It's more common in Asian states like China, India, and other countries, Brazil and America. The severity of diabetes in these countries highlights the large cases of retinopathy, nephropathy, and some heart attack cases as well [26]. In Brazil, the National Health Service policy stated extract of herbs cures lipid profile and insulin level of diabetes patient, phytotherapy is complimentary recommended for such cases [27]. This recommendation knowledge is based on clinical experimental evidence and positive results by health experts and researchers internationally [28]. Curcumin extracted from turmeric is a phytochemical that has been proved anti-diabetic in clinical studies, and in vitro studies show many benefits and potential effects on diabetes-related conditions [29]. Curcumin activates the plasma membrane and membrane of cell organelles of the pancreas to release insulin [30]. The three major bioactive components of turmeric that take a role in hyperglycemia to cure are curcumin, cumin aldehyde, cuminol; they improve the functioning of the pancreas insulin stimulating beta cells [31]. According to the Journal of the American College of Nutrition, adipose tissue releases leptin when its secretion increases, the apoptosis rate in pancreas beta cells increases, and it causes inhibitory effects on insulin function [32]. Interestingly, the effective properties of curcumin are observed both on the cell-cultured animals, and results are the same when it is practically observed on humans [33]. If we give a diabetic patient a curcumin capsule at a dose of 300mg / per day who is also obese, then the patient may reduce their BMI, LDL, fasting sugar, 17% blood glucose level will be maintained [34]. According to Toronto General Research Institute, diabetic patients' body weight decreases and body fat content in the high-fat diet; if a patient is taking a curcumin capsule daily, almost five experiments proved that it slows down adipose cells expansion [35].

Curcumin and Cardiovascular Diseases

Curcumin, the major curcuminoid found in the turmeric rhizome (*Curcuma longa*), has the property to reduce inflammation, inhibit oxidation, show anti-apoptotic and cardioprotective properties [36]. Curcumin has been shown to lower the production of reactive oxygen species, exert expression to protect cells and their properties, and reduce oxidative stress and inflammation in several in vitro and in vivo investigations [47]. In myocardial ischemia, several pathways are engaged, and their role in ischemic myocardial cell injury and death has been well-characterized at the molecular level. For example, in

cardiac ischemia, the production of reactive oxygen species becomes high as feedback of the loss of oxygen the substrate's surface energy. Increased reactive oxygen stress can cause cardiomyopathy deformities and other sub-cellular structure disturbances because high oxygenated stress damages lipid, protein, and DNA [38]. In comparison to the negative control groups, Liu et al. found that giving rats curcumin (10, 20, or 30 mg/kg/d) as a complement reduces oxidative stress (3-fold) and infarct size (2.5-fold) [39]. In the case of post-Myocardium Infraction, which is very common these days in every developed country, it could be the result of a high level of apoptosis; in other words, it is also called the end of cell cycle or cell death because, at the most damaged part in myocardium infraction reports of apoptosis seen abnormal, early treatment of ventricles can prevent heart attack. Curcumin can decrease the apoptosis process, regarded as one of the most important goals for avoiding heart failure development in individuals who have had a cardiac attack. In the most frequently used inbred strain of mice, the C57 black 6 (C57BL/6) mice have consistently shown that curcumin may have cardiac myocytes counter normal cell death induced by deficiency of oxygen [40]. Curcumin protects against cancer via up-regulating miR-7a/b genes; these genes protect the individual from cardiomyocyte in ischemia, according to the researchers. Curcumin has also been shown to affect the SIRT3 genes (regulate cardiac energy) reaction pathway, lowering the activity of other apoptosis indicators, including protein Bax, a large group of proteins that control APOPTOSIS acetylated superoxide dismutase 2, an enzyme that reduces oxygenated stress [41].

Curcumin link to Inflammatory Bowel Disease

In the gut, microflora bacteria digest macronutrients and make intestines healthy when there is any disruption of this bacteria or any other environmental negative factor or foreign particle attack on the gastrointestinal tract, intestinal bowel disease develops [42]. Curcumin is proved safe to be used in many clinical trials; it is stated that it can cure irritable bowel disease (IBD). After much research, it is demonstrated that inflammation of the gastrointestinal tract, such as inflammatory bowel disease, e.g., Crohn's disease, ulcerative colitis, may cause colon cancer [43]. In 2012, the American Journal explained curcumin's reaction with inflammatory bowel disease; a small experiment was done on 9 patients [44]. Curcumin dose of 550 mg given twice a day for one month then next month they give the same dose of curcumin three times daily for a month to 5 patients who are already suffering from inflammatory bowel disease and taking corticosteroids therapy; after this experiment, the patient result seems positive condition was improved as compared to before

experiment. Another four patients out of nine stopped taking their corticosteroids therapy because they cure only with curcumin Phytotherapy. A patient with Crohn's disease takes curcumin therapy to follow up for one month and cure symptoms like body pain, bloating, dehydration, and normal stools. curcumin is an antioxidant that cures inflammation of the gastrointestinal tract and is used in multiple pharmacological experiments [45]. In another research, a patient having ulcerative colitis disease with multiple symptoms like abdominal cramps, blood in stools, weakness, bloating, given 500mg dose of curcumin per day with a combination of prednisone by the oral route of this phytotherapy feeding, express positive results after one year of this treatment, patient report no blood in stools no cramps [46].

Antimicrobial Activity

Turmeric is used as a food preservative [47]; spices have a significant hand in the pharmaceutical industry and are also shown to extend the shelf life of food due to its antimicrobial activities. Antimicrobial activities range from acting against total aerobic mesophilic bacteria (TAMB) and total aerobic psychotropic bacteria (TAPB) [48]. Streptococcus, Staphylococcus, Klebsiella pneumonia, Helicobacter pylori, Bacillus subtilis, Vibrio cholera. It has been effective against Streptococcus is also in line with other studies [49]. An inhibition zone is seen against E. coli and S. Aureus, thus essential in healing wounds. Turmeric is also working in sync with various anti-biotics such as ampicillin oxacillin and norfloxacin [50]. Farming turmeric in nutrient-rich soils would contribute to the expansion of sustainable and industrial agriculture, leading to massive employment and, therefore, improving the country's economic status, as seen in Nsukka [51].

CONCLUSIONS

Turmeric is a one-of-a-kind source of a number of chemical compounds that are involved in a variety of biological processes. Although several studies have been conducted on turmeric, further research is required to determine its other medicinal properties in the fight against illness. A drug development program should be initiated to create current medications. While crude extracts of the plant's leaves or rhizomes have medicinal properties, modern drugs can only be developed following extensive investigation of the plant's pharmacotherapeutics, bioactivity, mechanism of action, and toxicities, as well as following proper standardization and clinical trials. As the worldwide landscape is shifting toward the use of non-toxic plant products with traditional therapeutic uses, it is critical to focus the creation of new pharmaceuticals derived from C. longa for the management of various illnesses. Additional research on C. longa is necessary to

elucidate the hidden regions and their practical therapeutic uses that can benefit humanity

REFERENCES

- [1] Yadav RP, Tarun G, Roshan C, Yadav P. Versatility of turmeric: A review the golden spice of life. *Journal of Pharmacognosy and Phytochemistry*. 2017;6(1):41-6.
- [2] Nair KP. Turmeric (*Curcuma Longa L.*) and Ginger (*Zingiber Officinale Rosc.*)-World's Invaluable Medicinal Spices: The Agronomy and Economy of Turmeric and Ginger. Springer International Publishing; 2019 Oct 25. doi.10.1007/978-3-030-29189-1
- [3] Akaberi M, Sahebkar A, Emami SA. Turmeric and Curcumin: From Traditional to Modern Medicine. In *Studies on Biomarkers and New Targets in Aging Research in Iran 2021* (pp. 15-39). Springer, Cham. doi.10.1007/978-3-030-56153-6_2
- [4] Kaur A. Historical background of usage of turmeric: A. *Journal of Pharmacognosy and Photochemistry*. 2019; 8(1): 2769-2771.
- [5] Bhat KK. *Agrotechnology of aromatic plants*. K. TULEY DE SILVA. 1995 Nov:13.
- [6] Singletary K. Turmeric: potential health benefits. *Nutrition Today*. 2020 Jan 1;55(1):45-56. doi: 10.1097/NT.0000000000000392
- [7] Timba PP, Giri SG, Panchal RV. Health benefits and possible risks of turmeric, garlic and ginger: a short. *Health*. 2019 Apr;6(4):4656-9.
- [8] Gupta H, Gupta M, Bhargava S. Potential use of turmeric in COVID-19. *Clinical and experimental Dermatology*. 2020 Oct 1; 45(7):902-3. doi.org/10.1111/ced.14357
- [9] Nwaekpe JO, Anyaegbunam HN, Okoye BC, Asumugha GN. Promotion of turmeric for the food/pharmaceutical industry in Nigeria. *American Journal of Experimental Agriculture*. 2015;8(6):335-41. doi.10.9734/AJEA/2015/16517
- [10] Chumroenphat T, Somboonwatthanakul I, Saensouk S, Siriamornpun S. Changes in curcuminoids and chemical components of turmeric (*Curcuma longa L.*) under freeze-drying and low-temperature drying methods. *Food Chemistry*. 2021 Mar 1;339: 128121. doi.10.1016/j.foodchem.2020.128121
- [11] Xu LL, Shang ZP, Lu YY, Li P, Sun L, Guo QL et al . Analysis of curcuminoids and volatile components in 160 batches of turmeric samples in China by high-performance liquid chromatography and gas chromatography mass spectrometry. *Journal of Pharmaceutical and Biomedical Analysis*. 2020 Sep 5;188:113465. doi.10.1016/j.jpba.2020.113465
- [12] Singletary K. Turmeric: potential health benefits. *Nutrition Today*. 2020 Jan 1;55(1):45-56.. doi: 10.1097/NT.0000000000000392
- [13] 13. de Oliveira Filho JG, de Almeida MJ, Sousa TL, dos Santos DC, Egea MB. Bioactive Compounds of Turmeric (*Curcuma longa L.*). *Bioactive Compounds in Underutilized Vegetables and Legumes*. 2021:297-318. doi.10.1007/978-3-030-57415-4_37
- [14] 14. Joshi P, Joshi S, Semwal DK, Bisht A, Sharma S, Dwivedi J. Chemical composition, antioxidative and antimicrobial activities of turmeric spent oleoresin. *Industrial Crops and Products*. 2021 Apr 1;162:113278. doi.10.1016/j.indcrop.2021.113278
- [15] 15. Mitchem H. Determining Best Practice for Occupational Therapy and Obesity Intervention (Doctoral dissertation, The College of St. Scholastica).
- [16] 16. Bradford PG. Curcumin and obesity. *Biofactors*. 2013 Jan;39(1):7887. <https://doi.org/10.1002/biof.1074>
- [17] 17. World Health Organization. Fact sheet 311: Obesity and overweight. <http://www.WHO.int/media/centre/factsheets/fs311/en/index.HTML>, 2011.
- [18] 18. Aggarwal BB. Targeting inflammation-induced obesity and metabolic diseases by curcumin and other nutraceuticals. *Annual review of nutrition*. 2010 Aug 8;30:173. /doi.10.1146/annurev.nutr.012809.104755
- [19] 19. Weisberg SP, Leibel R, Tortoriello DV. Dietary curcumin significantly improves obesity-associated inflammation and diabetes in mouse models of diabetes. *Endocrinology*. 2008 Jul 1;149(7):3549-58. doi.10.1210/en.2008-0262
- [20] 20. Eaton SL, Roche SL, Llaverro Hurtado M, Oldknow KJ, Farquharson C, Gillingwater TH, Wishart TM. Total protein analysis as a reliable loading control for quantitative fluorescent Western blotting. *PloS one*. 2013 Aug 30;8(8):e72457. doi: 10.1371/journal.pone.0028784
- [21] Costa G, Francisco V, C Lopes M, T Cruz M, T Batista M. Intracellular signaling pathways modulated by phenolic compounds: application for new anti-inflammatory drugs discovery. *Current medicinal chemistry*. 2012 Jun 1;19(18):2876-900. doi.10.2174/092986712800672049
- [22] Panzhinskiy E, Bashir R, Bagchi D, Nair S. Effect of curcumin and α -lipoic acid in attenuating weight gain and adiposity. *Journal of the American College of Nutrition*. 2019 Aug 18;38(6):493-8. doi.10.1080/07315724.2018.1557572
- [23] Lekshmi PC, Arimboor R, Indulekha PS, Nirmala Menon A. Turmeric (*Curcuma longa L.*) volatile oil inhibits key enzymes linked to type 2 diabetes. *International journal of food sciences and nutrition*.

- 2012Nov1;63(7):8324..doi.10.3109/09637486.2011.607156
- [24] Sousa DF, Araújo MF, de Mello VD, Damasceno MM, Freitas RW. Cost-effectiveness of passion fruit albedo versus turmeric in the glycemic and lipaemic control of people with type 2 diabetes: Randomized clinical trial. *Journal of the American College of Nutrition*. 2021Nov10;40(8):67988.doi.10.1080/07315724.2020.1823909
- [25] de Araújo MF, Veras VS, de Freitas RW, de Paula MD, de Araújo TM, Uchôa LR et al. The effect of flour from the rind of the yellow passion fruit on glycemic control of people with diabetes mellitus type 2: a randomized clinical trial. *Journal of diabetes & metabolic disorders*. 2017 Dec;16(1):1-7.1-7 doi.10.1186/s40200-017-0300-z
- [26] Thota RN, Acharya SH, Garg ML. Curcumin and/or omega-3 polyunsaturated fatty acids supplementation reduces insulin resistance and blood lipids in individuals with high risk of type 2 diabetes: a randomised controlled trial. *Lipids Health Diseases*. 2019 Jan 26;18(1):31. doi: 10.1186/s12944-019-0967-x..
- [27] Weisberg SP, Leibel R, Tortoriello DV. Dietary curcumin significantly improves obesity-associated inflammation and diabetes in mouse models of diabetes. *Endocrinology*. 2008 Jul;149(7):3549-58. doi: 10.1210/en.2008-0262.
- [28] Na LX, Zhang YL, Li Y, Liu LY, Li R, Kong T, Sun CH. Curcumin improves insulin resistance in skeletal muscle of rats. *Nutr Metab Cardiovasc Dis*. 2011 Jul;21(7):526-33. doi: 10.1016/j.numecd.2009.11.009
- [29] Ghorbani Z, Hekmatdoost A, Mirmiran P. Anti-hyperglycemic and insulin sensitizer effects of turmeric and its principle constituent curcumin. *Int J Endocrinol Metab*. 2014 Oct 1;12(4):e18081. doi: 10.5812/ijem.18081.
- [30] Bi X, Lim J, Henry CJ. Spices in the management of diabetes mellitus. *Food Chem*. 2017 Feb 15;217:281-293. doi: 10.1016/j.foodchem.2016.08.111.
- [31] Navekar R, Rafrat M, Ghaffari A, Asghari-Jafarabadi M, Khoshbaten M. Turmeric Supplementation Improves Serum Glucose Indices and Leptin Levels in Patients with Nonalcoholic Fatty Liver Diseases. *J Am Coll Nutr*. 2017 May-Jun;36(4):261-267. doi: 10.1080/07315724.2016.1267597
- [32] Maradana MR, Thomas R, O'Sullivan BJ. Targeted delivery of curcumin for treating type 2 diabetes. *Mol Nutr Food Res*. 2013 Sep;57(9):1550-6. doi: 10.1002/mnfr.201200791.
- [33] Rivera-Mancia S, Trujillo J, Chaverri JP. Utility of curcumin for the treatment of diabetes mellitus: evidence from preclinical and clinical studies. *Journal of Nutrition & Intermediary Metabolism*. 2018 Dec1;14:29-41.doi.10.1016/j.jnim.2018.05.001
- [34] Jin T, Song Z, Weng J, Fantus IG. Curcumin and other dietary polyphenols: Potential mechanisms of metabolic actions and therapy for diabetes and obesity. *American Journal of Physiology-Endocrinology and Metabolism*. 2018 Mar 1.doi.10.1152/ajpendo.00285.2017
- [35] Kargozar S, Bains F, Hoseini SJ, Verdi J, Asadpour S, Mozafari M. Curcumin: footprints on cardiac tissue engineering. *Expert Opinion on Biological Therapy*. 2019Nov2;19(11):1199205.doi.10.1080/14712598.2019.1650912
- [36] Lundvig DM, Pennings SW, Brouwer KM, Mtaya-Mlangwa M, Mugonzibwa EA, Kuijpers-Jagtman AM et al. Curcumin induces differential expression of cytoprotective enzymes but similar apoptotic responses in fibroblasts and myofibroblasts. *Experimental cell research*. 2015 Jan 15;330(2):429-41./doi.10.1016/j.yexcr.2014.10.006
- [37] Uğuz AC, Öz A, Nazıroğlu M. Curcumin inhibits apoptosis by regulating intracellular calcium release, reactive oxygen species and mitochondrial depolarization levels in SH-SY5Y neuronal cells. *Journal of Receptors and Signal Transduction*. 2016 Jul3;36(4):395401.doi.10.3109/10799893.2015.1108337
- [38] Panth N, Paudel KR, Parajuli K. Reactive oxygen species: a key hallmark of cardiovascular disease. *Advances in medicine*. 2016 Oct;2016. /doi.10.1155/2016/9152732
- [39] Liu H, Wang C, Qiao Z, Xu Y. Protective effect of curcumin against myocardium injury in ischemia reperfusion rats. *Pharmaceutical Biology*. 2017 Jan 1;55(1):1144-8.doi.10.1080/13880209.2016.1214741
- [40] Li R, Geng HH, Xiao J, Qin XT, Wang F, Xing JH et al. miR-7a/b attenuates post-myocardial infarction remodeling and protects H9c2 cardiomyoblast against hypoxia-induced apoptosis involving Sp1 and PARP-1. *Scientific reports*. 2016 Jul 7;6(1):1-11.doi.10.1038/srep29082
- [41] Wang R, Zhang JY, Zhang M, Zhai MG, Di SY, Han QH et al. Curcumin attenuates IR-induced myocardial injury by activating SIRT3. *Eur Rev Med Pharmacol Sci*. 2018 Feb 1;22(4):1150-60.
- [42] Sreedhar R, Arumugam S, Thandavarayan RA, Karuppagounder V, Watanabe K. Curcumin as a therapeutic agent in the chemoprevention of inflammatory bowel disease. *Drug discovery today*. 2016May1;21(5):8439.https://doi.org/10.1016/j.drudis.2016.03.007

- [43] Fadus MC, Lau C, Bikhchandani J, Lynch HT. Curcumin: An age-old anti-inflammatory and anti-neoplastic agent. *Journal of traditional and complementary medicine*. 2017 Jul 1;7(3):339-46.[doi:10.1016/j.jtcme.2016.08.002](https://doi.org/10.1016/j.jtcme.2016.08.002)
- [44] Midura-Kiela MT, Radhakrishnan VM, Larmonier CB, Laubitz D, Ghishan FK, Kiela PR. Curcumin inhibits interferon- γ signaling in colonic epithelial cells. *American Journal of Physiology-Gastrointestinal and Liver Physiology*. 2012 Jan;302(1):G8596.<https://doi.org/10.1152/ajpgi.00275.2011>
- [45] Vecchi Brumatti L, Marcuzzi A, Tricarico PM, Zanin V, Girardelli M, Bianco AM. Curcumin and inflammatory bowel disease: potential and limits of innovative treatments. *Molecules*. 2014 Dec 16;19(12):2112753. <https://doi.org/10.3390/molecules191221127>
- [46] Lahiff C, Moss AC. Curcumin for clinical and endoscopic remission in ulcerative colitis. *Inflammatory Bowel Diseases*. 2011 Jul 1;17(7):E66. E66 <https://doi.org/10.1002/ibd.21710>
- [47] Rajendran N, Kumar D. Role of diet in the management of inflammatory bowel disease. *World journal of gastroenterology: WJG*. 2010 Mar 3;16(12):1442.[doi: 10.3748/wjg.v16.i12.1442](https://doi.org/10.3748/wjg.v16.i12.1442)
- [48] Uchejeso, O. M., Raphael, O. C., Etukudoh, N. S., & Obiora, E. R. (2021). Use of turmeric against COVID-19 in Nsukka; the need for massive farming
- [49] Samuel-Penu B, Baridakara SC. Anti-Microbial Activities of Turmeric and Ginger on Bacterial Isolates of Normal Skin Flora. DOI: 10.9734/JAMB/2021/v21i330336
- [50] Adhikary T, Hossain CM, Mallick S, Paul S, Banerjee N, Basak P. Revisiting Therapeutic Potentials of Ethanolic Extract of *Curcuma longa* L. rhizomes to Evaluate wound Healing Progression upon Topical Application of its Ointment. *Indian Journal of Pharmaceutical Education and Research*. 2021 Jan 1;55(1):174-83. [doi:10.5530/ijper.55.1.19](https://doi.org/10.5530/ijper.55.1.19)
- [51] Uchejeso OM, Raphael OC, Etukudoh NS, Obiora ER. Use of turmeric against COVID-19 in Nsukka; the need for massive farming. [doi:10.26765/DRJPHET87125908](https://doi.org/10.26765/DRJPHET87125908)



Original Article

Association of Quadriceps Femoris Muscle Weakness with Symptomatic Osteoarthritis of Knee

Arfa Zuha¹, Sarwat Anees², Muhammad Usman Jameel¹, Adnan Hashim^{1*}¹University Institute of Physical Therapy, The University of Lahore, Lahore, Pakistan²Department of Physiotherapy, Social Security Hospital, Lahore, Pakistan

ARTICLE INFO

Key Words:

Quadriceps femoris muscles weakness, knee osteoarthritis, kneepain

How to Cite:

Zuha, A. ., Anees, S. ., Usman Jameel, M. ., & Hashim, A. . (2022). Association Of Quadriceps Femoris Muscle Weakness with Symptomatic Osteoarthritis of Knee: Quadriceps Femoris Muscle Weakness with Symptomatic Osteoarthritis of Knee. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.543>

*Corresponding Author:

Adnan Hashim
 University Institute of Physical Therapy, The University of Lahore, Lahore, Pakistan
adnanhashim199@gmail.com

Received Date: 10th June, 2022

Acceptance Date: 27th June, 2022

Published Date: 30th June, 2022

ABSTRACT

The most widely recognized kind of joint sickness, osteoarthritis, influences in excess of 30 million individuals in the United States alone. It is the biggest reason for tireless handicap in more established people, with a yearly expense of \$185 billion. Degenerative circumstances coming about because of the biochemical breakdown of articular (hyaline) ligament may be considered. Osteoarthritis, the most widely recognized outer muscle problem, is a drawn-out ongoing sickness portrayed via ligament diminishing in joints. **Objective:** The aim of this study was to evaluate the association of quadriceps femoris muscle weakness with symptomatic osteoarthritis of knee. **Methods:** A cross sectional study was conducted on 196 participants from the general population of Lahore. Non probability Convenient Sampling was used. Knee injury and osteoarthritis outcome criteria for knee osteoarthritis and MMT (manual muscle testing) for quadriceps weakness. **Results:** The result exhibited that the p-value for association of quadriceps weakness with symptomatic knee osteoarthritis is 0.097 which shows that there is no association. P value explains there is no association between these two variables. **Conclusion:** In this study, there was not direct interactive association between quadriceps muscles weakness with symptomatic knee osteoarthritis among general population.

INTRODUCTION

Both utilitarian knee joint dependability and knee joint stacking are supported by the quadriceps muscle. At the point when frail quadriceps muscles can't handle tibial interpretation during ambulation, dynamic knee joint dependability might be diminished, expanding the gamble of joint harm [1]. Besides, frail quadriceps muscles can promptly become exhausted, bringing about poor neuromuscular control and maybe permitting pathologic joint development. Proprioceptive tactile capacity plays a part in the planning of basic biomechanical occasions [2]. Quadriceps muscle reinforcing is suggested in clinical rules for the treatment of knee OA. Be that as it may, it's indistinct in the event that quadriceps muscle shortcoming expands

the possibility creating knee OA or propelling the illness. In spite of the fact that there is a rationale for supporting quadriceps muscle reinforcing in the people who have or are in danger of knee OA to decrease utilitarian limitations, more examination is expected to check whether such suggestions can really forestall disease [3]. accordingly, the objective of this paper is to survey the proof on the connection between quadriceps muscle debilitating and the beginning and movement of knee OA. Various cross-sectional examinations have demonstrated that quadriceps muscle shortcoming is clear in people who have knee OA even from the get-go in the periods of ligament diminishing and relates with Kellgren-Lawrence

(KL) grade of radiographic seriousness [4]. One exceptionally prominent cross-sectional examination, which has been referenced in excess of 400 papers as per Google Scholar, offered roundabout proof that quadriceps muscle debilitating may exist preceding the advancement of knee OA [5]. Because of its basic capacity in the transmission, retention, and rearrangement of stresses during everyday exercises, the knee has gotten a great deal of logical consideration. In ambulation across different territories, a solid knee empowers for joint steadiness. The versatility and strength of the lower appendage are seriously hampered by essential knee osteoarthritis [6]. Since there is no known remedy for this dynamic degenerative condition, exhaustive recovery is fundamental. Modifiable gamble factors like dreary joint developments, weight, contamination, and mishaps, among numerous others, may decrease the illness' defenselessness in individuals in danger. Aside from other pre-laid out factors affecting knee osteoarthritis, quadriceps muscle strength has been found to impact agony and hindrance in the lower appendages. Knee uneasiness is a significant clinical indication of knee osteoarthritis [7]. Muscle shortcoming exasperated or exacerbated knee OA. The objective of this study was to decide isometric quadriceps strength in subjects with suggestive osteoarthritis of the knee, to decide the connection between quadriceps strength and agony and handicap in knee osteoarthritis patients, and to contrast quadriceps strength in subjects and gentle, moderate, and extreme radiological knee osteoarthritis [8]. When contrasted with control people, individuals with knee osteoarthritis have powerless knee extensor muscles. Knee extensor muscle shortcoming has been distinguished as a gamble factor for knee osteoarthritis, especially in ladies, as per individual exploration. More prominent quadriceps solid strength was viewed as related with a diminished frequency of episode suggestive knee osteoarthritis, yet not radiographic knee osteoarthritis. Different investigations have investigated the meaning of unfortunate muscle work as a gamble factor for knee osteoarthritis, yet no conclusive ends have been reached [9]. It's pivotal to get a superior comprehension of whether knee extensor muscle shortcoming is a gamble factor for knee osteoarthritis, on the grounds that strong strength is a possibly modifiable gamble factor. There has been no precise review and meta-investigation as far as anyone is concerned to decide this [10]. Knee osteoarthritis (OA) is an essential wellspring of handicap in more seasoned people, and the predominance of this sickness is anticipated to soar in the following twenty years. Patients with knee OA have a more unfortunate utilitarian capacity, which can be connected with joint inconvenience, firmness, and a

deficiency of lower furthest point muscle strength. Thus, knee OA shouldn't be visible just as a ligament infection, and clinical treatment of the sickness should incorporate record for related muscle shortfalls. Patients with knee OA frequently have reduced force-creating capacity in the quadriceps because of solid decay and strong restraint, which is the failure to completely and volitionally enact the muscle [11,12]. Muscle debilitations in knee OA patients to explore the connection between muscle hindrances and actual capacity, to make sense of the likely job of muscle disabilities in the beginning and movement of knee OA, and to sum up the best proof looking at the adequacy of activities that target muscle impedances in knee OA patients [13]. There are 2 joints in the knee which are tibiofemoral and patellofemoral joint. Transmission of weight of body from femur to tibia is by tibiofemoral joint like hinge. There is small degree of tibial axial rotation take place in sagittal plane. Patellofemoral articulation is used for the extension mechanism. Quadriceps muscles are working eccentrically in some positions such as in gait, jumping or running position. For the extensor mechanism medial and lateral retinacular ligaments. These ligaments are distally attached to bones of tibia and anterior bones of menisci. Quadriceps muscles present on the anterior portion of the thigh [17]. In quadriceps muscle of thigh is present in the anterior side of leg, vastus lateralis is present outside portion, vastus medialis present on inner side and the vastus intermedius is present on the posterior of the thigh. Origin of femoris is from anterior superior iliac supine. Composition of rectus femoris consist of four muscles bellies [18]. For the treatment and improvement of knee osteoarthritis is such as: Decrease the pain and stiffness in the knee joint. Maintains of joint mobility is very important. Engage person in certain tasks for the improvement of daily life activities. Improvement in person daily activities related to health. Control the further damage of knee joint. Guide the patient about his problem and educate them how to manage their problems [19]. Some other interventions are using for the control of knee pain such as a narrow-woven fabric is used around the patella of knee, invigorating the patella of knee, these interventions are using for the improvement of knee pain, quadriceps strengthening is one of the best techniques which is used for the strengthening of the quadriceps muscles [20]. The aim of this study was to evaluate the association of quadriceps femoris muscle weakness with symptomatic osteoarthritis of knee.

METHODS

A cross sectional study was conducted on 196 people from general population of Lahore. Non-Probability Convenient Sampling was used. After the consent was taken, MMT

grades will be used for the quadriceps weakness. Standardized questionnaire criteria were used for the knee osteoarthritis. For this current study KOOS knee injury and osteoarthritis outcome was used for the conformation of osteoarthritis and manual muscles testing used for muscles weakness.

RESULTS

The results from this study were, the mean age of patient is 53.9 and S.D was 13.60. Maximum age was 83 and minimum age is 23 years. There were 103(103%) females and 93(93%) females in a sample size (n) of 196 participants. Table 1 shows that 56(28.6%) of people were in grade 2 and 9(4.6%) of participants out of 196 sample size were in grade 5.

MMT	Frequency	Percent
Grade 0	17	8.7
Grade 1	39	19.9
Grade 2	56	28.6
Grade 3	46	23.5
Grade 4	29	14.8
Grade 5	9	4.6

Table 1: Descriptive statistics of manual muscle testing for quadriceps weakness

There was no association between quadriceps femoris muscle weakness and symptomatic knee osteoarthritis (p value is 0.097), because P value is greater than 0.097, Table 2.

Knee osteoarthritis	Weak	Strong	Total
Yes	44	43	87
No	68	41	109
Total	112	84	196

Table 2: Knee osteoarthritis with quadriceps femoris muscle weakness

Chi square = 2.756, P value = 0.097

This table explains that there was no association between quadriceps femoris muscle weakness and symptomatic knee osteoarthritis (p value is 0.097).

DISCUSSION

Sheila C O'Reilly directed this review, and as per him, volunteers with knee inconvenience had lower quadriceps strength than those without torment. The p esteem was (p0.005) on the grounds that there was a connection between quadriceps muscle debilitating and indicative knee osteoarthritis. As per this review, quadriceps initiation was additionally lower, albeit this didn't totally make sense of why quadriceps strength was decreased. Quadriceps strength is firmly connected to local area based hindrance and knee distress. (14) There was no connection between quadriceps femoris muscle debilitating and suggestive knee osteoarthritis in this ongoing examination. The ongoing review's P esteem was (p> 0.005). Men with more vulnerable quadriceps strength

didn't have a higher rate of knee torment, as indicated by this review. The ladies, then again, had a higher possibility weakening knee distress. Subjects were shown how to support routine quadriceps exercises that they might do at home consistently. In ladies, quadriceps shortcoming was connected to a higher probability of knee distress demolishing over the long run, yet not in men. The joint appendage was considerably more vulnerable, had lower volitional muscle initiation, and had a more modest LMCSA (fit muscle cross sectional region) than the contralateral, as indicated by this review. Quadriceps strong shortcoming is brought about by both decreased volitional muscle actuation and LMCSA (slender muscle cross sectional region) in those with knee OA. LMCSA (slender muscle cross sectional region) was uncovered to be the most grounded indicator of solidarity in the contralateral, illness free appendage, though volitional muscle actuation was viewed as the critical determinant of solidarity in the osteoarthritis appendage. Volitional muscle actuation shortages might lessen the viability of volitional fortifying regimens in OA patients with quadriceps shortcoming [15]. Those without radiographic osteoarthritis had a 22 percent higher quadriceps strength than ladies with osteoarthritis (P 0.05). When contrasted with ladies with Noyes' grades by and large utilizing fat immersed proton thickness groupings 2 and 3-5, quadriceps strength was comparatively higher in ladies with Noyes' average tibial and femoral ligament scores of 0 (P 0.05). Ladies with early indications of osteoarthritis showed lower quadriceps strength than ladies who didn't have osteoarthritis [16]. According to the discoveries of this ongoing examination, which incorporated an example size of 196 individuals, there was no connection between quadriceps femoris muscle shortcoming and suggestive knee osteoarthritis. Extra exploration ought to be led for the affiliation. The current investigations' p esteem is (p> 0.097).

CONCLUSION

In this study, there was no direct interactive association between the quadriceps femoris muscles with osteoarthritis of knee among the general population of Lahore. According to this study muscles weakness was not present. Further studies and investigations are required to assess the association between quadriceps weakness and knee osteoarthritis.

REFERENCES

- [1] Segal NA, Glass NA. Is quadriceps muscle weakness a risk factor for incident or progressive knee osteoarthritis? *Physics Sports medical*. 2011 Nov;39(4):44-50. doi: 10.3810/psm.2011.11.1938
- [2] Bennell KL, Wrigley TV, Hunt MA, Lim BW, Hinman RS. Update on the role of muscle in the genesis and

- management of knee osteoarthritis. *Rheumatic Disease Clinic North Am.* 2013 Feb;39(1):145-76. doi: 10.1016/j.rdc.2012.11.003.
- [3] Eckstein F, Hitzl W, Duryea J, Kent Kwok C, Wirth W; OAI investigators. Baseline and longitudinal change in isometric muscle strength prior to radiographic progression in osteoarthritic and pre-osteoarthritic knees—data from the Osteoarthritis Initiative. *Osteoarthritis Cartilage.* 2013 May;21(5):682-90. doi: 10.1016/j.joca.2013.02.658.
- [4] Segal NA, Glass NA, Torner J, Yang M, Felson DT, Sharma L, Nevitt M, Lewis CE. Quadriceps weakness predicts risk for knee joint space narrowing in women in the MOST cohort. *Osteoarthritis Cartilage.* 2010 Jun;18(6):769-75. doi: 10.1016/j.joca.2010.02.002.
- [5] Arden N, Blanco F, Cooper C. *Atlas of Osteoarthritis.* Tarporley: Springer Healthcare Ltd. 2014;21. Kraus V, Blanco F, Englund M, Karsdal M, Lohmander L. Call for standardized definitions of osteoarthritis and risk stratification for clinical trials and clinical use. *Osteoarthritis Cartilage.* 2015; 23(8):1233-1241. doi.org/10.1016/j.joca.2015.03.036
- [7] Pal CP, Singh P, Chaturvedi S, Pruthi KK, Vij A. Epidemiology of knee osteoarthritis in India and related factors. *Indian Journal Orthopedics.* 2016 Sep; 50(5):518-522. doi: 10.4103/0019-5413.189608.
- [8] Muraki S, Akune T, Teraguchi M, Kagotani R, Asai Y, Yoshida M et al. Quadriceps muscle strength, radiographic knee osteoarthritis and knee pain: the ROAD study. *BMC Musculoskeletal Disorder.* 2015 Oct; 16:305. doi: 10.1186/s12891-015-0737-5.
- [9] Luc-Harkey BA, Safran-Norton CE, Mandl LA, Katz JN, Losina E. Associations among knee muscle strength, structural damage, and pain and mobility in individuals with osteoarthritis and symptomatic meniscal tear. *BMC Musculoskeletal Disorder.* 2018 Jul; 19(1):258. doi: 10.1186/s12891-018-2182-8.
- [10] Ruhdorfer A, Wirth W, Eckstein F. Relationship between isometric thigh muscle strength and minimum clinically important differences in knee function in osteoarthritis: data from the osteoarthritis initiative. *Arthritis Care Research (Hoboken).* 2015 Apr; 67(4):509-18. doi: 10.1002/acr.22488.
- [11] Luc-Harkey BA, Safran-Norton CE, Mandl LA, Katz JN, Losina E. Associations among knee muscle strength, structural damage, and pain and mobility in individuals with osteoarthritis and symptomatic meniscal tear. *BMC Musculoskeletal Disorder.* 2018 Jul; 19(1):258. doi: 10.1186/s12891-018-2182-8.
- [12] Mentiplay BF, Perraton LG, Bower KJ, Adair B, Pua YH, Williams GP, et al. Assessment of Lower Limb Muscle Strength and Power Using Hand-Held and Fixed Dynamometry: A Reliability and Validity Study. 2015 Oct; 10(10): e0140822. doi: 10.1371/journal.pone.0140822.
- [13] Kim SG, Lee YS. The intra- and inter-rater reliabilities of lower extremity muscle strength assessment of healthy adults using a hand held dynamometer. *J Phys Ther Sci.* 2015 Jun; 27(6):1799-801. doi: 10.1589/jpts.27.1799.
- [14] O'Reilly SC, Jones A, Muir KR, Doherty M. Quadriceps weakness in knee osteoarthritis: the effect on pain and disability. *Ann Rheum Dis.* 1998 Oct; 57(10):588-94. doi: 10.1136/ard.57.10.588.
- [15] Petterson SC, Barrance P, Buchanan T, Binder-Macleod S, Snyder-Mackler L. Mechanisms underlying quadriceps weakness in knee osteoarthritis. *Med Science Sports Exerc.* 2008 Mar; 40(3):422-7. doi: 10.1249/MSS.0b013e31815ef285.
- [16] Palmieri-Smith RM, Thomas AC, Karvonen-Gutierrez C, Sowers MF. Isometric quadriceps strength in women with mild, moderate, and severe knee osteoarthritis. *Journal of Physical Medical Rehabilitation.* 2010 Jul; 89(7):541-8. doi: 10.1097/PHM.0b013e3181ddd5c3.
- [17] van der Esch M, Steultjens M, Harlaar J, Knol D, Lems W, Dekker J. Joint proprioception, muscle strength, and functional ability in patients with osteoarthritis of the knee. *Arthritis Rheumatism.* 2007 Jun 15; 57(5):787-93. doi: 10.1002/art.22779.
- [18] Barker K, Lamb SE, Toye F, Jackson S, Barrington S. Association between radiographic joint space narrowing, function, pain and muscle power in severe osteoarthritis of the knee. *Clinic Rehabilitation.* 2004 Nov; 18(7):793-800. doi: 10.1191/0269215504cr754oa.
- [19] Baliunas AJ, Hurwitz DE, Ryals AB, Karrar A, Case JP, Block JA, et al. Increased knee joint loads during walking are present in subjects with knee osteoarthritis. *Osteoarthritis Cartilage.* 2002 Jul; 10(7):573-9. doi: 10.1053/joca.2002.0797.
- [20] Al-Johani AH, Kachanathu SJ, Ramadan Hafez A, Al-Ahaideb A, Algarni AD, Meshari Alroumi A et al. Comparative study of hamstring and quadriceps strengthening treatments in the management of knee osteoarthritis. *Journal of Physical Therapy Science* 2014 Jun; 26(6):817-20. doi: 10.1589/jpts.26.817



Original Article

Breast Cancer Screening Practices Amongst Female Students In Pakistan

 Ismail Anwar Khokhar¹, Mohammad Musa Asif¹, Muhammad Mashood¹, Mominah Zulfiqar¹, Minahil Ismail¹ and Ayesha Asjad²
¹University Institute of Physical Therapy, The University of Lahore, Pakistan

²Medicare Polyclinic, Lahore, Pakistan

ARTICLE INFO

Key Words:

Breast Cancer; Breast Self-Examination; clinical breast examination; Mammography

How to Cite:

 Khokhar, I. A., Musa Asif, M., Mashood, M., Zulfiqar, M., Ismail, M., & Asjad, A. (2022). Breast Cancer Screening Practices Amongst Female Students in Pakistan: Breast cancer screening practices. *Pakistan BioMedical Journal*, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.523>

*Corresponding Author:

 Ismail Anwar Khokhar
 University Institute of Physical Therapy, The University of Lahore, Pakistan
ismailanwerkhokhar@gmail.com

Received Date: 6th June, 2022

Acceptance Date: 22nd June, 2022

Published Date: 30th June, 2022

ABSTRACT

Cancer is currently responsible for around 6 million deaths worldwide. Cancer-related deaths are predicted to rise to 74% in the next several years which is alarming for the developing countries. Breast cancer is one of the most common cancers in women and is also the leading cause mortality. **Objective:** The purpose of this study was to determine the practices opted by Pakistani women about breast self and clinical Examination and screening modalities. **Methods:** Total 453 selected female University students using the "Epitool" online sample calculation website with a 95% confidence interval and a 5% margin of error were selected. All girls between the age of 18-55 years who were currently enrolled in one of the study programs and could complete the English questionnaire were included in the study. The Breast Cancer Investigation Questionnaire (BCIQ) was used in study. SPSS version 25.0 was used to analyze the data. **Results:** The respondents' mean age was 22.87 ± 4.67 years. The prevalence of knowledge of breast cancer screening techniques was high 341 (75.3%), 245(53.3%) and 273 (60%), respectively, for breast self-examination, clinical breast examination, and mammography. However, only 345 (75.1%), 303 (36.9%), and 255 (56.2%) knew BSE, CBE, and mammography are helpful in breast cancer diagnosis respectively. **Conclusion:** Even though many females were aware of breast cancer and self-examination, the number of women who do BSE was alarmingly low.

INTRODUCTION

At present, cancer is responsible for roughly 6 million deaths globally, or about 12% of all fatalities. The fact that cancer-related fatalities are expected to climb to 75% in the coming years, up from 60% currently, is concerning for the developing world. Breast cancer is one of the most prevalent types of cancer, and it is also the main cause of cancer deaths among women, therefore it must be treated thoroughly. Breast cancer claims the lives of around 375,000 people each year, with up to 1 million new cases being diagnosed each year. Breast cancer is more common in women over the age of 60. Despite the efficacy of mammography and several advertising of screening programs, a substantial proportion of women who are

eligible do not practice routine breast cancer screening [1]. In 2006, the breast health global initiative (BHGI) was found with the goal of increasing breast cancer awareness and breast self-examination (BSE) in poor nations with limited resources. It has helped to raise breast cancer awareness in several poor nations, including Pakistan [2]. Pakistan continues to have the highest breast cancer incidence rate, with 1 out of every 9 women in Pakistan getting breast cancer at some point in their lives [3]. Inherited genetic mutation, along with hyperplasia and a personal or family history of breast cancer, is one of the primary variables that raises the risk of breast cancer in women [4]. Obesity, menopause, and oral contraceptives, hormonal therapy

after menopause or radiation exposure, first childbirth beyond the age of 35, and excessive alcohol use are some of the additional risk factors [5, 6]. Regular physical activity, a healthy body weight, and breastfeeding are only a few of these factors that can help to lower the chance of breast cancer [7, 8]. Because breast cancer is a progressive illness, early diagnosis can assist enhance the survival rate. Mammography, Breast self-examination (BSE), and clinical breast examination (CBE) are some of the screening procedures utilized [9]. However, because of issues such as limited resources and low literacy, mammography is not widely available in nations such as Pakistan [10]. Physical activity is being utilized as a supplement during chemotherapy and radiation to alleviate illness and therapy-related issues [11]. Although the influence of physical exercise on the immune system of healthy people has been examined, the effect of physical activity on the immune system of cancer patients has yet to be investigated [12]. Some studies have shown that exercising on regular basis can have a positive impact on the body's immune response [13, 14]. Environmental and lifestyle variables, including alcohol and tobacco use, physical activity, and a high-fat diet, can contribute to the development of breast cancer, and that removing these factors (primary prevention) can help to reduce morbidity and death. The diagnostic methods (secondary prevention) such as mammography, BSE, MRI, and ultrasonography, are available and are considerably more successful in the early identification of cancers or abnormalities that predispose to tumors [15]. Because breast cancer is such a complex illness, genetic and environmental factors have a role. The cause for various cancers' hostile behavior is breast cancer stem cells (BCSCs), which are also one of the primary therapeutic difficulties [16]. Prior to the advent of immunotherapy and targeted medicines, breast cancer treatment was generally limited to surgical procedures and radical mastectomies [17]. Metastatic breast cancer (MBC) is also known as secondary breast cancer and arises when cells from a primary breast tumor spread from the breast to other regions of the body via the lymphatic system or circulation [18]. Over the last few years, the mortality rate of breast cancer has decreased while the occurrence rate has increased [19]. Breast cancer can occur at any time, and it is highly probable that the entire family will be impacted. For a patient with early diagnosis of breast cancer and subsequent lifestyle changes are critical [20]. The goal of this study was to observe the percentage of females in Pakistan who are aware of the initial screening procedures for the early diagnosis of the breast cancer and to analyze the major screening practices in regard to self-breast examination and clinical breast examinations.

METHODS

Female students from private sector institutions were invited to participate in this descriptive cross-sectional research. A total of 453 female University students using the "Epitool" online sample calculation website were selected [21] with a simple non-probability selection approach. There was a 95% confidence interval and a 5% margin of error. The sample ranged in age from 18 to 55 years old and included undergraduate, master's, and doctorate students. Before being included in the study, each participant signed an informed consent form. The Ethical Review committee deemed that no ethical approval was required for the study; subsequently the entire study was conducted in accordance with the declaration Helsinki [22]. The study included all females who were presently enrolled in one of the study programs and could complete the questionnaire in English. The exclusion criteria prohibited any male students from accessing the response sheet, as well as female students who could not read English questions, because there was no Urdu translation and validation research for the questionnaire used in the study. The Breast Cancer Investigation Questionnaire (BCIQ), which was employed in the research; divided into five distinct parts. Section A is about demographics, Section B is about breast cancer awareness, Section C is about breast self-examination (BSE), Section D is about clinical breast examination (CBE), and Section E is about mammography utilization. The questionnaire had a total of 38 questions, which were then utilized to analyze the results [23]. The information was gathered utilizing a pre-tested, structured questionnaire. Data on sociodemographic, breast cancer awareness, knowledge, and practice of Breast Self-Examination (BSE), Clinical Breast Examination (CBE), and mammography were collected. After the questionnaires were selected for completeness and data extraction, the data was input and analyzed using Statistical Package for Social Sciences (SPSS) version 25.0. The level of statistical significance was established at 95% confidence interval for cross tabulating the variables.

RESULTS

A total of 453 people completed the BCIQ questionnaire, used in the previous literature [23]. When questioned about their marital status, 378 (83.3%) of the study's participants said they were single or had never been married before. As a result, the majority of the study's participants were single, the remaining participants were married 72 (15.9%) and widowed 3 (0.8%). The participants' greatest level of education was tertiary school or graduation, with 283 (62.5%) having completed it, 73 (16.1%) having completed senior secondary schools, 57 (12.6%)

completed junior secondary and 25(5.5%) of the females of the sample had completed primary school. Students 235 (51.9%), doctors 132(29.1%), and office employees 42(9.3%) made up the majority of the sample, others included pharmacists 10 (2.2%), cleaning staff 19(4.2%) and laboratory staff workers 15 (3.3%). Breast cancer knowledge was present in the majority of the sample, with 439 (96.7 %) individuals stating that they had heard about breast cancer previously while only 14 (3.3%) females were unaware of the breast cancer. Media 229 (50.6 %), books and other reading material 144 (31.8%) were the most prevalent sources of breast cancer information among the research participants. Other sources included hospitals 8(1.8%) medical lectures 13 (2.9%) medical conferences or seminars 29 (6.4%), relatives and friends 20 (6.6%). 162 (35.9%) out of 453 total participants had relatives with breast cancer. 7 (4.3%) participants' mothers, 91 (56.1%) aunts, 4 (2.5%) sisters, 9 (5.6%) cousins had been diagnosed with breast cancer while 51 (31.5%) had other family members with breast cancer. The majority of the participants 341(75.1%) had heard of breast self-examination, and the same number of them said they thought BSE was an essential and effective technique for early breast cancer diagnosis. Although there is a lack of knowledge about breast self-examination among the participants. Only half of the participants 241(53.2%) knew how to perform a BSE, and 119 (26.3%) had no notion, as shown in Table 1.

Questions Asked	n (%)
Ever heard of BSE (n=453)	
Yes	341(75.3)
No	112(24.7)
Is BSE a useful tool for early detection of Breast cancer?(n=453)	
Yes	340 (75.1)
No	113(24.9)
Have you been taught how to do BSE?(n=453)	
Yes	241(53.2)
No	212(46.8)
If yes, who taught you?(n=241)	
Parents	16(6.6)
Teacher	25(10.4)
Doctor	41(17.0)
Nurse	3(1.2)
Friend	16(6.6)
Other	140(58.2)
Parents	16(6.6)
At what age should BSE be started?(n=453)	
From birth	10(2.2)
From puberty	128(28.3)
From 30 years	27(6)
From 20 years	88(19.4)
After menopause	20(4.4)
No idea	180(39.7)
How often should BSE be done?(n=453)	
Daily	23(5.1)
Weekly	98(21.6)
Monthly	132(29.1)

Yearly	38(8.4)
No idea	162(35.8)
What is the best time to do BSE?(n=453)	
During menstrual flow	64(14.1)
A week after period	83(18.3)
No idea	296(65.2)
BSE should be done by (n=453)	
Doctor	97(21.4)
Trained nurse	26(5.7)
The individual	275(60.7)
Other	55(12.1)
BSE is done by (n=453)	
Inspecting the breast in the mirror	324(71.5)
Feeling the breast with the hand	3(0.7)
Feeling the armpit with the hand	2(0.4)
Doing ultrasound of the breast	2(0.4)
Mammography	3(0.7)
No idea	119(26.3)

Table 1: Respondents' knowledge of breast self-examination

The sample had an excellent understanding of breast self-examination and practiced it. 329 (72.6%) of the participants were aware that if their BSE was abnormal, they should consult a doctor. However, just 277 (61.1%) of the respondents did BSE, with 36.1% doing it only sometimes and 53 (19.1%) doing it regularly. Those who did not practice BSE, 176 (38.9%) claimed that it was either not in their family's DNA (22.7%) or that it was unnecessary (26.7 percent). Table 2 lists all the participants' reasons in detail.

Questions Asked	n (%)
If you discover any abnormality during BSE, what will you do?(n=453)	
Do some lab tests	49(10.8)
Pray over it	13(2.9)
See a doctor	329(72.6)
Do Nothing	62(13.7)
Benefits of BSE (n=453)	
Familiar with breast texture	24(5.3)
Early detection of breast cancer	204(45.0)
Detection of abnormal changes	198(43.7)
A good breast exercise	27(6.0)
Do you practice BSE?(n=453)	
Yes	277(61.1)
No	176(38.9)
If yes, how often?(n=277)	
Weekly	53(19.1)
Monthly	50(18.1)
Occasionally	74(26.7)
Rarely	100(36.1)
If no, why not?(n=176)	
Don't know how to do it	23(13.1)
Breast cancer not in my family	40(22.7)
Don't remember	13(7.4)
Don't think it is necessary	47(26.7)
Don't have the time	16(9.1)
Not heard about it	21(11.9)
No reason	16(9.1)
If you have been practicing BSE, have you ever discovered any abnormality in your breast?(n=277)	
Yes	77(27.8)
No	200(72.2)

If yes, what did you do? (n=77)	
Prayed over it	22 (28.6)
Saw a doctor	55 (71.4)
Do you think BSE is a good practice? (n=453)	
Yes	400 (88.3)
No	53 (11.7)

Table 2: Respondents' practice of breast self-examination

Table 3 shows the participants' comprehensive and detailed responses to their knowledge of clinical breast examination. Only 238 (52.2%) of the participants had heard of clinical breast examination (CBE), indicating that almost half of the sample was unaware of CBE and had no knowledge about it. When asked about why they haven't undergone mammography procedure ever? there were multiple answers which were included into one option "not enough knowledge" 121 (26.7). These options included not old enough, financial constraints, didn't find need to do mammography, unavailability mammography, not yet compulsory, never felt the need, no symptoms are present, never felt of getting one, didn't need it and didn't find any reason.

Questions Asked	n (%)
Ever heard of CBE? (n=453)	
Yes	245 (53.9)
No	209 (46.0)
Is CBE a useful tool for detection of breast CA? (n=453)	
Yes	303 (66.9)
No	150 (33.1)
Do not know CBE should be done by (n=453)	
Doctor	308 (68.0)
Trained nurse	74 (16.3)
The individual	48 (10.6)
No idea	23 (5.1)
CBE should be done using (n=453)	
Ultrasound	106 (23.4)
Mammography	220 (48.6)
Hand	98 (21.6)
No idea	29 (6.4)
How often should CBE be done? (n=453)	
Daily	21 (4.6)
Weekly	22 (4.9)
Monthly	74 (16.3)
Yearly	53 (11.7)
When abnormality is found on BSE	127 (28.0)
No idea	156 (34.4)
Have you heard of mammography?	
Yes	273 (60.0)
No	159 (35.0)
Is mammography a useful tool for the early detection of breast cancer?	
yes	265 (58.4)
no	43 (9.4)
Don't Know	145 (32.0)
At what age should mammography be started	
After menopause	23 (5.0)
From 20	62 (13.6)
From 40	80 (17.6)
From birth	17 (3.7)
From puberty	66 (14.5)
No idea	205 (45.2)

How often should mammography be done?	
Monthly	131 (28.9)
Yearly	192 (42.3)
Weekly	97 (21.4)
No Idea	23 (5.0)
Have you ever done a mammography?	
No	381 (84.1)
Yes	72 (15.8)
If no to question above, why not?	
Not old	233 (51.4)
Financial Issue	99 (21.8)
Not enough Knowledge (Multiple Answers)	121 (26.7)

Table 3: Respondents' knowledge and practice of CBE and mammography

DISCUSSION

Breast cancer is one of the leading causes of death worldwide [1]. It is one of those diseases that, if detected early, may be completely cured, allowing the survivor to live a happy life [9]. Lack of knowledge among young girls, resulting in undetected cases that end in terrible circumstances. The primary objective of this study was to assess female knowledge of breast cancer and, the procedures utilized for early detection or screening of breast cancer. The study found that while a large number of females do not have basic information of breast cancer, the percentage of females who conduct basic breast self-examination is alarmingly low; over half of the sample participants did not undertake self-breast exams and the majority did not know how to do so. Following the basic breast self-examination, the clinical breast examination is performed, which most of the female participants are unfamiliar with. In 2015, the authors Noreen M et al., conducted research and found that a high number of public awareness initiatives are urgently needed. Looking at their findings and current results, it is that they are in accordance with one another, and that not much has been done in the previous 6 years to promote breast cancer awareness among women [24]. Current study showed how often women self-examined their breasts, and it is discovered that just a small percentage of women did so on a weekly basis. Although the degree of awareness among medical students is good owing to their practice, Qasim, S. mentioned in their 2020 article. In their study, the number of females conducting BSE was also quite small, and they suggested that further research and public awareness campaigns be done in this area. Similarly, Ullah Z et al, Zia Ullah et al, and Arif S. et al. also indicated that there was insufficient knowledge of breast cancer among females in all types of communities. And the BSE, which is an important part of the early screening and diagnostic procedure, was only used by a small percentage of girls in their research [25]. Current research adds to the body of knowledge on breast cancer and its early screening

measures in the Pakistani community. However, it raises serious concerns regarding the use of basic self-examination for breast cancer screening and an inadequate knowledge of clinical breast inspection.

CONCLUSION

Although a high percentage of individuals are aware of breast cancer and breast self-examination, the number of women who do BSE is dangerously low. As a result, measures should be done to promote awareness, particularly among students, in order to avert any avoidable consequences.

REFERENCES

- [1] Edgar L, Glackin M, Hughes C, Rogers KM. Factors influencing participation in breast cancer screening. *British Journal of Nursing*. 2013 Sep; 22(17):1021-6. doi: 10.12968/bjon.2013.22.17.1021.
- [2] Gilani SI, Khurram M, Mazhar T, Mir ST, Ali S, Tariq S, Malik AZ. Knowledge, attitude and practice of a Pakistani female cohort towards breast cancer. *JPMA. The Journal of the Pakistan Medical Association*. 2010 Mar; 60(3):205.
- [3] Zaheer S, Shah N, Maqbool SA, Soomro NM. Estimates of past and future time trends in age-specific breast cancer incidence among women in Karachi, Pakistan: 2004-2025. *BMC Public Health*. 2019 Dec; 19(1):1-9. doi: 10.1186/s12889-019-7330-z.
- [4] Sun YS, Zhao Z, Yang ZN, Xu F, Lu HJ, Zhu ZY, et al. Risk Factors and Preventions of Breast Cancer. *International journal of biological sciences*. 2017 Nov; 13(11):1387-1397. doi: 10.7150/ijbs.21635.
- [5] Wang K, Li F, Chen L, Lai YM, Zhang X, Li HY. Change in risk of breast cancer after receiving hormone replacement therapy by considering effect-modifiers: a systematic review and dose-response meta-analysis of prospective studies. *Oncotarget*. 2017 Aug; 8(46):81109-81124. doi: 10.18632/oncotarget.20154.
- [6] Aurin J, Thorlacius H, Butt ST. Age at first childbirth and breast cancer survival: a prospective cohort study. *BMC Research Notes*. 2020 Jan; 13(1):9. doi: 10.1186/s13104-019-4864-1.
- [7] Niehoff NM, Nichols HB, Zhao S, White AJ, Sandler DP. Adult Physical Activity and Breast Cancer Risk in Women with a Family History of Breast Cancer. *Cancer Epidemiol Biomarkers Prevention*. 2019 Jan; 28(1):51-58. doi: 10.1158/1055-9965.EPI-18-0674.
- [8] Picon-Ruiz M, Morata-Tarifa C, Valle-Goffin JJ, Friedman ER, Slingerland JM. Obesity and adverse breast cancer risk and outcome: Mechanistic insights and strategies for intervention. *CA Cancer J Clin*. 2017 Sep; 67(5):378-397. doi: 10.3322/caac.21405.
- [9] Wang L. Early Diagnosis of Breast Cancer. *Sensors (Basel)*. 2017 Jul; 17(7):1572. doi: 10.3390/s17071572.
- [10] Saeed S, Asim M, Sohail MM. Fears and barriers: problems in breast cancer diagnosis and treatment in Pakistan. *BMC Womens Health*. 2021 Apr; 21(1):151. doi: 10.1186/s12905-021-01293-6.
- [11] Ferioli M, Zauli G, Martelli AM, Vitale M, McCubrey JA, Ultimo S, et al. Impact of physical exercise in cancer survivors during and after antineoplastic treatments. *Oncotarget*. 2018 Feb; 9(17):14005-14034. doi: 10.18632/oncotarget.24456.
- [12] Schmidt T, van Mackelenbergh M, Wesch D, Mundhenke C. Physical activity influences the immune system of breast cancer patients. *Journal of Cancer Research and Therapeutics*. 2017 Jul; 13(3):392-8. DOI: 10.4103/0973-1482.150356
- [13] Bartlett DB, Willis LH, Slentz CA, Hoselton A, Kelly L, Huebner JL, et al. Ten weeks of high-intensity interval walk training is associated with reduced disease activity and improved innate immune function in older adults with rheumatoid arthritis: a pilot study. *Arthritis research & therapy*. 2018 Jun; 20(1):127. doi: 10.1186/s13075-018-1624-x.
- [14] Campbell JP, Turner JE. Debunking the Myth of Exercise-Induced Immune Suppression: Redefining the Impact of Exercise on Immunological Health Across the Lifespan. *Frontiers in immunology*. 2018 Apr; 9:648. doi: 10.3389/fimmu.2018.00648.
- [15] Kamińska M, Sygit K, Budny A, Surdyka D, Kukiełka-Budny B, Burdan F. Primary and secondary prevention of breast cancer. *Annals of Agricultural and environmental Medicine*. 2017 Jun; 24(4):549-53. doi.org/10.26444/aaem/75943
- [16] Barzaman K, Karami J, Zarei Z, Hosseinzadeh A, Kazemi MH, Moradi-Kalbolandi S, et al. Breast cancer: Biology, biomarkers, and treatments. *International immunopharmacology*. 2020 Jul; 84:106535. doi: 10.1016/j.intimp.2020.106535.
- [17] Barzaman K, Moradi-Kalbolandi S, Hosseinzadeh A, Kazemi MH, Khorramdelazad H, Safari E, et al. Breast cancer immunotherapy: Current and novel approaches. *International Immunopharmacology*. 2021 Sep; 98:107886. doi.org/10.1016/j.intimp.2021.107886
- [18] Henriques B, Mendes F, Martins D. Immunotherapy in breast cancer: when, how, and what challenges?. *Biomedicines*. 2021 Nov; 9(11):1687. doi.org/10.3390/biomedicines9111687
- [19] Pudkasam S, Tangalakis K, Chinlumprasert N, Apostolopoulos V, Stojanovska L. Breast cancer and exercise: The role of adiposity and immune markers.

- Maturitas. 2017 Nov; 105:16-22. doi: 10.1016/j.maturitas.2017.04.022.
- [20] Choudhury R, Pujadas-Botey A, Wheeler L, Marlett N, Estey A. The standardised cancer booklet and beyond: Patient perspectives on patient education for breast cancer care. *Health Education Journal*. 2020 Oct;79(6):712-23. doi.org/10.1177/0017896920911690
- [21] Sergeant E. Epitools Epidemiological Calculators: Ausvet; 2018 [18 september 2021]. Available from: <http://epitools.ausvet.com.au>.
- [22] Mundial AM. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013 Nov; 310(20):2191-4. doi: 10.1001/jama.2013.281053.
- [23] Madubogwu CI, Egwuonwu AO, Madubogwu NU, Njelita IA. Breast cancer screening practices amongst female tertiary health worker in Nnewi. *Journal of cancer research and therapeutics*. 2017 Apr-Jun; 13(2):268-275. doi: 10.4103/0973-1482.188433.
- [24] Noreen M, Murad S, Furqan M, Sultan A, Bloodsworth P. Knowledge and awareness about breast cancer and its early symptoms among medical and non-medical students of Southern Punjab, Pakistan. *Asian Pacific Journal of Cancer Prevention*. 2015 Mar; 16(3):979-84. doi: 10.7314/apjcp.2015.16.3.979.
- [25] Arif S, Baloch Q, Zaheer F, Agheem R, Ariff M, Ahmed M. The adequate breast cancer knowledge assessment: A cross-sectional study done among nonmedical women of Karachi. *J Educ Health Promot*. 2018 Dec;7:169. doi: [10.4103/jehp.jehp_177_18](https://doi.org/10.4103/jehp.jehp_177_18)



Original Article

Clinical Presentation of Gastroesophageal Reflux Among Children With Chronic Constipation

Amna Hussain¹, Zaigham Hashir¹, Bushra Gohar Shah², Riffat Farrukh³, Shaheen Masood⁴¹Pakistan Institute of Medical Sciences, Islamabad, Pakistan²Sahara Medical College, Narowal, Pakistan³Department of Pediatrics, Karachi Medical and Dental College and Abbasi Shaheed Hospital, Karachi, Pakistan⁴Assistant Professor Pediatrics, Karachi Medical and Dental College, Karachi, Pakistan

ARTICLE INFO

Key Words:

Functional gastrointestinal disorder (FGID), functional constipation, gastro-esophageal reflux diseases (GERD).

How to Cite:

Hussain, A. ., Hashir, Z. ., Gohar Shah, B. ., Farrukh, R. ., & Masood, S. . (2022). Clinical Presentation Of Gastroesophageal Reflux Among Children With Chronic Constipation: Gastroesophageal Reflux Among Children with Chronic Constipation. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.520>

*Corresponding Author:

Amna Hussain
 Pakistan Institute of Medical Sciences, Islamabad, Pakistan
amnahussain08@gmail.com

Received Date: 2nd June, 2022

Acceptance Date: 20th June, 2022

Published Date: 30th June, 2022

ABSTRACT

The gastro-esophageal reflux disease is the type of gastrointestinal disorder which is very common in children. To evaluate the overlap and correlation between different gastrointestinal track disorders different epidemiological studies are conducted. The chronic constipation and gastroesophageal reflux are the functional disorder of gastrointestinal (GI) track with the significant correlation. **Objective:** The purpose of the study was to elaborate the relationship between the very common and functional disorders of the gastrointestinal (GI) track; the gastroesophageal reflux and the functional constipation. The percentage frequency of gastroesophageal reflux in the children was calculated. **Methods:** This was a cross-sectional study with statistical approach, conducted in Pakistan Institute of Medical Sciences, Islamabad and Abbasi Shaheed Hospital, Karachi for the duration of six months from December 2020 to May 2021. Those patients who referred to pediatric gastroenterology department of hospital were included in the study. The children were diagnosed with functional constipation. For the diagnosis of FC the Rome III criteria was applied. Two groups were established. There were 34 number of patients diagnosed with FC in the experimental group, while 36 children suspicion of GERD disease were placed in control group. **Results:** The mean age of the children referred to the pediatric gastroenterology lab was observed to be 8 years. Out of 34 patients included in the experimental group the 15 were male and other 29 were female. Similarly out of the 36 patients included in the control group the 16 were males and other 16 were females. The 24 months was observed as the mean duration of functional constipation. The 50% were experiencing hiccups in the experimental group, while 22% in the control group. The 75% patients in the control group suffering from chronic cough, while regurgitation were reported in other 72%. The 50% in the experimental group experienced belching. Coughing and regurgitation were seen in about 47% patients. **Conclusion:** The one of the most considered factors in treatment and monitoring of chronic constipation is functional gastrointestinal disorder. The symptoms of gastroesophageal reflux can be improved by treating chronic constipation.

INTRODUCTION

The functional gastrointestinal disorder (FGID) developed as a results of ENS adaptive responses to the physiological triggers. The gastroesophageal reflux disease is most common type of FGID in the children. The scientist are willing to uncover the factors involve in pathogenesis of gastroesophageal reflux disease and functional constipation. At the instant general hypothesis is that different psychogenic and hormonal elements are involved

in causing these FGID diseases. The gastric content flows back to the esophagus. The complications caused by this retrograded flow are defined as gastroesophageal reflux diseases (GERD). It is the one of the most prevalent complication of childhood. The delay in gastric emptying is a major risk factor associated with the disease. The other risk factors are nutritional habits of the childhood. The gastrointestinal motility of gastric content is highly

affected by functional constipation²⁻³. During functional constipation the transit time of colon lengthen that ultimately leads to temporary increased in intra-abdominal pressure. Due to changing living conditions, the functional constipation is observed in majority of children. The reported percentage of functional constipation is 8.3%. The functional constipation can lead to colon distention. The gastric waves are impaired by rectal distention. The most commonly observed symptoms in GRED patients are temporary heartburn⁴⁻⁵. The irregular vomiting followed by early satiety are also observed in children suffering from FC. The motility and microcirculation of the gut is normally controls by enteric nervous system(ENS)⁶. The continuous maintenance therapy is required for the treatment of GRED. The commonly used first-line diagnosis and treatment therapy for gastroesophageal reflux disease is proton pump inhibitor⁷⁻⁸. The purpose of the study was to elaborate the interrelationship exist between constipation and reflux. The chronic upper intestinal infections occur in correlation with functional constipation. The overlaps between the different gastric functional disorders need to evaluate for controlling the percentage of FGID patients in pediatric gastroenterology clinics⁹⁻¹⁰.

METHODS

This was a cross-sectional study with statistical approach, conducted in Pakistan Institute of Medical Sciences, Islamabad and Abbasi Shaheed Hospital, Karachi for the duration of six months from December 2020 to May 2021. The children referred to pediatric gastroenterology department of our hospital were included in the study. The children had the complaint of functional constipation. The mean age of the children included in the study was between 4-16 years. The Rome III criteria were applied for the FC diagnosis. The children suffering from mental retardation were excluded from the study. Those who were allergen to foods and showed abnormal thyroid functions were excluded. The ethical committee of the hospital approved the present study. But it didn't approve the group of healthy children to be included in the control group. Therefore the patient suspicions of having GERD disease were included in the control group. The Rome III was also applied on this group. Basically in the present study two groups was established. One is experimental with 34 numbers of patients which are diagnosed with FC, while the other is control group with 36 children suspicion of GERD disease. The results were recorded. After the recording of clinical findings, a questionnaire about reflux related symptoms were given to every patient for further evaluation of the findings. The Antimony dual canal probe was used to monitor esophagus pH of every patient. The 10cm signal meter probe were used for monitoring pH of the patient

having age above 5 years, while 5cm signal meter probe was used for the patients having age below 5 years. The electrodes of the pH meter were placed in-accordance with esophageal X-ray graphics. The pH meter probe distal end was inserted nasopharyngeal to the esophagus, while proximal end was inserted to the upper sphincter of esophagus. After 24 hours of strict monitoring of pH, the children were allowed to go back home. The esophageal pH less than 4 were defined as acid reflux. The total episodes of this reflux were greater than 40. The lasting time for this reflux was 15 seconds. While the acid reflux having pH less than 4 with the lasting time of 5 mints were seen in 5 patients. These were calculated with the help of distal probe. The reflux index calculated by using proximal probe of pH meter was 1% while using distal probe of the pH meter was 5%. The t-test and chi-square test was used for the statistical analysis of the data. A comparison between the findings of control and experimental groups was made. The results were reported.

RESULTS

The mean age of the patient attended the pediatric gastroenterology lab was calculated. It was observed to be 8 years. The 24 months was observed as the mean duration of functional constipation. In about 50% patients included in experimental group had the complaint of hiccup and belching. Coughing and regurgitation were observed in about 47% patients. While in the control group 75% patients had complaint of chronic cough, while regurgitation were reported in other 72% (showed in table 1). The more common symptoms in patient diagnosed with FC was hiccups and belching. While the chronic cough was more common in the patients with the reflux related symptoms. The distal channel acid reflux was observed in 26% patients of experimental group, while 35% had proximal channel acid reflux. The distal channel acid reflux was seen in 30% patients of control group while, other 33% had proximal channel acid reflux.

The observed symptoms	Experimental group (n=34)	Percentage	Control group (n=36)	Percentage	Calculated P-value
Hiccups	17	50%	8	22.2%	0.021
Regurgitation	16	47%	26	72.2%	0.071
Vomiting	6	17.6%	10	27.7%	0.456
Pyrosis	9	26.4%	15	41.6%	0.708
Bronchitis	8	23.5%	11	30.5%	0.708
Wheezing	9	26.4%	14	38.8%	0.297
Chronic cough	16	47%	27	75%	0.012
Belching	17	50%	6	16.6%	0.002
Hoarseness	11	32.3%	11	30%	0.924

Table 1: The percentage of reflux related symptoms observed in experimental and control group;

From pH monitoring the percentage of acid reflux episodes were calculated. It was observed that 38% of patients of

experimental group and 41% patients of control group had the acid reflux (involving lower part of esophagus). The 26% patients of experimental group had distal channel acid reflux, while 35% had proximal channel acid reflux.

Esophageal pH monitoring parameters	Experimental group	Percentage	Control group	Percentage	P value
Proximal probe with reflux index greater than 5%	12	35.2%	12	33.3%	0.86
Distal probe with reflux index greater than 1%	9	26.4%	11	30%	0.95
Positivity of proximal and distal probe	13	38.2%	15	41%	0.75
Acid reflux episodes greater than fifty	3	8.8%	3	8.3%	0.67
Acid reflux lasts for more than 5 minutes	7	20.5%	13	36.1%	0.26
Mean of the distal reflux index	1.2	3.3%	1.3	3.53%	0.82
Mean of the proximal distal index	0.6	1.08%	0.3	0.8%	0.61

Table 2: The percentage of esophageal pH monitoring parameters in experimental and control group

The 30% patients of control group had distal channel acid reflux, while other 33% had proximal channel acid reflux. The results of group I and II were compared and findings were reported for further evaluation (shown in table 2).

DISCUSSION

The two most common disorder of gastrointestinal tract are GERD and FC. These occur simultaneously at the instant. The knowledge about their pathologies and overlap is still need to uncover. The children diagnosed with FC are more prone to symptoms like, GERD and abnormal acid flux. It was observed that about 60-65% of the children diagnosed with FC had the GERD symptoms while, other 50% had symptom of abnormal acid reflux. With the increase in defecation frequency has a strong impact on the abnormal acid reflux¹¹. While in other the increase in defecation frequency don't have any effect, the abnormal acid reflux remain continue. The abnormal acid reflux can be reduced by treatment of constipation. It also reduce the symptoms of GERD. According to the data obtained from the questionnaire, it was observed that about 50% of the patients involved in present study had the history atopy of GERD. The one of the highly known risk factor of the GERD disease is positive family history of GERD¹²⁻¹³. The prevalence of atopic conditions in the patient diagnosed with FC is higher than the patient included in the control group. GERD is affected by many factors; it is known to be a multifactorial disease. The limited knowledge is present about this disease. The need of the hour is to uncover the pathophysiology of the disease. This will not only help to plan better treatment strategies but also give insights into the correlation and overlap between the FC and GERD¹⁴⁻¹⁵. The symptoms of upper gastrointestinal tract are observed

in the patients with slow transit constipation. These includes vomiting, regurgitation and dyspepsia. The cologastric brake mechanism is used to explain the emptying of gastric¹⁶. Fecal stasis (rectum or anus) and delayed gastric emptying is observed in the patients suffering from constipation. The gastric emptying is highly controlled by the feces retention in the rectum. The only reasonable explanation at the moment for the continuous abnormal acid reflux instead of increasing frequency of defecation, is that the FC overlap with the GERD¹⁷. After the treatment of chronic constipation the reflux index of acid and its growling was significantly reduced. On the other hand the defecation frequency increases always. The enteric system of young children response more frequently and strongly to the constipation treatment. Comparing this observation with the adolescent children, the response slow down¹⁸⁻¹⁹. Constipation among the children having age up to 12 years have no gender predominance. It was observed that there is no significant relationship between the bowel habits and constipations. The episodes of acid reflux and defecation frequency are negatively related with each other. The gastric motility increased by the decrease in intra-abdominal pressure. This ultimately leads to decrease in acid reflux episodes.²⁰ The Borowitz et al. conducted the similar research and findings of the present study and his are highly comparable with each other. After the treatment of patient with chronic constipation the patient diagnosed with GERD don't complaint about the symptoms such as intermittent vomiting and heartburn, hence these also vanished with the FC treatment. The patient having complaint of chronic constipation, can also have GERD disease. For the in-depth exploitation of the correlation between the FC and GERD the further studies are required²¹. The pH meter impedance analysis must be carried out in the next studies. The symptoms of GERD varied, these variations are less common among the adults. For the clear diagnosis of non-acid reflux the esophageal pH monitoring don't correlate. Acid reflux is more commonly caused by delayed is gastric emptying. The emptying time of gastric was not determined in the present study. The pretreatment and post treatment data was compared and the constipation treatment efficacy in acid reflux was determined in the patients with Fc²².

CONCLUSION

The GERD and FC overlap in many cases, and this overlap has increased the risk of percentage mortality in the children. The post-treatment data of the patient suffering from FC and GERD, showed that the reflux symptoms reduced. Therefore for the treatment of the patient having complaint of FC, the GERD must be considered. It will help in better treatment and monitoring of functional

constipation.

REFERENCES

- [1] Baran M, Ozgenc F, Arikan C, Cakir MU, Ecevit C, Aydoğdu S, Yagci R. Gastroesophageal reflux in children with functional constipation. *Turkish Journal of Gastroenterology*. 2012;23(6).
- [2] Momma E, Koeda M, Tanabe T, Hoshikawa Y, Hoshino S, Kawami N, Kawagoe T, Tatsuguchi A, Kaise M, Iwakiri K. Relationship between gastroesophageal reflux disease (GERD) and constipation: laxative use is common in GERD patients. *Esophagus*. 2021 Jan;18(1):152-5.
- [3] Baran M, Cagan Appak Y, Karakoyun M, Yalcinkaya S, Eliacik K, Dundar BN. The overlap of gastroesophageal reflux disease and functional constipation in children: the efficacy of constipation treatment. *European Journal of Gastroenterology & Hepatology*. 2017 Nov 1;29(11):1264-8.
- [4] Dehghani SM, Poorghaiomi R, Javaherizadeh H. Clinical Manifestation of Gastroesophageal Reflux among Children with Chronic Constipation. *Middle East journal of digestive diseases*. 2020 Jul;12(3):178.
- [5] Baran M, Ozgenc F, Arikan C, Cakir MU, Ecevit C, Aydoğdu S, Yagci R. Gastroesophageal reflux in children with functional constipation. *Turkish Journal of Gastroenterology*. 2012;23(6).
- [6] Van Den Berg MM, Benninga MA, Di Lorenzo C. Epidemiology of childhood constipation: a systematic review. *Official journal of the American College of Gastroenterology | ACG*. 2006 Oct 1;101(10):2401-9.
- [7] Borowitz SM, Sutphen JL. Recurrent vomiting and persistent gastroesophageal reflux caused by unrecognized constipation. *Clinical pediatrics*. 2004 Jun;43(5):461-6.
- [8] Hyman PE, Milla PJ, Benninga M. A., Davidson GP, Fleisher DF, Taminiau J. Childhood functional gastrointestinal disorders: neonate/toddler. *Gastroenterol*. 2006;130:1519-26.
- [9] Hyams JS, Di Lorenzo C, Saps M, Shulman RJ, Staiano A, van Tilburg M. Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology*. 2016 May 1;150(6):1456-68.
- [10] Ekingen G, Ceran C, Guvenc BH, Tuzlaci A, Kahraman H. Early enteral feeding in newborn surgical patients. *Nutrition*. 2005 Feb 1;21(2):142-6.
- [11] Suri S, Eradi B, Chowdhary SK, Narasimhan KL, Rao KL. Early postoperative feeding and outcome in neonates. *Nutrition*. 2002 May 1;18(5):380-2.
- [12] Mamatha B, Alladi A. Early oral feeding in pediatric intestinal anastomosis. *Indian Journal of Surgery*. 2015 Dec;77(2):670-2.
- [13] Fernandes VP, Lima MC, Camargo EE, Collares EF, Bustorff-Silva JM, Lomazi EA. Gastric emptying of water in children with severe functional fecal retention. *Brazilian Journal of Medical and Biological Research*. 2013 Mar 15;46:293-8.
- [14] Bouchoucha M, Deutsch D, Uong P, Mary F, Sabate JM, Benamouzig R. Characteristics of patients with overlap functional gastrointestinal disorders. *Journal of Gastroenterology and Hepatology*. 2021 Aug;36(8):2171-9.
- [15] Yousefi A, Ardakan MT, Nakhaei S, Najafi M, Behnoud N. A Study of Familial Aggregation of Habitual Constipation. *Iranian Journal of Pediatrics*. 2019 Aug 1;29(4).
- [16] Igor'V M, Osadchuk MM, Osadchuk MA. Cross-Functional Syndrome of Gastrointestinal Diseases in Adults and Children in the Context of Their Continuity. *Annals of the Russian academy of medical sciences*. 2021 Nov 30;76(5):458-64.
- [17] Mahoney LB, Rosen R. The spectrum of reflux phenotypes. *Gastroenterology & Hepatology*. 2019 Dec;15(12):646.
- [18] Di Stefano M, Pucci E, Miceli E, Pagani E, Brondino N, Nappi G, Corazza GR, Di Sabatino A. Prevalence and pathophysiology of post-prandial migraine in patients with functional dyspepsia. *Cephalalgia*. 2019 Oct;39(12):1560-8.
- [19] Burns G, Pryor J, Holtmann G, Walker MM, Talley NJ, Keely S. Immune activation in functional gastrointestinal disorders. *Gastroenterology & hepatology*. 2019 Oct;15(10):539.
- [20] Wang XJ, Camilleri M. Personalized medicine in functional gastrointestinal disorders: Understanding pathogenesis to increase diagnostic and treatment efficacy. *World journal of gastroenterology*. 2019 Mar 14;25(10):1185.
- [21] Reina J, Smith JW. Medical treatment of irritable bowel syndrome. *Clinics in colon and rectal surgery*. 2005 May;18(02):102-8.
- [22] Fujiwara Y, Arakawa T. Epidemiology and clinical characteristics of GERD in the Japanese population. *Journal of gastroenterology*. 2009 Jun;44(6):518-34.



Original Article

Comparative Effects of Therapeutic Massage and Acupressure on Neck Pain

Saba Mengal¹, Aamir Gul Memon^{2*}, Fatima Chaudhary³, Saleh Shah⁴, Muhammad Faheem Afzal⁵, Muhammad sanaullah², Sumaira Nawaz⁶, Falak Abdul Latif⁷

¹Physical Therapy Department, Isra University Hyderabad, Pakistan

²Physical Therapy Department, Riphah International University, Lahore, Pakistan

³Institute of health and management sciences IHMS, Islamabad, Pakistan

⁴Superior University, Lahore, Pakistan

⁵PSRD, College of Rehabilitation Sciences, Lahore, Pakistan

⁶Rashid medical hospital Dubai

⁷Department of Physical Therapy, Suleman Roshan Medical College, Sindh, Pakistan

ARTICLE INFO

Key Words:

Acupressure, Disability, Neck pain, Rehabilitation, Therapeutic massage

How to Cite:

Mengal, S., Memon, A. G., Chaudhary, F., Shah, S., Afzal, M. F., Sanaullah, M., Nawaz, S., & Abdul Latif, F. . (2022). Comparative Effects of Therapeutic Massage and Acupressure on Neck Pain: Therapeutic Massage and Acupressure in Neck Pain. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.505>

*Corresponding Author:

Aamir Gul Memon
 Physical Therapy Department, Riphah International University, Lahore, Pakistan
aamir_mmn642@yahoo.com

Received Date: 3rd June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Depending on the cause, neck pain can persist anywhere from a few days to several years; Osteoarthritis, spinal stenosis, ruptured disc, pinched nerves, emotional and physical stress, strain, bad posture, tumor, and other disorders are among the most common causes acupressure on local and distal acupuncture sites may provide drowsiness and relaxation, which may help to relieve chronic neck discomfort. **Objective:** To compare the effects of therapeutic massage and acupressure on neck pain. **Methods:** ISRA University Hospital Karachi conducted a randomized clinical trial. A total of n=30 individuals were between the ages of 20 and 35, with neck discomfort ranging from 3-6 on the VAS scale. The n=30 participants were separated into two groups: therapeutic massage (n=14) and acupressure (n=15). The data was analyzed using the SPSS version 22.0. **Results:** Mean age of study participants was 24.34± 4.3 years. A total of n=12 were female, and the remaining n=18 were male. The analysis showed that pain and neck disability significantly improved in both groups (p<0.05). When compared in both groups, the intensity of pain was not significantly different in both groups, but neck disability was significantly improved in the acupressure group as compared to the massage group after six weeks of intervention. **Conclusion:** The study concluded that both techniques benefit neck pain and disability and found significant results. But results show that acupressure was found to be more beneficial and significant than the therapeutic massage.

INTRODUCTION

Neck discomfort is a debilitating condition that goes through remissions and relapses and causes considerable movement restrictions in late-twentieth-century computer users [1]. The majority of cases follow an episodic pattern [2]. Trapizus myalgia (38%), tension neck syndrome (17%), and cervicgia are the most common neck pain cases base on clinical symptoms and indicators (17%). Myofascial pain syndrome (MPS) of the neck and shoulder [3] and the formation of myofascial trigger points

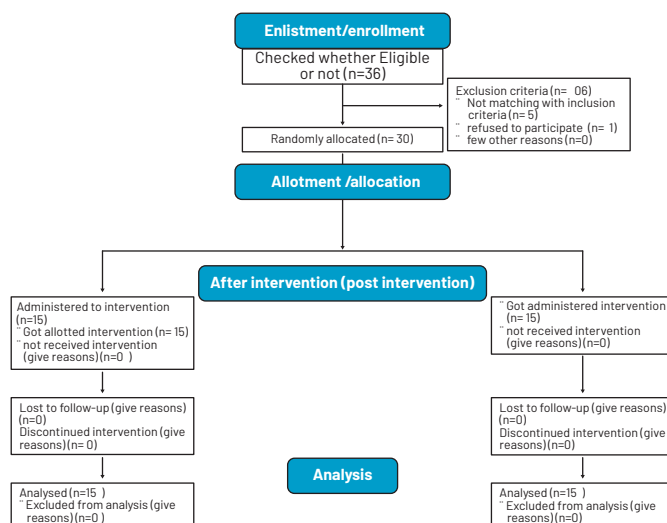
(MTrPs) on the trapezius, on the other hand, have been proposed as pain-causing mechanism [4]. Trauma, infections or inflammatory illnesses, rheumatic disorders, and congenital disease can all cause neck pain; however, in the majority of cases, no specific cause can be found, and the condition is characterized as nonspecific neck pain[5]. According to the Global Burden of Disease (GBD), musculoskeletal disease is the second greatest cause of global disability, with 43 percent of people experiencing it

in 2017 [5]. Neck pain is more common in women (48%) than in men (38%) in the general population. Working women had higher neck pain than older women. Chronic neck discomfort, which is defined as pain that lasts longer than six months, was shown to be more common in women (22% vs. 14%) than in men (14%) [6]. When it comes to work-related musculoskeletal disorders, work-related neck pain (WRNP) is more common among computer users, according to the research (WRMSDs). Nigeria (33.9%), Turkey (21.6%), Estonia (51%), Sweden (50%), Finland (20.7%), Iran (54.9%), India (45%), and Pakistan (45%) attest to this truth, according to the literature (16.8%) [7]. Maintaining proper posture is still essential for avoiding neck pain. Several interventions have been proposed to enhance computer users' posture through self-efficacy, such as internet training [6] and real-time visual feedback [8]. The cost-effectiveness planes revealed that 98% of the bootstrapped ratio for pain intensity, 85% for perceived recovery, and 87% for QALY were located in the southeast quadrant, demonstrating that manual treatment dominates physiotherapy. In a patient with mechanical neck pain, an impairment-based MTE resulted in clinically and statistically significant short and long-term improvements in pain disability and patient-perceived recovery when compared to a programme consisting of advice, a mobility exercise, and sub-therapeutic ultrasound [9]. The recommended strengthening exercise may have increased the extensibility and flexibility of the soft tissues, resulting in less pain and more range of motion [10]. Major purpose of this study is to see how therapeutic massage and acupressure can help with neck pain. The impact of this study on the community will be to provide novel treatment techniques even yet, there isn't much research comparing massage and acupressure.

METHODS

After receiving consent from the Department of Physical Therapy, ISRA University Karachi Campus, a randomized clinical trial investigation was done at the Physiotherapy OPD, ISRA University Hospital, from February to July 2018. Participants in the study gave their written informed consent, and their personal information was kept private in accordance with the Helsinki Declaration. The no probability convenience sampling technique was used in this study. The sample size was calculated by Epi-tool [11] and n=30 participants were divided into two groups (Group A: Massage Therapy and Group B: Acupressure) via a lottery method. The study participant was the participant between 20-35 years having neck pain between 3-6 intensity of VAS were included in the study. Radiating neck pain or cases of cervical spondylosis, systemic and metabolic diseases fracture the cervical spine,

participants with a whiplash injury, and cervical spine surgery were excluded from the study. The VAS was for pain assessment; the neck disability index was used to determine functional limitations due to neck pain. The assessment was taken at the baseline after three weeks of intervention. The therapeutic massage group received three weeks of treatment sessions of friction massage with 10 minutes of the hot pack before the session. After selecting and examining the trapezius muscle, gently with the sweeping thumb and palm, circular friction is performed in small circles, moving deeper and deeper into the tissue to the maximum depth and then released. Repeat this action three times on the same spot [12]. Acupressure groups received three weeks of treatment sessions of acupressure with 10 minutes given three times a week, three sets of the intensity of acupressure applied on the trapezius. Through right thumb in a rotatory fashion at 20-25 cycles per minute for 30 seconds. The subjects were observed for a further 10 minutes [13].



RESULTS

The mean age of 30 participants was 34.80 ± 4.746 . A total of n=16 (53.33%) of participants were male, and 14 (46.67%) were female, as shown in Table 1.

Variables	Construct	Frequency	Percentage %
Marital status	Married	19	63.33%
	Unmarried	11	36.67%
Occupation	Housewife	6	20%
	Driver	2	6.67%
	Clerk	5	16.67%
	Computer Operator	6	20%
	Nurse	6	20%
	Teacher	1	3.33%
	Tailor	4	13.33%

Table 1: Demographic data of the study participants

In Group A of pretreatment, 15 participants had moderate

disability, but 7 had a moderate disability after the treatment, and 8 had a mild type of disability. In Group B of pretreatment, 15 participants had moderate disability, but 5 had a moderate disability after the treatment, and 10 had a mild type of disability. Group-A, the mean difference of pain intensity within groups was 1.77 ± 0.53 , and neck disability was 7.1 ± 0.8 . Group-B's mean pain intensity difference within groups was 2.34 ± 0 , and neck disability was 9.19 ± 0.19 . Pre and post-treatment of pain intensity between groups were 0.34 ± 0.2 and 0.23 ± 0.11 . Pre and post-treatment of neck disability were 0.01 ± 0.39 and 2.1 ± 0.22 . The analysis showed that pain intensity and neck disability significantly improved ($p < 0.05$) after 3 weeks of intervention in therapeutic massage and acupressure groups. When comparing both groups, improvement in the pain intensity was not statistically ($p \geq 0.05$) significant, while neck disability significantly improved ($p < 0.05$) in the acupressure group as compared to the massage group after three weeks of intervention, Table 2.

Variables	Group A	Group-B	Mean Different	p-value
Pre Pain Intensity	5.00 ± 0.66	5.34 ± 0.2	0.34 ± 0.2	0.059
Post Pain Intensity	3.23 ± 0.130	3.00 ± 0.02	0.23 ± 0.11	0.079
Mean different	1.77 ± 0.53	2.34 ± 0.98		
p-value	0.04*	0.001**		
Pre Neck Disability	25.90 ± 3.80	25.89 ± 3.41	0.01 ± 0.39	0.764
Post Neck Disability	18.80 ± 3.00	16.70 ± 3.22	2.1 ± 0.22	0.04*
Mean Different	7.1 ± 0.8	9.19 ± 0.19		
p-value	0.0054**	0.00002***		

Level of significance: $p < 0.05^*$, $p < 0.01^{**}$, $p < 0.001^{***}$
 < 0.05 p-value consider significant result.

Table 2: With-in and between-group analysis

DISCUSSION

This study will help to improve patient outcomes and neck pain and ultimately reduce the severity of mechanical neck pain symptoms and expertise in physical intervention/therapies. This study will also help promote these therapeutic massages versus acupressure and their benefits in improving the condition of patients who suffer from Neck Pain. A study was conducted to explore the usefulness and comparative effectiveness of mobilization and muscle energy techniques to improve range of motion and physical functioning among patients with mechanical neck pain. The study concluded that both techniques are more effective in treating mechanical neck pain [14]. Study examined the efficacy of deep transverse friction massage and myofascial release among patients with the trapezius. The finding showed a significant improvement in pain and range of motion within groups. In contrast, the two intervention groups found no significant difference in pain and range of motion. The study concluded that the myofascial trigger release technique is more effective for

patients with the trapezius [15]. A study concluded that acupressure might be effective on the neck. However, it is not conclusive in line with the low evidence level and low methodological quality of included studies [16]. Another study looked into the effects of acupuncture on adults suffering from neck pain. Moderate quality data also suggests that acupuncture is more beneficial than inactive treatment for pain relief at short term follow-up, according to a study [17]. In chronic neck pain patients, acupuncture outperforms Sham in terms of decreasing motion-related pain and range of motion after just one treatment session. Acupuncture at far sites increases ROM more than D. D.N. is ineffective for motion-related discomfort [18]. Massage appears to be safe and may have clinical benefits for treating persistent neck pain, at least in the short term, according to an old study [19, 20]. Therapeutic massage was found to be useful for neck discomfort in this study. Acupressure, on the other hand, is more effective than therapeutic massage. Because the sample size was limited and the treatment period was short, there was no evidence of long-term improvement in functional impairment. Data should be collected based on gender-based disparities in pain and functional impairments in future investigations. To evaluate the long-term impact on functional impairment, the treatment time should be increased.

CONCLUSIONS

This study concluded that both techniques benefit neck pain and disability and found significant results. But in, in between-group results show that acupressure was found to be more beneficial and significant than the therapeutic massage.

REFERENCES

- [1] Park DJ, Park SY. Long-term effects of diagonal active stretching versus static stretching for cervical neuromuscular dysfunction, disability and pain: An 8 weeks' follow-up study. *Journal of back and musculoskeletal rehabilitation*. 2019 Jan ; 32(3): 403-10. doi: 10.3233/BMR-171107
- [2] Xie Y, Szeto G, Dai J. Prevalence and risk factors associated with musculoskeletal complaints among users of mobile handheld devices: A systematic review. *Applied ergonomics*. 2017 Mar; 59:132-42. doi.org/10.1016/j.apergo.2016.08.020
- [3] Gaudez C, Cail F. Effects of mouse slant and desktop position on muscular and postural stresses, subject preference and performance in women aged 18-40 years. *Ergonomics*. 2016 Nov; 59(11):1473-86. doi.org/10.1080/00140139.2016.1148783
- [4] Gerber LH, Shah J, Rosenberger W, Armstrong K, Turo D, Otto P, et al. Dry needling alters trigger points in the upper trapezius muscle and reduces pain in

- subjects with chronic myofascial pain. *PM&R*. 2015 Jul; 7(7):711-8. doi.org/10.1016/j.pmrj.2015.01.020
- [5] Rostron S. The Effects of Massage Therapy on a Patient with Migraines and Cervical Spondylosis: A Case Report. *International Journal of Therapy Massage and Bodywork*. 2021; 14(3):15-21. doi:10.3822/ijtm.v14i3.629
- [6] Bakken AG, Eklund A, Warnqvist A, O'Neill S, Axén I. The effect of two weeks of spinal manipulative therapy and home stretching exercises on pain and disability in patients with persistent or recurrent neck pain; a randomized controlled trial. *BMC Musculoskeletal Disorders*. 2021 Oct; 22(1):903. doi: 10.1186/s12891-021-04772-x.
- [7] Hasanat MR, Ali SS, Rasheed A, Khan M. Frequency and Associated Risk Factors for Neck Pain Among Software Engineers in Karachi, Pakistan. *JPMA: The Journal of the Pakistan Medical Association*. 2017 Jul; 67(7):1009-12.
- [8] Shirvani H, Salesi M, Samadi M, Shamsoddini A. Design and Development of a 3-Axis Accelerometer Biofeedback System for Real-Time Correction of Neck Posture for Long-Time Computer Users. *Journal of Medical Signals and Sensors*. 2021; 11(4):269-273. doi: 10.4103/jmss.JMSS_56_20
- [9] Fritz JM, Kim M, Magel JS, Asche CV. Cost-Effectiveness of Primary Care Management with or Without Early Physical Therapy for Acute Low Back Pain: Economic Evaluation of a Randomized Clinical Trial. *Spine (Phila Pa 1976)*. 2017 Mar; 42(5):285-290. doi: 10.1097/BRS.0000000000001729.
- [10] Ganesh GS, Mohanty P, Pattnaik M, Mishra C. Effectiveness of mobilization therapy and exercises in mechanical neck pain. *Physiotherapy Theory and Practice*. 2015 Feb; 31(2):99-106. doi: 10.3109/09593985.2014.963904.
- [11] Ho K, Spence J, Murphy MF. Review of pain-measurement tools. *Annals of emergency medicine*. 1996; 27:427-432.
- [12] Coulter ID, Crawford C, Vernon H, Hurwitz EL, Khorsan R, Booth MS, et al. Manipulation and mobilization for treating chronic nonspecific neck pain: a systematic review and meta-analysis for an appropriateness panel. *Pain physician*. 2019 Mar; 22(2):E55.
- [13] Kay TM, Gross A, Goldsmith CH, Rutherford S, Voth S, Hoving JL, et al. Exercises for mechanical neck disorders. *Cochrane Database Systematic Review*. 2012 Aug; (8):CD004250. doi:10.1002/14651858.CD004250.pub4.
- [14] Anwar N, Khalid K, Rana AA, Hayat MK, Idrees MQ, Zafar S. Efficacy of Kalenborn grade III mobilization, muscles energy techniques and their combination to improves range of motion and functional ability in adults with mechanical neck pain; *International Journal of Physiotherapy*. 2016; 3(4): 482-486. doi.org/10.15621/ijphy/2016/v3i4/111059
- [15] Mane P, Pawar A, Warude T. Effect of Myofascial Release and Deep Transverse Friction Massage as an Adjunct to Conventional Physiotherapy in Case Unilateral Upper Trapezitis - Comparative Study; *International Journal of Science and Research*; 2017: 6(3)644-647. doi: 10.21275/SR21330105408
- [16] Kwon CY, Lee B. Clinical effects of acupressure on neck pain syndrome (nakchim): a systematic review. *Integrative Medicine Research*. 2018 Sep; 7(3):219-230. doi: 10.1016/j.imr.2018.01.002.
- [17] Trinh K, Graham N, Irnich D, Cameron ID, Forget M. Acupuncture for neck disorders. *Cochrane Database Systematic Review*. 2016 May; (5):CD004870. doi: 10.1002/14651858.CD004870.pub4.
- [18] Irnich D, Behrens N, Gleditsch JM, Stör W, Schreiber MA, Schöps P, et al. Immediate effects of dry needling and acupuncture at distant points in chronic neck pain: results of a randomized, double-blind, sham-controlled crossover trial. *Pain*. 2002 Sep; 99(1-2):83-9. doi: 10.1016/s0304-3959(02)00062-3.
- [19] Sherman KJ, Cherkin DC, Hawkes RJ, Miglioretti DL, Deyo RA. Randomized trial of therapeutic massage for chronic neck pain. *The Clinical Journal of Pain*. 2009; 25(3):233-238. doi:10.1097/AJP.0b013e31818b7912
- [20] Bronfort G, Haas M, Evans R, Leininger B, Triano J. Effectiveness of manual therapies: the UK evidence report. *Chiropractic & osteopathy*. 2010 Dec; 18(1):1-33.



Original Article

Comparison of Diclofenac Suppository with Injection Tramadol in Postoperative Pain

Abdul Rab¹, Sughra Parveen¹, Asif Ali¹, Ali Nawaz¹, Shahzore Gul¹ and Muhammad Musadaq¹¹Jinnah Postgraduate Medical Center, Karachi, Pakistan

ARTICLE INFO

Key Words:

Abdominal Surgery, Post-Operative Pain, Diclofenac Suppository, Injection Tramadol, and Analgesic Efficacy.

How to Cite:

Rab, A. ., Parveen, S. ., Ali, A. ., Nawaz, A. ., Gul, S. . & Musadaq, M. . (2022). Comparison Of Diclofenac Suppository with Injection Tramadol In Postoperative Pain: Diclofenac Suppository with Injection Tramadol in Postoperative Pain. Pakistan BioMedical Journal, 5(6).

<https://doi.org/10.54393/pbmj.v5i6.591>

*Corresponding Author:

Abdul Rab
 Jinnah Postgraduate Medical Center, Karachi,
 Pakistan
harm.version02@gmail.com

Received Date: 19th May, 2022
 Acceptance Date: 26th May, 2022
 Published Date: 31st May, 2022

ABSTRACT

Pain and damage to tissue structure is frequently observed after surgical procedures. Management of postoperative pain has always been remained a challenge to surgeons because of its detrimental effect on patient's satisfaction, early mobilization and regaining of functionality. **Objective:** To compare the analgesic efficacy of diclofenac suppository with injection tramadol 100 mg for postoperative pain relief after abdominal surgeries. **Methods:** This Randomized Double-Blind Controlled Trial was conducted upon a sample of 98 patients, aged 12 to 60 years and undergoing abdominal surgery (elective and emergency) divided into two groups (Group A: Diclofenac Suppositories 100 mg, and Group B: Injection Tramadol 100 mg), of 49 patients each. Visual Analogue Scale (VAS) was used for measuring the severity of pain at 0, 1, 6, 12, 18 and 24 hours, following surgeries. **Results:** The mean age of the sample stood at 31 (SD ± 03) years, with most of the sample comprising of males (72.45%). Postoperative pain was experienced by patients in both groups, with group A reporting less severe pain than group B but no statistical difference was found between the severity. **Conclusion:** After careful consideration, it may be concluded that both agents, namely Diclofenac Suppositories 100 mg, and Injection Tramadol 100 mg are efficacious at managing the postoperative pain hence both may be used interchangeably or in conjunction among patients undergoing abdominal surgeries.

INTRODUCTION

Trauma elicited by surgical incisions nearly always manifests pain and managing that postoperative pain effectively has remained a challenge for healthcare professionals around the world. Much emphasis is laid onto effective management of postoperative pain which has always been remained a challenge to surgeons because of its detrimental effect on patient's satisfaction, early mobilization and regaining of functionality [1]. Ineffective relief from pain is known to adversely impact patient health in various ways. Firstly, the pain causes acute distress, and secondly, it hampers the mobility thereby leading to complications associated with delayed mobility. The incumbent anxiety and psychological distress have

profound impact on the general health and wellbeing of the individuals [2,3]. Certain factors play a role in determining the extent and duration of pain that follows a surgery, namely the incision (type, site, size, and closure technique), the surgery (type, level of invasiveness, and the duration) and underlying health conditions [4,5]. Attempts to modulate the factors and prevent postoperative pain are made routinely in many forms especially the administration of pre-emptive analgesia [6]. "However, it is not clear how successful preventative methods may be in preventing severe and prolonged pain. but it is highly probable that early intervention (when early signs are first noticed) is more likely to be advantageous [7,8]. Opioids have been

used since long to prevent postoperative pain but the associated adverse events such as nausea/vomiting, respiratory depression, and ileus, have forced healthcare professionals to reconsider the choice of analgesia [9]. Alternatives to opioids, include "systemic analgesics tramadol and ketamine as well as regional analgesia techniques like neuraxial and peripheral blocks". Tramadol is a synthetic 4-phenyl-piperidine analogue of codeine. It is a central analgesic with a low affinity for opioid receptor. It inhibits serotonin and norepinephrine neuronal reuptake [10]. Tramadol is "increasingly used for the treatment of acute post-operative and chronic pain of intermediate or severe intensity. One of the NSAIDs used for acute pain management is diclofenac in suppository form. Many studies have been conducted to compare NSAIDs with opioids, but there have been no studies to determine the efficacy of suppository diclofenac and injection Tramadol after abdominal surgery. This study was designed to evaluate this idea in postoperative pain relief" after abdominal surgery[11].

METHODS

This Randomized Double-Blind Controlled Trial was conducted upon a sample of 98 patients, aged 12 to 60 years and undergoing abdominal surgery (elective and emergency) divided into two groups (Group A: Diclofenac Suppositories 100 mg, and Group B: Injection Tramadol 100 mg), of 49 patients each. Visual Analogue Scale (VAS) was used for measuring the severity of pain at 0, 1, 6, 12, 18 and 24 hours, following surgeries. "Scores were recorded by making a handwritten mark on a 10-cm line that represents a continuum between no pain and worst pain." All consecutive patients presenting to the ward 3, Jinnah Postgraduate Medical Centre, Karachi, from November 2020 to November 2021 and meeting the eligibility criteria were allocated to either of the groups (A or B) using computer generated simple randomized numbers. Data was analyzed using the IBM SPSS v. 21.0 and M.S Excel 2013. "Descriptive statistics such as mean \pm standard deviation (SD) was used for continuous variables such as age and VAS Score. Numbers and percentages were used to describe the proportion of categorical variables such as sex".

RESULTS

The mean age of the sample stood at 31(SD \pm 03) years, with most of the sample comprising of males (72.45%). The summary of descriptive statistics is tabulated below:

Variable	Group A	Group B	Cumulative	
Mean Age	31.5 (SD \pm 03)	30.5 (SD \pm 03)	31 (SD \pm 03)	
Gender	Male	35 (71.43%)	36 (73.47%)	71 (72.45%)
	Female	14 (28.57%)	13 (26.53%)	27 (27.55%)
Type of Surgery	Elective	37 (75.55%)	41 (83.67%)	78 (79.59%)
	Emergency	12 (24.49%)	08 (16.33%)	20 (20.41%)
Mean Duration of Surgery (mins)	61 (SD \pm 7.7)	60 (SD \pm 5.3)	60.5 (SD \pm 6.1)	

Postoperative pain was experienced by patients in both groups, with group A reporting less severe pain than group B. There was no statistical difference between the severity of the pain though.

Postoperative Pain	Group A	Group B	P Value
0 Hours	1.61	2.21	0.081
1 Hour	2.19	2.43	0.093
6 Hours	2.66	2.91	0.131
12 Hours	2.95	3.68	0.064
18 Hours	2.87	3.59	0.059
24 Hours	2.71	3.40	0.061

DISCUSSION

The analgesic regimen needs to meet the goals of providing safe, effective analgesia, with minimal side effects. However, most new analgesic agents are not available in many hospitals since they are expensive and require trained personnel and special equipment. The age-old agents, namely diclofenac and tramadol are thus commonly employed and need to be researched well enough [12,13]. Tramadol is known to be a potent analgesic however, when administered intravenously (and even orally) the peak concentrations of the drug are reached rapidly and oftentimes lead to severe post-operative nausea and vomiting. Rectal administration of Tramadol may be an alternative in this situation, but that too yields uncomfortable side effects. Diclofenac is believed by many to be a better choice for suppository [14-17]. Joshi et al, compared diclofenac suppository with tramadol suppository. It was noted that "in diclofenac group at 4 hours mean VAS score 2.1, at 6 hours it was 2.63 and at 8 hours mean VAS was 2.07, after that rescue analgesia was given. After 8 hours 60% patients needed first rescue analgesia in diclofenac group. While when compared compared diclofenac suppository with tramadol suppository, it was found mean VAS was less in diclofenac group and this difference was statistically significant. Also no side effect was found in diclofenac group. Thus, rectal suppository of diclofenac is better alternative for postoperative analgesia in as compared to tramadol" [18-20]. Sahil et al, too compared the same and it was noted that "mean VAS score showed significantly better pain relief with diclofenac suppository compared to tramadol group over a period of 12 hours after surgery (for e.g., mean VAS score for diclofenac group at 4 and 6 hours was 2.6 and

2.83 as compared to 3.12 and 3.36 of tramadol group. Better pain relief with diclofenac suggests better efficacy as compared to tramadol injection [21-22]. This research however, had a few limitations; the first being the absence of a control / placebo group and the second being the small sample size and single study setting. In future, the research may be replicated with a more extensive sample and a control group for greater methodological rigor.

CONCLUSION

After careful consideration, it may be concluded that both agents, namely Diclofenac Suppositories 100 mg, and Injection Tramadol 100 mg are efficacious at managing the postoperative pain hence both may be used interchangeably or in conjunction among patients undergoing abdominal surgeries.

REFERENCES

- [1] Pereira S, Portela F, Santos MF, Machado J, Abelha A. Predicting type of delivery by identification of obstetric risk factors through data mining. *Procedia Computer Science*. 2015 Jan 1;64:601-9. doi.org/10.1016/j.procs.2015.08.573
- [2] Verstraete S, Van de Velde M. Post-cesarean section analgesia. *Acta Anaesthesiologica Belgica* 2012;63(4):147-67.
- [3] Harper CM, Lyles YM. Physiology and complications of bed rest. *Journal of the American Geriatrics Society* 1988 Nov;36(11):1047-54. doi: 10.1111/j.1532-5415.1988.tb04375.x.
- [4] Kehlet H, Dahl JB. The value of "multimodal" or "balanced analgesia" in postoperative pain treatment. *Anesthesia and analgesia*. 1993 Nov;77(5):1048-56. doi: 10.1213/00000539-199311000-00030.
- [5] Chan A, Dore CJ, Ramachandra V. Analgesia for day surgery: Evaluation of the effect of diclofenac given before or after surgery with or without bupivacaine infiltration. *Anaesthesia*. 1996 Jun;51(6):592-5. DOI: 10.1111/j.1365-2044.1996.tb12574.x
- [6] Munishankar B, Fettes P, Moore C, McLeod GA. A double-blind randomised controlled trial of paracetamol, diclofenac or the combination for pain relief after caesarean section. *International journal of obstetric anesthesia* 2008 Jan;17(1):9-14. doi: 10.1016/j.ijoa.2007.06.006.
- [7] Booth JL, Harris LC, Eisenach JC, Pan PH. A Randomized Controlled Trial Comparing Two Multimodal Analgesic Techniques in Patients Predicted to Have Severe Pain After Cesarean Delivery. *Anesthesia and analgesia*. 2016 Apr;122(4):1114-9. doi:10.1213/ANE.0000000000000695.
- [8] Merrikhihaghi S, Farshchi A, Farshchi B, Farshchi S, Abedin-Dorkoosh F. Tramadol versus diclofenac in pain management after cesarean section: A cost analysis study. *Journal of Pharmacoeconomics and Pharmaceutical Management*. 2015 Oct 5;1(1/2):22-4.
- [9] Darvish H, Memar Ardestani B, Mohammadkhani Shali S, Tajik A. Analgesic Efficacy of Diclofenac and Paracetamol vs. Meperidine in Cesarean Section. *Anesthesia and Pain Medicine* 2013 Dec 26;4(1):e9997. doi: 10.5812/aapm.9997.
- [10] Taneja A, Kaur T, Sood IV. Comparative Study on The Effect of Paracetamol, Diclofenac and their Combination in Post-Operative Pain Relief of Cesarean Section. *JK Science*. 2015;17(1):30.
- [11] Nikooseresht M, Seifrabiei MA, Davoodi M, Aghajanlou M, Sardari MT. Diclofenac suppository vs. IV acetaminophen combined with IV PCA for postoperative pain management in patients undergoing laminectomy: a randomized, double-blinded clinical trial. *Anesthesiology and pain medicine*. 2016 Jun;6(3). DOI:10.5812/aapm.36812
- [12] Hooda R, Pathak P, Chavhan R. Comparative study of diclofenac suppository with tramadol suppository in addition to acetaminophen for post caesarian analgesia. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2020 Apr 1;9(4):1372-7. doi.org/10.18203/2320-1770.ijrcog20201086
- [13] Joshi Vyankatesh S, Vyavahare Ramesh D, Khade Ganesh DS, Jamadar NP. Comparative study of analgesic efficacy of rectal suppository of tramadol versus diclofenac in suppressing postoperative pain after Cesarean section. *International journal of biomedical research* 2013 Jan;1(2):32-7.
- [14] Sahil S, Mane M, Paranjap J. Comparison of diclofenac suppository with tramadol suppository for post-operative analgesia in abdominal hysterectomy patient. *Medpulse International Journal of Medicine* 2017;4(5):606-9.
- [15] Smith CA, Ruth-Sahd L. Reducing the incidence of postoperative nausea and vomiting begins with risk screening: An evaluation of the evidence. *Journal of PeriAnesthesia Nursing*. 2016 Apr 1;31(2):158-71. DOI: 10.1016/j.jopan.2015.03.011
- [16] Atashkhoei S, Bilehjani E, Fakhari S, Hanieh FA. Postoperative Nausea and Vomiting Prophylaxis with Ondansetron in Diagnostic Gynecologic Laparoscopy: Preemptive versus Preventive Method. *Advances in Reproductive Sciences*. 2017 Jan 13;5(1):1-9. DOI:10.4236/arsci.2017.51001
- [17] Awad K, Ahmed H, Abushouk AI, et al. Dexamethasone combined with other antiemetics

- versus single antiemetics for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy: An updated systematic review and meta-analysis. *International journal of surgery*. 2016 Dec 1; 36:152-63. DOI: 10.1016/j.ijssu.2016.10.034
- [18] Firdaus K, Dan A, Maaya M, Rahman RA, Kamaruzaman E, Manap NA, et al. Dexamethasone 8 mg Versus Dexamethasone 4 mg with Propofol 0.5 mg/kg for the Prevention of Postoperative Nausea and Vomiting after Laparoscopic Gynaecology Procedure. *International Medical Journal*. 2016 Feb 1;23(1).
- [19] Munishankar B, Fettes P, Moore C, McLeod GA. A double-blind randomised controlled trial of paracetamol, diclofenac or the combination for pain relief after caesarean section. *International journal of obstetric anaesthesia* 2008 Jan;17(1):9-14. doi: 10.1016/j.ijoa.2007.06.006.
- [20] Chan A, Dore CJ, Ramachandra V. Analgesia for day surgery: Evaluation of the effect of diclofenac given before or after surgery with or without bupivacaine infiltration. *Anaesthesia*. 1996 Jun;51(6):592-5. DOI: 10.1111/j.1365-2044.1996.tb12574.x
- [21] Krzyzanowski SA, Kim K, Smith DC, Young M, Buffington CK. The Effects of a Dexamethasone-based Prophylaxis Protocol on Postoperative Nausea and Vomiting (PONV) and the Duration and Associated Cost of the Hospital Stay. *Surgery for Obesity and Related Diseases*. 2018 Nov 1;14(11): S7. doi.org/10.1016/j.soard.2018.09.474
- [22] Gao C, Li B, Xu L, Lv F, Cao G, Wang H, et al. Efficacy and safety of ramosetron versus ondansetron for postoperative nausea and vomiting after general anesthesia: a meta-analysis of randomized clinical trials. *Drug Design Development Therapy*. 2015 Apr 23;9:2343-50. doi: 10.2147/DDDT.S80407.



Original Article

Comparison of Sevoflurane and Propofol for Insertion of I-Gel in Patients Undergoing Minor Elective Surgical Procedures Under General Anesthesia

Shumaila Ashfaq¹, Faheem Asghar², Shahid Adalat Chaudhry³, Muhammad Nadeem Khan⁴, Sajid Razzaque⁵, Usman Habib Virk⁶

¹Department of Anesthesia, Islam Medical College Sialkot, Pakistan

²Department of Anesthesia, M. Islam Medical College Gujranwala, Pakistan

³Department of Anesthesiology, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur AJ&K, Pakistan

⁴Department of Anesthesia, Mohtarma Benazir Bhutto Shaheed Medical College, Medical College Mirpur AJ&K, Pakistan

⁵Department of Surgery, CMH Rawalakot, Pakistan

⁶M. Islam Medical College Gujranwala, Pakistan

ARTICLE INFO

Key Words:

I-Gel, Sevoflurane, Insertion, Anesthetics, Surgery

How to Cite:

Ashfaq, S. ., Asghar, F. ., Adalat Chaudhry, S. ., Nadeem Khan, M. ., Razzaque, S. . & Habib Virk, U. . (2022). Comparison of Sevoflurane and Propofol for Insertion Of I-Gel in Patients Undergoing Minor Elective Surgical Procedures Under General Anesthesia: Sevoflurane and Propofol for Insertion of I-Gel in Patients. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.518>

***Corresponding Author:**

Shumaila Ashfaq

Department of Anesthesia, Islam Medical College Sialkot, Pakistan

shumailach2003@yahoo.com

Received Date: 2nd June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

The usage of Propofol is the most common method for the sake of insertion of I-Gel. But when propofol is used it may cause serious problems like swelling or inflammation at the injection site, low blood pressure, and apnea. There is a need to find another better method for providing anesthetics during the insertion of I-Gel. **Objective:** To find out the effects of two anaesthetics propofol and sevoflurane during the insertion of I-Gel. **Methods:** For the sake of the study a group of 66 patients were selected. All of these patients have to go under some surgeries using commonly available anaesthetics. The patients were divided into two groups 33 patients in each group. One group received Propofol before surgery and the other group receive sevoflurane. Then after the insertion of I-Gel, patients were analyzed in detail for all the changes that took place. **Results:** After the insertion of I-Gel, all the physical changes of the patients were analyzed in detail. Both of the study groups were given different drugs, but after surgery, no difference was observed between two groups having different anaesthetic. Both of the group have same heart rate, blood pressure and other insertion details except that Sevoflurane need much time to perform its anaesthetic function as compared to Propofol. **Conclusion:** After all these experiments, it is inferred that, when the effects of both drugs were compared, Sevoflurane has stability in the case of hemodynamics, it can replace propofol in a number of procedures due to its stability. Propofol does not have so much hemodynamic stability. But when I-Gel insertion has to be performed, Propofol has a better rate of induction as compared to sevoflurane.

INTRODUCTION

In recent years, a new device name "Supraglottics" device is much popular during surgeries on the Air passage way. I-Gel is a cuff less gadget belonging to the second generation. It has a non-billow seal which diminishes different constrictive trauma which is a side effect of other devices. It provides some internal anatomical insignia to the laryngeal, pharyngeal, and per laryngeal assembly. The usage of I-Gel has many advantages like minimization of hemodynamic alterations, laryngoscopy, and relaxation of

the muscular system. An adequate quantity of anesthetic is required for the insertion of I-Gel in non-paralyzed patients. For the I-Gel surgery, this device is designed in such a way that, it consists of a mask having morphology like a larynx. By the use of this device, the air passageway received only a limited amount of oxygen. Insertion of I-Gel is that it provides a controlled amount of oxygen to the patient by creating positive pressure. But before the insertion of I-Gel, different anesthetics are given to the

patients [1]. The main purpose of these anesthetics is to induce unconsciousness before insertion, relaxation of jaws, and controlled oxygen supply without disturbing the heart-related mechanisms. So, before insertion, usually, propofol is recommended in the protocol, but when all the characteristics of different anesthetics were compared, another drug named Sevoflurane came as an option because this drug has much stability in terms of hemodynamics. Sevoflurane has one more advantage, it smells non-pungent as compared to propofol and this drug is not soluble in blood or water, so it can also be an ideal choice for its usage as an anesthetic in case of insertion of I-Gel. This drug has one more advantage it does not cause any irritation in the respiratory system. When this drug was given to the patients it may cause cough, shortness of breath, and laryngospasm [2-3]. This drug also facilitates the rapid insertion of the I-Gel by quickly inducing its effect in the patient. Its induction capacity is quite high as compared to propofol. It leads to unconsciousness for a long time as compared to the other drug. In this study different hemodynamic alteration was observed within two groups having these anesthetics before surgery [4-6]. The efficiency of both of the drugs was compared in this study, to find which one is better and has low side effects as an anesthetic during insertion of I-Gel and is more beneficial with regard to cost and providing better results in case of other surgeries as well [5-8].

METHODS

For this study, clearance from the ethical committee of the institute was got as well as all the information from the patients was taken with their consent. Patients were selected from December 2020 to December 2021. A group of 66 patients was selected and their average age was from 20 to 60 years. All of these patients have to undergo I-Gel insertion. These patients were divided into two groups, i.e. 33 patients in each group. One group was given propofol drug as Anesthesia and the other group was given sevoflurane. Before the insertion of I-Gel, patients were not given food for 6 hours. Before the start of treatment, Anesthesia was given to both of the groups in prescribed quantities (3 mg/kg of propofol with 0.2 mg of glycopyrrolate), in the case of sevoflurane 8% was given to the patients. After providing Anesthesia, its reaction was observed in the patient. The duration of the effect of Anesthesia was also measured and analyzed. Before giving the dose of Anesthesia, the weight of the patients was measured, and the dose was decided according to the weight of the patient. The assessment of the effect of anesthetics was predicted by calling patients by their names. The peak point of Anesthesia was when the reflex action of eyelashes is lost for that particular time. After

observing the general aspects of both anesthetics, other parameters were also assessed such as blood pressure, heart rate, the solubility of drugs within the blood, and oxygen absorbance capacity of the blood after giving the dose. The exact dose required to develop complete unconsciousness was also optimized. To analyze the results different statistical approaches were applied such as a t-test for the prediction of alterations in hemodynamics. Probability of error less than 0.05 was considered significant.

RESULTS

A total of 33 patients were taken in group 1 and group 2 respectively. There was no difference found between the age groups in case of both groups. And the results were not significantly variable with respect to body weight distribution as well. The average of the age was 37 ± 7.2 (SD) and in group S it was 39 ± 6 (SD). The mean weight that was observed after compiling results came out to be 54 ± 6 (SD) in case of group P and in case of group S it was 57 ± 6 (SD) as described in Table 1.

1. Group P or group 1 : Propofol 2.5 mg/kg body weight
2. Group S or group 2: Sevoflurane 8% was introduced

Characteristics	Group 1	Group 2	Unpaired	p-value
	Average+SD	Average+SD	T- test	
Age in years	37+7	39+6	-0.99	0.4
Weight (kg)	54+6	57+6	-2.0	0.052

Table 1: Demographic features of the patients

After using IV propofol the induction was more strongly observed. And the mean of the time of induction that was carried out in group P was 28 ± 7 (SD) and in case of group S it was 49 ± 9 (SD). ($p=0.005$). It was found that there was no change in the mean time of I- Gel incorporation in the two groups. The mean time that was recorded in sec for I- Gel insertion in case of Group P was 10 ± 3 (SD) sec and in case of other group 11 ± 5 (S.D), Table 2.

Variables	Propofol	sevoflurane	p-value
Induction time in sec	28 ± 7	49 ± 9	0.001
I Gel time of insertion in sec	10 ± 3	11 ± 5	0.57

Table 2: Induction time and insertion of I Gel

The first attempt to place I-Gel in all patients was successful. There was no statistical significance found between groups in the insertion of I-Gel. The conditions of I-Gel insertions in 27 (80%) patients were found to be successful with a score of 18. And in the remaining 7(21%) of the patients the result came out to be average, Table 3.

Grading	Propofol group	Sevoflurane group	p-value
Excellent	31(93%)	27(80%)	0.2
Satisfactory	2(6%)	7(21%)	0.18

Table 3: Grading of state for I Gel insertion

Average arterial blood pressure	Baseline	At 1 min	2 min	3 min	4 min	5 min
Group S	98.4	81.5	78.5	78	78.2	78
Group P	92.7	0.7	79.8	68.3	68.1	68
p-value	.3	6.45	.28	.14	.4	.04
Rate of Heart beat						
Group S	95.5	84.5	82	82	82	880
Group P	88.1	76.9	74.3	75	75	75
p-value	0.38	0.18	0.78	0.2	0.17	0.06

Table 4: Assessment of haemodynamic parameters

DISCUSSION

Muhammad A. Nasir invented I-Gel in cooperation with the inter surgical company in 2007. This gel is now very important in the air way control and is used in surgeries with successful rate. After the induction of Anesthesia, a very promising and satisfactory insertion of I-Gel is required with a sufficient depth and a proper blunting of airway reflexes is also needed. As compared with endotracheal incubation, the installment of I-Gel is linked with less intense variations in hemodynamics [9-11]. In this study the patients were divided into two groups each containing 33 patients. All the patients were confirmed for fasting and the pre-evaluation of the patients was carried out before administration of Anesthesia [12,13]. Due to its enhanced negative effect on reflexes of airway and because of its prominent jaw relaxation properties, propofol is used as a successful intravenous induction agent. However, it has some adverse side effects including pain, apnea, hypotension etc. If we look that the inhalational induction agents that can used, it was found that sevoflurane is the most effective because of its nice smell and, quick and smooth induction, and less irritation in the respiratory tract as compared to other induction agents. The vital capacity of both sevoflurane is relatable to the bolus introduction of propofol. This is linked with efficient hemodynamic stability and elevated patient approval range [14-16]. It was found that the I-Gel insertion was superior to the working of propofol than the sevoflurane. The excellent conditions that were found were 93% in case of propofol and 80% in case of sevoflurane [17-18]. Quite similar results were found in a study carried out by Chavan et al., by using an exact point of induction in there was loss of eye lash function in both of the participating individuals. Moreover, sevoflurane has been compared to the working of propofol in many studies for the I-Gel analysis. And it was later on found that the reliability, excellent quality and safety of sevoflurane makes it an excellent alternative for propofol in case of adults [19]. The studies show that the comparisons of hemodynamic aspects (heart rate, arterial pressure) between the two groups revealed that there was a prominent difference between these aspects in the two groups. The propofol group depicted lessened arterial

pressure as compared to the sevoflurane one. ($p=0.007$). But after the insertion of I-Gel there was a mean decrease in arterial blood pressure in both groups. There was no prominent variation found the heart rates in both groups. ($p=0.09$) Moreover, if the heart rate was discussed in the group after every minute there was a significant decrease in the heart rate in case of both groups after the insertion of I-Gel as compared to the other strategy mean arterial pressure (MAP). In this study I-Gel was able to be effectively inserted in the patients in the first try. The induction duration was found to be significantly higher in sevoflurane as compared to propofol. These findings are almost same as found by Kannaujia et al., In the present study it was revealed that the hemodynamic parameters were constant and similar in case of both group of patients. However, there was a statistically prominent difference between heart rate (HR) and MAP in propofol group after 3 minutes of induction [20]. Ahmeduddin et al., later on relate the results that the hemodynamic characteristics were constant in case of both groups. Thus we can say that the insertion and the fitting of I-Gel is done speedily and with proper safety in case of propofol. But as far as sevoflurane is concerned it has very efficient hemodynamic response. Sevoflurane can prove to be very useful in case of cardiovascular disorder. If VCB technique is used sevoflurane 8% can be compared to intravenous delivery of propofol in adults that are carrying out general surgical procedure under Anesthesia. Although according to the studies there is a reasonable amount of time that is required to relax the jaws after using sevoflurane which can lead to hindrance in I-Gel insertion. Sevoflurane can prove to be an excellent alternative of intravenous induction especially in patients that have cardiovascular disease at critical stage or in any case where the propofol can't be used. Sevoflurane is the most desirable alternative of propofol and is used in I-Gel insertions in case of adults [21-22].

CONCLUSION

Propofol is proved to be an efficient for the installment of I-Gel. It is also calmer to perform as compared to other drugs. But sevoflurane has an advantage that it has effective hemodynamic stability therefore it can be efficiently used for patients suffering from cardiovascular disorders.

REFERENCES

- [1] Mahajan R. Comparison of Sevoflurane and Propofol for Insertion of I-Gel in Patients Undergoing Minor Elective Surgical Procedures under General Anesthesia. JK Science. 2020; 22(1):24-8.
- [2] Cohen IT, Finkel JC, Hannallah RS, Hummer KA, Patel KM. Rapid emergence does not explain agitation following sevoflurane Anesthesia in infants and

- children: a comparison with propofol. *Pediatric Anesthesia*. 2003 Jan; 13(1):63-7. doi: 10.1046/j.1460-9592.2003.00948.x.
- [3] Song D, Joshi GP, White PF. Fast-track eligibility after ambulatory anesthesia: a comparison of desflurane, sevoflurane, and propofol. *Anesthesia & Analgesia*. 1998 Feb; 86(2):267-73. doi: 10.1097/00000539-199802000-00009.
- [4] Raeder J, Gupta A, Pedersen FM. Recovery characteristics of sevoflurane- or propofol-based Anesthesia for day-care surgery. *Acta Anaesthesiologica Scandinavica*. 1997 Sep; 41(8): 988-94. doi: 10.1111/j.1399-6576.1997.tb04825.x.
- [5] Kanaya A, Kuratani N, Satoh D, Kurosawa S. Lower incidence of emergence agitation in children after propofol anesthesia compared with sevoflurane: a meta-analysis of randomized controlled trials. *Journal of anesthesia*. 2014 Feb; 28(1):4-11. doi: 10.1007/s00540-013-1656-y.
- [6] Jellish WS, Lien CA, Fontenot HJ, Hall R. The comparative effects of sevoflurane versus propofol in the induction and maintenance of anesthesia in adult patients. *Anesthesia & Analgesia*. 1996 Mar; 82(3):479-85. doi: 10.1097/00000539-199603000-00009.
- [7] Zhang Y, Shan GJ, Zhang YX, Cao SJ, Zhu SN, Li HJ, et al. Propofol compared with sevoflurane general Anesthesia is associated with decreased delayed neurocognitive recovery in older adults. *British Journal of Anesthesia*. 2018 Sep; 121(3):595-604. doi.org/10.1016/j.bja.2018.05.059
- [8] Hagberg C, Arttime C. Airway management in the adult. *Miller's Anesthesia*. 8th ed. Philadelphia. Churchill Livingstone 2015; 1647-58.
- [9] Beylacq L, Bordes M, Semjen F, Cros AM. The I-gel, a single-use supraglottic airway device with a non-inflatable cuff and an esophageal vent: an observational study in children. *Acta Anaesthesiologica Scandinavica*. 2009 Mar; 53(3): 376-9. doi: 10.1111/j.1399-6576.2008.01869.x.
- [10] Ahmeduddin S, Amjad A, Sadqa A. Comparison of propofol and sevoflurane for laryngeal mask airway insertion. *Journal of Rawalpindi Medical College (JRMC)*; 2013; 17(2):268-70.
- [11] Rustagi PS, Nellore SS, Kudalkar AG, Sawant R. Comparative evaluation of i-gel® insertion conditions using dexmedetomidine-propofol versus fentanyl-propofol - A randomised double-blind study. *Indian Journal of Anaesthesia*. 2019 Nov; 63(11):900-907. doi: 10.4103/ija.IJA_313_19.
- [12] Dwivedi R, Dwivedi S, Chourasia HK. A comparative study of sevoflurane and propofol for laryngeal mask airway insertion in adults. *International Journal of Scientific Study*. 2015; 3:67-71.
- [13] El Radaideh KM, Al Ghazo MA. Single breath vital capacity induction of anesthesia with 8 % sevoflurane versus intravenous propofol for laryngeal tube insertion in adults. *Saudi Medical Journal*. 2007; 28:3640.
- [14] Kannaujia A, Srivastava U, Saraswat N, Mishra A, Kumar A, Saxena S. A preliminary study of I-gel: A new supraglottic airway device. *Indian journal of anaesthesia*. 2009 Feb; 53(1):52.
- [15] Sengupta J, Sengupta M, Nag T. Agents for facilitation of laryngeal mask airway insertion: a comparative study between thiopentone sodium and propofol. *Annals of African medicine*. 2014 Jul-Sep; 13(3):124-9. doi: 10.4103/1596-3519.134405.
- [16] Sukhupragarn W, Leurcharusmee P, Sotthisopha T. Cardiovascular effects of volatile induction and maintenance of anesthesia (VIMA) and total intravenous anesthesia (TIVA) for laryngeal mask airway (LMA) anesthesia: A comparison study. *J Med Assoc Thai* 2015; 98:388-93.
- [17] Negargar S, Peirovifar A, Mahmoodpoor A, Parish M, Golzari SE, Molseqi H, et al. Hemodynamic parameters of low-flow isoflurane and low-flow sevoflurane anesthesia during controlled ventilation with laryngeal mask airway. *Anesthesiology and Pain Medicine*. 2014 Dec; 4(5): e20326. doi: 10.5812/aapm.20326.
- [18] Topuz D, Postaci A, Sacan O, Yildiz N, Dikmen B. A comparison of sevoflurane induction versus propofol induction for laryngeal mask airway insertion in elderly patients. *Saudi Medical Journal*. 2010; 31:1124-29.
- [19] Chavan SG, Mandhyan S, Gujar SH, Shinde GP. Comparison of sevoflurane and propofol for laryngeal mask airway insertion and pressor response in patients undergoing gynecological procedures. *Journal of anaesthesiology, clinical pharmacology*. 2017 Jan Mar; 33(1):97-101. doi:10.4103/joacp.JOACP_31_3_15.
- [20] Ravi S, Krishnamoorthy K, Ganesan I. Comparison of sevoflurane and propofol for laryngeal mask airway in children. *Indian journal of clinical anaesthesia*. 2015; 2:137-40.
- [21] Vora K, Shah V, Patel D, Modi M, Parikh G. Sevoflurane versus propofol in the induction and maintenance of Anesthesia in children with laryngeal mask airway. *Sri Lanka Journal of Child Health*. 2014 Jun; 43(2). doi.org/10.4038/sljch.v43i2.7004
- [22] Enlund M, Berglund A, Ahlstrand R, Walldén J, Lundberg J, Wärnberg F, et al. Survival after primary

breast cancer surgery following propofol or sevoflurane general anesthesia-A retrospective, multicenter, database analysis of 6305 Swedish patients. *Acta Anaesthesiologica Scandinavica*. 2020 Sep; 64(8):1048-1054. doi:



Original Article

Correlation of Sonographic Gestational Age with Fetal Kidney Length in Normal Pregnancy

Areej Zamir¹, Sadia Azam¹, Abid Ali¹, Rehan Afsar¹, Aneeqa Khalid¹ and Waqar Mehmood Dar¹¹University Institute of Radiological and Medical Imaging Sciences, University of Chenab, Gujrat, Pakistan

ARTICLE INFO

Key Words:

Ultrasonography, Length of Fetal Kidney, Gestational Age

How to Cite:

Zamir, A. ., Azam, S., Ali, A. ., Afsar, R. ., Khalid, A. ., & Mehmood Dar, W. . (2022). Correlation of Sonographic Gestational Age with Fetal Kidney Length in Normal Pregnancy: Sonographic Gestational Age with Fetal Kidney Length in Normal Pregnancy. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.532>

*Corresponding Author:

Areej Zamir
 The University of Chenab, Gujrat, Pakistan
areejzamir99@gmail.com

Received Date: 8th June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Precise evaluation of gestational age is essential for quality maternity care. Ultrasonography is the most readily available and reliable method to establish gestational age. This study aims to use the length of the fetal kidney as a reliable parameter to measure gestational age in late second and third trimesters. **Objective:** To determine the relationship between fetal kidney length and gestational age in weeks during the late 2nd and 3rd trimester of normal pregnancy. **Methods:** It was a prospective cross-sectional study conducted on 105 singleton normal pregnant females between 24th and 40th weeks of gestation who came to the obstetrics and gynecology department at a private sector hospital in Kharian, Pakistan. The duration of the study was four months. Bi-parietal diameter, femur length, and fetal kidney lengths were measured. Statistical analyses were applied using SPSS version 22.0. **Results:** A moderately significant positive correlation was identified between different gestational age measuring parameters and fetal kidney length. The correlation was significant at the level of 0.01. The correlational values of GA according to LMP with FKLL and FKLR were ($r = .85^{**}$) and ($r = .87^{**}$) respectively. GA with BPD indicates a moderately significant positive correlation with FKLL and FKLR ($r = .94^{**}$) and ($r = .94^{**}$). GA with FL also shows a moderately significant positive correlation with FKLL and FKLR ($r = .83^{**}$) and ($r = .83^{**}$), respectively. **Conclusion:** In conclusion, fetal kidney length in millimeters correlates well with gestational age in weeks and shows linear growth with gestational age throughout pregnancy. Gestational age estimated from fetal kidney length gives improved dating of fetal age.

INTRODUCTION

Accurate estimation of gestational age is essential for assuring fetal well-being and management of pregnancies [1]. Estimating the delivery date, especially for those who present late for maternal care and those uncertain about their LMP, always remained a challenge [2]. If the gestation age is not measured accurately, it can result in fetal premature birth or post-maturity, increasing the chances of fetal morbidity and mortality [3]. In the first trimester, the date of pregnancy is determined by the first day of the previous menstrual cycle, the diameter of the gestational sac, and the crown lump length. The most common parameters used to determine pregnancy dates in the second trimester are the fetal Bi-parietal diameter, femur length, head circumference, and abdominal circumference, with an accuracy of +/-10 to 14 days [4,5].

Many of these parameters can predict gestational age with great precision. However, as gestational age increases, these parameters become more and more unreliable due to physical size variations of organs. They can also be affected in certain medical conditions like oligohydromnios, polyhydromnios, breech presentation, IUGR, etc [6,7]. They show discrepancies from the expected average gestational age [8,9]. Therefore, accurate pregnancy dating remained a challenge in the late 2nd or 3rd trimester. It requires a valuable parameter that can independently predict gestational age accurately [10,11]. Other non-traditional parameters being studied to measure gestational age include trans cerebellar diameter, the transverse diameter of the colon, amniotic fluid volume, hard palate width, and fetal sacral length [12]. The fetal

kidney is one parameter to measure the fetus's gestational age in the second and third trimesters [13,14]. The renal length of the fetus showed a fortnightly growth rate of 1.7mm with gestational age during pregnancy [15]. Fetal kidneys are easy to visualize after the 18th week of gestation. In the early stage before 17th week, kidneys are just homogeneous structures except at the central collecting structure. Lately, one can easily differentiate between renal parenchyma, collecting structures, adrenal glands, cortex, medulla, and renal pelvis [16]. Fetal kidneys are seen in the transverse plane as two circular structures along both sides of the spine. While longitudinally, they appear as two small bean-shaped structures in the paravertebral region. Fetal kidney length correlated with gestational age, and its linear progression with gestational age has been demonstrated on MRI. After 24 week of gestation FKL is more accurate way of measuring gestational age than FL, BPD, AC, and HC [17,18]. High-risk pregnancies like hypertension, diabetes mellitus, IUGR, oligohydramnios, polyhydramnios, and placental abnormalities affects BPD, FL, HC and AC [19]. Length of fetal kidney in millimeters approximates fetal gestational age in weeks [20]. This growth of the fetal kidneys remains unaffected by abnormalities; therefore, it can effectively measure gestational age as an adjunct to other routinely used parameters [21,22].

METHODS

A prospective cross-sectional study was conducted at a private sector hospital's obstetrics and gynecology department in Kharian, Pakistan. The sample size for this study was selected using a convenient sampling technique. One hundred five females with singleton normal pregnancies between 24 to 40 weeks of gestational age who were sure about their LMP were included in the study. Females with pregnancies below the 24th week of gestation, multiple pregnancies, diabetes mellitus, hypertension, oligohydromnios and polyhydromnios were excluded from the study. GE Logic P7 Ultrasound Machine with a 3.5MHz frequency convex transducer was used for scanning the fetus. Fetal kidneys were visualized in a transverse plan below the stomach level. Then the probe was rotated to 90 degrees to image the kidneys' longitudinal axis in the left and right paravertebral region. Kidney length was measured from the lower to upper pole, excluding the adrenal gland. All participants gave written consent. Data was analyzed using SPSS version 22.

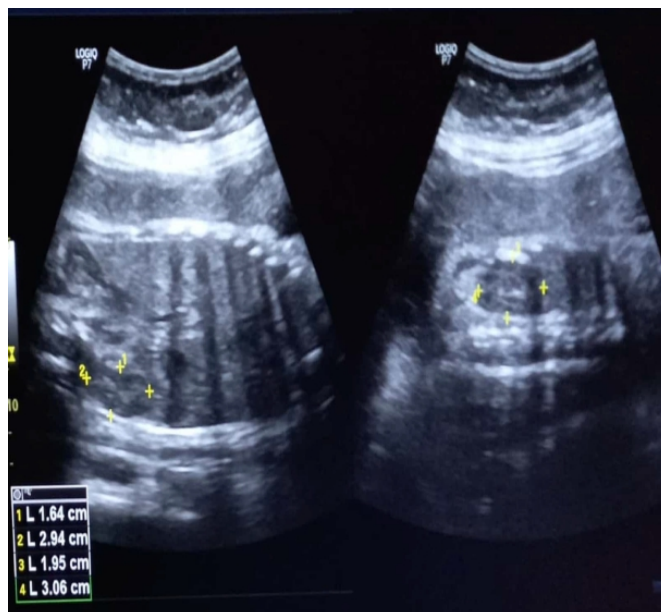


Figure 1: Fetal right and left Kidney measured from one pole to another at 30th weeks of gestation 29.4(right), 30.6(left)

RESULTS

The study included one hundred five females with gestational age between 24 to 40 weeks of normal pregnancy. All of the participant's age range from 22-40 years. Out of 105 subjects, 15 were between 25-29 weeks of gestation, 44 were between 30-34 weeks, and 46 were between 35-39 weeks. There were 22.9% (24) primigravida and 77.1% (81) multigravida subjects. The mean value of gestational age according to LMP, BPD, FL, FKLL, and FKLR was 33.56 weeks, 32.68 weeks, 32.66 weeks, 32.61 weeks, and 32.38 weeks respectively with a standard deviation of 3.14, 3.29, 3.18, 3.42, and 3.42 respectively. A moderately significant positive correlation was identified between different gestational age measuring parameters and fetal kidney length. The correlational values of GA according to LMP and GA with BPD, GA with FL, FKLL and FKLR were ($r = .87^{**}$), ($r = .75^{**}$), ($r = .85^{**}$) and ($r = .87^{**}$) respectively significant at 0.01. GA with BPD indicates a moderately significant positive correlation with FKLL and FKLR ($r = .94^{**}$) and ($r = .94^{**}$) significant at 0.01. GA with FL also shows a moderately significant positive correlation with FKLL and FKLR ($r = .83^{**}$) and ($r = .83^{**}$), respectively significant at 0.01, as shown in Table 1.

Parameters	R	P value
GA with LMP*GA with BPD	.87**	0.01
GA with LMP*GA with FL	.75**	0.01
GA with LMP* FKLL	.85**	0.01
GA with LMP* FKLR	.87**	0.01
GA with BPD* FKLL	.94**	0.01
GA with BPD* FKLR	.94**	0.01

GA with FL* FKLL	.83**	0.01
GA with FL* FKLR	.83**	0.01

BPD= Bi parietal diameter, FL=Femur Length, FKLL=Length of fetal left kidney, FKLR=Length of Fetal right kidney, GA= Gestational age

Table 1: Correlation between GA with LMP, GA with BPD, GA with FL, FKLL and FKLR

The simple linear regression model shows a strong positive linear relationship between gestational age with LMP and BPD, FL, FKLL, and FKLR, as shown in Table 2.

Independent Variables	A	B	P	R ²	Sum of Error
BPD	3.89	0.363	0.00	0.774	0.00
FL	13.7	0.310	0.00	0.633	0.00
FKLL	7.46	0.792	0.00	0.726	0.00
FKLR	7.43	0.796	0.00	0.762	0.00

BPD=Bi parietal diameter, FL=Femur Length, FKLL=Length of fetal left kidney, FKLR=Length of Fetal right kidney, GA=Gestational age

Table 2: Simple Linear regression between Gestational Age with LMP and BPD, FL, FKLL and FKLR

The overall growth of fetal right and left kidney length with their standard deviation according to gestational age is shown in Table 3.

GA weeks		FKLL (mm)	FKLR (mm)
25-29	Mean	28.0133	27.4533
	N	15	15
	Sd	2.05804	1.95553
30-34	Mean	31.9636	31.8023
	N	44	44
	Sd	2.36418	1.91839
35-39	Mean	35.5391	35.5283
	N	46	46
	Sd	1.95885	2.14628
Total	Mean	32.9657	32.8133
	N	105	105
	Sd	3.38125	3.44470

FKLL= Length of Fetal left kidney, FKLR= Length of Fetal right kidney

Table 3: Distribution of cases based on gestational age with right and left kidney length

DISCUSSION

Ultrasound is an easily available modality that can image various organs in utero, allowing adequate estimation of the fetal GA. This study was conducted on 105 pregnant females to determine the relationship between the length of the fetal right and left kidney and gestational age between 24-40 weeks. Fetal kidney length shows a statistically significant positive correlation with weeks of gestation. FKL gives reliable estimate of gestational age. Mean value of fetal left kidney was 32.61 mm and mean length of fetal right kidney was 32.38 mm. The left kidney correlation coefficient was slightly lower than from the right kidney. The best correlation coefficient was found between LMP and BPD derived gestational age. The correlation coefficient values of GA according to LMP with

FKLL and FKLR were ($r= 0.85^{**}$) and ($r= 0.87^{**}$). A previous study conducted by Sanjib Kumar Das et al. 2018 showed a significant positive correlation between the length of fetal kidneys and gestational age according to LMP with a correlation coefficient ($r=0.907$) which is slightly higher than our study [1]. The correlation coefficient values of GA according to BPD with FKLL and FKLR were ($r= 0.94^{**}$) and ($r= 0.94^{**}$). The correlation coefficient values of GA according to FL with FKLL and FKLR were ($r= 0.83^{**}$) and ($r= 0.83^{**}$). A previous study conducted by Jayati Bardhan et al. 2016 showed a significant positive correlation between the length of fetal kidneys and sonographic gestational age with a correlation coefficient ($r=0.99$) which is slightly higher than our study A simple linear regression model shows a positive relationship between gestational age according to LMP and FKLL, FKLR with a determination coefficient of 0.72 and 0.76, respectively. The regression equation used to estimate gestational age with BPD, FL, FKLL, and FKLR was $Y = \alpha + \beta(x)$. The regression model with GA according to BPD as an independent variable showed a regression equation as: GA according to LMP = $3.89 + 0.36$ (BPD). The regression model with GA according to FL as an independent variable showed a regression equation as: GA according to LMP = $13.7 + 0.31$ (FL). The regression model with GA according to FKLL as an independent variable showed a regression equation as: GA according to LMP = $7.46 + 0.79$ (FKLL). The regression model with GA according to FKLR as an independent variable showed a regression equation as: GA according to LMP = $7.43 + 0.79$ (FKLR). A previous study conducted by Mahmoud Mohamed Ghaleb et al. 2021 found a positive linear relationship between gestational age according to LMP and FKLL, FKLR with determination coefficients of 0.67, 0.86 respectively which are in accordance with our study [13]. FKL may be a more helpful method in cases when other traditionally used parameters are difficult to obtain and show considerable differences with GA. Because the GA is still traditionally determined, in some places, by LMP, the chances of error increase, necessitating the use of USG investigation as the only measuring tool for GA determination.

CONCLUSION

This study concludes that length of the fetal right and left kidney in millimeters shows linear progression with gestational age in weeks. It gives reliable estimation of gestation age without using any software. Ultrasonography is readily available and the safest modality to use during pregnancy which can be used to measure length of fetal kidneys accurately. Gestational age estimated from fetal kidney length gives improved dating of fetal age.

REFERENCES

- [1] Das SK, Acharya I, Pariida S, Mohanty J, Singh M, Swain BM. Correlation of gestational age with fetal renal length in third trimester pregnancy. *Journal of Medical Sciences and Health*. 2018;4(1):18-22.
- [2] Yusuf N, Moslem F, Haque JA. Fetal kidney length: can be a new parameter for determination of gestational age in 3rd trimester. *TAJ: Journal of Teachers Association*. 2007;20(2):147-150. <https://doi.org/10.3329/taj.v20i2.3078>
- [3] Ugur MG, Mustafa A, Ozcan HC, Tepe NB, Kurt H, Akcil E, et al. Fetal kidney length as a useful adjunct parameter for better determination of gestational age. *Saudi Medical Journal*. 2016 May;37(5):533-7. doi: 10.15537/smj.2016.5.14225.
- [4] Butt K, Lim K; diagnostic imaging committee. Determination of gestational age by ultrasound. *J Obstet Gynaecol Can*. 2014 Feb; 36(2):171-181. doi: 10.1016/S1701-2163(15)30664-2.
- [5] Abonyi EO, Eze CU, Agwuna KK, Onwuzu WS. Sonographic estimation of gestational age from 20 to 40 weeks by fetal kidney lengths' measurements among pregnant women in Portharcourt, Nigeria. *BMC Med Imaging*. 2019 Aug; 19(1):72. doi: 10.1186/s12880-019-0371-z.
- [6] Akram MS, Yousaf M, Farooqi U, Arif N, Riaz A, Khalid M, et al., Estimation of Gestational Age from Fetal Kidney Length in the Second and Third Trimester of Pregnancy by Ultrasonography. *Saudi Journal of Medical and Pharmaceutical Sciences*. 2019;5:222-229. DOI:10.21276/sjmps.2019.5.3.10
- [7] Toosi FS, Rezaie-Delui H. Evaluation of the normal fetal kidney length and its correlation with gestational age. *Acta Medica Iranica*. 2013:303-306.
- [8] Peter M, Nayak AK, Giri PP, Jain MK. Fetal kidney length as a parameter for determination of gestational age from 20th week to term in healthy women with uncomplicated pregnancy. *International Journal of Research in Medical Sciences*. 2017 May; 5(5):1869-73. DOI: <http://dx.doi.org/10.18203/2320-6012.ijrms20171808>
- [9] Kaul I, Menia V, Anand AK, Gupta R. Role of Fetal Kidney Length in Estimation of Gestational Age. *JK science*. 2012 Apr;14(2).
- [10] Konje JC, Abrams KR, Bell SC, Taylor DJ. Determination of gestational age after the 24th week of gestation from fetal kidney length measurements. *Ultrasound Obstet Gynecol*. 2002 Jun; 19(6):592-7. doi: 10.1046/j.1469-0705.2002.00704.x.
- [11] Kiran L, Aneesh M, Thulaseedharan A, et al. Fetal kidney length in estimation of gestation age by sonography. *International Journal of Contemporary Medicine and Surgical Radiology*. 2019;4:C79-C81.
- [12] Chatterjee S, Yadav K, Prakash P, Shekhawat K. Foetal kidney length as a parameter for determination of gestational age in pregnancy by ultrasonography. *International journal of reproduction, contraception, obstetrics and gynecology*. 2016 Jun; 5(6):1949-53.
- [13] Ghaleb MM, Shokri AI, El Sokyary MS, El Shourbagy MM. Role of ultrasonographic measurement of fetal kidney length in determination of gestational age during third trimester of pregnancy. *Open Journal of Obstetrics and Gynecology*. 2021 Mar;11(03):221. 10.4236/ojog.2021.113022
- [14] Shivalingaiah N, Sowmya K, Ananya R, Kanmani TR, Marimuthu P. Fetal kidney length as a parameter for determination of gestational age in pregnancy. *International Journal of Reproductive and Contraception Obstetrics Gynecology*. 2014 Jun; 3:424-7. DOI: 10.5455/2320-1770.ijrcog20140628
- [15] Edevbie J, Akhigbe A. Ultrasound measurement of fetal kidney length in normal pregnancy and correlation with gestational age. *Nigerian journal of clinical practice*. 2018; 21(8):960-966. DOI: 10.4103/njcp.njcp_373_15
- [16] Gupta S, Gupta V, Mahajan M, et al. Fetal Kidney length as a parameter for determination of Gestational Age from 20 th Weeks to term in healthy women with uncomplicated pregnancy. *JMSCR*. 2019 Nov; 7(11); 6359. DOI:<https://dx.doi.org/10.18535/jmscr/v7i11.110>
- [17] Gayam S, Geethavani M, Paul S. Fetal kidney length for determining gestational age in third trimester. *Obs Rev: Journal of Obstetrics and Gynecology*. 2018 Sep; 4:49-54.
- [18] Al-Mlah S, Nasef A, El-Masry HA. Assessment of fetal kidney length as a parameter for detection of gestational age at the third trimester of pregnancy. *The Egyptian Journal of Hospital Medicine*. 2019 Apr; 75(5):2839-44. doi.org/10.21608/ejhm.2019.33002
- [19] Bardhan J, Ghosh SK, Sarkar KN, Sarkar M. Fetal kidney length as a parameter for gestational age determination and its comparative evaluation with other fetal biometric indices. *IAIM*. 2016 Aug; 3(8):36-44.
- [20] Ahmadi F, Taqi Dizaj AV, Akhbari F, Hohreh Irani S, Holamreza Khalili G. Fetal kidney measurement in 26-39 weeks gestation in normal fetuses of Iranian pregnant women. *Journal of Pregnancy Child Health*. 2015; 2:139. doi: 10.4172/2376-127X.1000139
- [21] Muthaian E, Selvaraj K. Accuracy of the fetal kidney length measurement by ultrasonography in the determination of the gestational age in pregnancy. *National Journal of Clinical Anatomy*. 2019 Jan;

8(01):018-21. doi.org/10.1055/s-0039-1688532

- [22] Hemraj S, Abraham SM, Vinayaka US, Ravichandra G, Acharya D. Sonographic correlation of gestational age with fetal kidney length. *International Journal of Infertility & Fetal Medicine*. 2016 Aug; 7(2):37-41.



Original Article

Development of Normative Data of Functional Reach Test In Young Adults of Lahore; A Cross Sectional Survey

Sheeza Aleen¹, Maliha Shafique¹, Khadija Liaquat Ali^{1*}, Arooba Mehmood², Komal Tehzeeb³¹Riphah College of Rehabilitation and Allied Health Sciences, Riphah International University, Lahore, Pakistan.²Tehsil Headquater Hospital Mian Channu, Pakistan³Greens International University, Lahore, Pakistan

ARTICLE INFO

Key Words:

Adults, Balance, Functional reach test, Posture, Risk of fall.

How to Cite:

Aleen, S. ., Shafique, M. ., Liaquat, K., Mehmood, A. ., & Tehzeeb, K. . (2022). Development Of Normative Data of Functional Reach Test in Young Adults of Lahore; A Cross Sectional Survey: Development of normative data of functional reach test in young Adults. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.446>

*Corresponding Author:

Khadija liaquat Ali
 Riphah College of Rehabilitation and Allied Health Sciences,
 Riphah International University, Lahore, Pakistan.
khadijaliaquat90@gmail.com

Received Date: 3rd June, 2022

Acceptance Date: 18th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Risk of fall is one of the serious health concern of human beings. Many tests have been developed clinically to measure risk of fall in adults. **Objective:** To develop preliminary normative data of functional reach test (forward reach) in young adults. **Methods:** A cross sectional survey was conducted in different geographical areas of Lahore. A sample of 500 healthy young adults was recruited in study through convenience sampling technique. To measure dynamic balance functional reach test (forward) was used. **Results:** A total sample of 500 young adults were included 22% of participants were females and 78% were males. The mean age of participants was 24 ± 4 years. The mean score of functional reach test (forward) was 9.87 ± 2.9 inches, the minimum score was 3.20 inches and maximum score was 15.09 inches. There was no statistically significant difference was observed in scores of FRT in across and within the groups of both gender as p-value was > 0.05 . There was also weak positive significant correlation between BMI and scores of functional reach test and $p < 0.05$. **Conclusion:** The study provided the normative value of functional reach test (forward) for young adults.

INTRODUCTION

Balance is a state of equilibrium and harmony. It is the ability to stay upright without falling or moving in one direction or another. In humans, balance is often achieved through the use of our sense of sight, which provides us information about our position and the position of our surroundings. When a person is standing still, they are in a state of equilibrium [1,2]. The risk of falling in humans is largely determined by the balance system, which is a set of neural, skeletal, balance is a critical part of our ability to function. Without it, we would likely fall and become injured [3]. The risk of falling is greater in older adults, who have a higher chance of developing a balance disorder such as

vertigo and are more likely to require a mobility device such as a cane. However, even young adults can be affected by a loss of balance, and muscular systems that allow humans to stay upright [3,4]. The prevalence of falling in young adults has been linked to several conditions, including aging, injuries, and disease. Aging is associated with a decrease in the strength, size, and function of the nervous system, which can lead to decreased balance and the risk of falling. Injuries, such as broken bones, also affect balance, as they can interfere with the neural, skeletal, and muscular systems that allow humans to stay upright [5]. Balance functional assessments emphasize static balancing,

postural stability, anticipatory response, and functional mobility. Tinetti Performance oriented mobility assessment, beg balance scale, timed walking test timed up and go exam, Multidirectional reach test, and Functional reach test are some of the functional balance standard tests. Duncan and coworkers created the Forward Functional Reach Test to identify people who have balance difficulties. It is simple, quick, reliable, user-friendly, and clinically accessible [6]. It is the distance measured one may extend forward at arm's length while standing on a fixed base of support. They have provided age-related reference values. The functional reach is affected by height and age. It provides baseline and outcome data, as well as being predictive of falls in elderly people. [7] For children, the young, and the elderly in western and other eastern populations, normative functional reach test values are available. [8] A research of 135 healthy people was conducted to establish the standards of Functional Reach Test (FRT) values among people of various backgrounds ranging in age from 20 to 87 years old, as well as to associate the mean of FRT. The average (SD) forward distance for Indian males are 35.70(5.15)cm and 27.82(9.25) cm for Indian females, according to the findings. [9] A research of 350 healthy children is done to establish normal values for lateral reach (LR) and functional reach (FR) in school children, as well as to compare anthropometric parameters to LR and FR values and the relationship between LR and FR scores. The normal mean values of the FR and LR varieties ranged from 22.7 cm to 37 cm and 16.3 cm to 22.5 cm, respectively, according to the results [10]. Body mass index is indicator of fat composition in a human body; core variables of BMI are weight and height. Height considerably associates with both FR and LR. In previous studies normative values of functional reach test had been reported for different populations across different parts of world. A study was conducted on 202 children to establish normative values of forward functional reach for age group of 5- 15 years in Indian children [11]. Normative reference data for the functional reach test is currently unavailable in clinical practice, but it is well-thought-out and based on a western population. However, there are no reference values for functional reach tests. The study's goal was to create normative functional reach test data for young adults.

METHODS

A sample of 500 healthy young adult age between 18-32 years were recruited from general community of Lahore. Convenient sampling technique was used for collection of data. The characteristics of participants were healthy young adults both male and female, able to stand independently, able to flex shoulder at 90degree. Healthy

individuals with following conditions were excluded from study. Written inform consent was taken from all participants. The study was approved by research ethical committee of Riphah International University, Lahore. To analyze data SPSS version 25.0 was used. The data were checked for its normality by Shapiro Wilk test and $p < 0.05$ so parametric test were used for analysis. To measure the score of functional reach test (forward reach) the descriptive statistics were calculated and data were presented in means and standard deviation. To measure the correlation of FRT scores with gender and BMI Pearson correlation coefficient was computed. To measure the scores of the FRT across three groups of the age ANNOVA was computed. Individuals were assessed for functional reach while stood beside the wall (without touching it), shoulder flexed to 90 degrees, elbow fully extended, and hand fist. The first mark was made along the meter rod on the wall at the position of the third metacarpal. The participants were then instructed to lean forward as far as they could without taking a step or losing their balance. The third metacarpal was used as a reference along the yardstick on the wall for the second marking. The forward reach distance used for the functional reach test was the difference between two marks.

RESULTS

Out of 500 participants 22% (108) were males and 78 % (392) were females. The minimum age of participants was 18 years and maximum age was 32 years. The mean and standard deviation of age was 24 ± 4 years. The mean of BMI of males and females was 22.02 ± 3.44 and 24.80 ± 4.39 respectively. The demographics of participants presented in the Table 1.

No of participants	500
Male (n)	108(22%)
Female (n)	392(78%)
BMI kg/m2 males	22.02(3.44)
BMI kg/m2 females	24.80(4.39)
Age in years	24.0(4.0)

Table 1: Demographics of participants

The mean score of the forward functional reach test was 9.87 ± 2.97 inches, the minimum score was 3.20 inches and maximum score was 15.09 inches. The mean score of the functional reach test (forward reach) was calculated across complete spectrum of age participants and it is presented in the Table 2.

Age in years	Mean+SD	Min	Max
18 (n=9)	9.21±2.8	3.5	13.5
19(n=26)	8.8±2.14	5	14
20(n=13)	10.08±2.44	6	14
21(n=35)	9.62±2.73	5	16
22(n=65)	9.93±2.17	5.2	15.1
23(n=54)	11.15±5.81	5	15.09

24(n=8)	7.25±2.31	4	10
25(n=125)	9.8±2.39	3.5	15
26(n=61)	10.07±2.54	4	15
27(n=33)	9.93±2.08	6	14.1
28(n=10)	9.81±1.52	7	12.2
29(n=8)	10.61±1.93	8	13
30(n=22)	9.35±2.26	3.2	12.7
31(n=17)	9.1±2.96	3.5	13
32(n=14)	9.8±1.46	6	11

Table 2: Descriptive statistics of scores of Functional Reach test (forward) across Age (18-32 years)

To see the effect of gender in functional reach test the scores of both groups were calculated and there was no significant difference in scores across the groups. The mean score of the functional reach test in males was 9.968 ± 2.29 , and in females was 9.92 ± 3.13 and the p value was > 0.05 which shows that gender did not affect the score of the functional reach test. The scores are shown in figure. 1. A and 1. B..

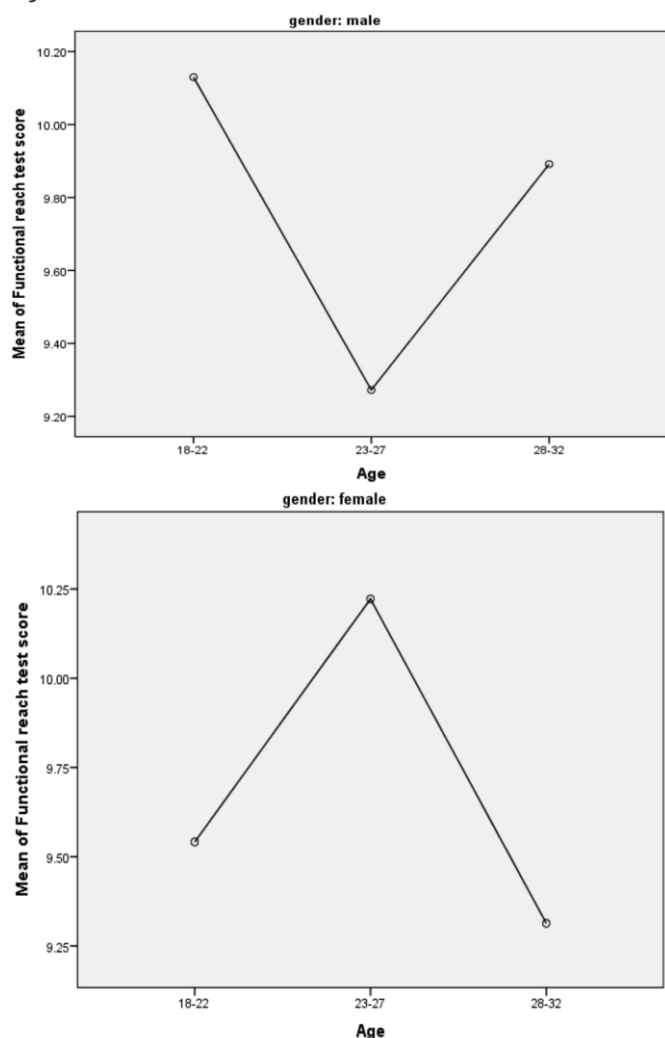


Figure 1: A). Scores of the Functional reach test (forward) in males. B). Scores of the Functional reach test (forward) in females.

The study was aimed to investigate the scores of FRT among three different age groups and impact of FRT scores on increasing age. The Anova test was used to find the difference of scores of FRT in three different age groups of both genders. The participants were divided into three age groups 18-22 years, 23-27 years and 28-32 years across both genders. The scores of functional reach test in males was 10.12 ± 2.40 , 9.27 ± 2.48 , 9.89 ± 1.84 respectively. The scores of functional reach test in females was 9.54 ± 2.37 , 10.22 ± 3.51 and 9.92 ± 3.13 respectively. There was no statistically significant difference was observed in scores of FRT in across and within the groups of both gender as p value was > 0.05 . Therefore, it reject the hypothesis that FRT scores declines with increasing age. The p values are shown in Table 3.

FRT	p-value
Males	>0.05
Males Between Groups	>0.05
Males Within Groups	>0.05
Females	>0.05
Females Between Groups	>0.05
Females Within Groups	>0.05

Table 3: p-value of the scores of Functional Reach Test (forward) and Age groups (18-22 years, 23-27 years and 28-32 years)

The Pearson correlation was calculated between gender and total score of functional reach test (forward), there was weak positive significant correlation between scores of both genders and p value was $p < 0.05$. There was also weak positive significant correlation between BMI and scores of functional reach test and $p < 0.05$. The correlations are shown in Table 4.

Functional reach test	Co - relation of FRT and gender and BMI
Gender male	$r = -0.029$, $p < 0.05$
Gender Females	$r = -0.005$, $p < 0.05$
BMI	$r = -0.002$, $p < 0.05$

Table 4: Correlation of functional reach test with gender and body mass index

DISCUSSION

The human postural control system is a system that enables a body to control its position and orientation in space, by moving its center of mass so that it is not displaced by the surrounding environment, while using other parts of the body as a support [1]. There was no decrease in FRT (forward) score with increasing age. This trend was attributed to the fact balance system did not decline between age 18- 40 years [7]. Human postural control system is the anterior-posterior balance control system of the body. It works to prevent falls by regulating how the body positions itself to preserve postural stability in spite of challenges imposed by the environment. The system also allows the body to act quickly on any

imbalance, allowing it to regain a stable posture quickly. Postural control is fully mature in adults and, it is maintained by feedback, anticipatory and feed forward mechanism [7]. To observe the difference of FRT scores across three age groups of adults we calculated ANOVA. There was no statistically significant difference was found in scores of FRT (forward) in three different age groups. The results were owned to the fact that postural control did not decline in adults [7]. We computed correlation between scores of FRT, and BMI. The results of negative correlations between FRT and BMI $r = -0.002$ [11,12]. The balance achieved by humans during walking, running, locomotion, and other movement is a dynamic balance between the forces of gravity acting on a body and the kinetic energy of the body's motion [12]. The body's efficiency in achieving this balance is the result of complex interactions between the body's structure and the forces its structure presents to the forces of gravity. The human body achieves dynamic balance through the integration of muscles and other systems [13]. The study aimed to develop normative value of functional reach test (forward) in young adults. The study showed the descriptive statistics of FRT (forward) scores between age 18-32 years. The results of test presented in means and standard deviation and minimum and maximum. The mean score of the FRT (forward) test had been varied across different ethnicity and geographical distribution, the difference in scores of FRT (forward) reach had occurred because of huge variation in age [14-17]. The mean score FRT (forward) test in present study was consistent with the study [6,18-20]. Anthropometric measurements changes in different regions and these measurements significantly impact FRT score. BMI is strongly correlated with health, but it does not take into account other factors that may influence health, such as fitness and postural control. The core elements of anthropometric measurements are height, weight and body mass index [6,19,20]. The study investigates the difference between postural control across gender. In present study there was no significant effect of gender on the mean score of FRT and the findings were similar as reported previously [18,21,22].

CONCLUSION

The study developed normative data of forward functional reach test in healthy adults of Lahore the study found negative correlation between FRT (forward reach) and age of participants. In addition, the study reported weak positive correlation between FRT (forward reach) and gender of participants.

REFERENCES

[1] Omaña H, Bezaire K, Brady K, Davies J, Louwagie N, Power S, et al. Functional reach test, single-leg stanc

test, and Tinetti performance-oriented mobility assessment for the prediction of falls in older adults: a systematic review. *Physical Therapy*. 2021 Oct; 101(10):pzab173. doi.org/10.1093/ptj/pzab173

- [2] Faris AJ. Is the Fullerton Advanced Balance scale responsive to change in balance performance? California State University, Fullerton; 2009. *-74
- [3] Umphred DA, Lazaro RT. *Neurological rehabilitation*. Elsevier Health Sciences; 2012 Aug 14.
- [4] Moriyama Y, Yamada T, Shimamura R, Ohmi T, Hirokawa M, Yamauchi T, et al. Movement patterns of the functional reach test do not reflect physical function in healthy young and older participants. *PLoS one*. 2022 Mar 31; 17(3):e0266195. doi.org/10.1371/journal.pone.0266195
- [5] Singh P, Hujon N. Normative data of Modified Functional Reach Test in younger and middle-aged North Eastern Indian population. *Archives of Medicine and Health Sciences*. 2013 Jul; 1(2):109. doi.org/10.4103/2321-4848.123018
- [6] Duncan PW, Weiner DK, Chandler J, Studenski S. Functional reach: a new clinical measure of balance. *Journal of Gerontology*. 1990 Nov; 45(6):M192-7. doi: 10.1093/geronj/45.6.m192.
- [7] O'Sullivan SB, Schmitz T, Fulk G. Examination of motor function: Motor control and motor learning. *Physical rehabilitation*. 2007:161-206.
- [8] Bohannon RW, Wolfson LI, White WB. Functional reach of older adults: normative reference values based on new and published data. *Physiotherapy*. 2017 Dec; 103(4):387-391. doi: 10.1016/j.physio.2017.03.006.
- [9] Mohammed R, Basha AS, Jungade S. Influence of age, gender, and body mass index on balance and mobility performance Indian community-dwelling older people. *Physical & Occupational Therapy in Geriatrics*. 2021 Apr; 39(2): 144-56. doi.org/ 10.1080/02703181.2020.1818909
- [10] Melam G, Buragadda S, Alhusaini A, Ibrahim AI, Kachanathu SJ. Gender differences in static and dynamic postural stability parameters in community dwelling healthy older adults. *Middle East Journal of Science and Research*. 2014; (22):1259-64. DOI: 10.5829/idosi.mejsr.2014.22.09.85208
- [11] Deshmukh AA, Ganesan S, Tedla JS. Normal values of functional reach and lateral reach tests in Indian school children. *Pediatric Physical Therapy*. 2011 Spring; 23(1):23-30. doi: 10.1097/PEP.0b013e3182099192.
- [12] Pires IM, Garcia NM, Zdravevski E. Measurement of Results of Functional Reach Test with Sensors: A Systematic Review. *Electronics*. 2020 Jun

- 30;9(7):1078. [/doi.org/10.3390/electronics9071078](https://doi.org/10.3390/electronics9071078)
- [13] Soke F, Eldemir S, Ozkan T, Ozkul C, Ozcan Gulsen E, Gulsen C, Eldemir K, Irkec C, Gonenli Kocer B, Batur Caglayan HZ, Guclu-Gunduz A. The functional reach test in people with multiple sclerosis: a reliability and validity study. *Physiotherapy Theory and Practice*. 2021 Jun 13;1-5. doi.org/10.1080/09593985.2021.1938308.
- [14] Dani VB, Shah R, Sheth R. Functional reach test: Establishing the reference value in healthy adults of Gujarat, India. *Acta Medica International*. 2019 Jul; 6(2):89. DOI: 10.4103/ami.ami_81_18
- [15] Schenkman M, Morey M, Kuchibhatla M. Spinal flexibility and balance control among community-dwelling adults with and without Parkinson's disease. *J Gerontol a Biol Sci Med Sci*. 2000 Aug; 55(8):M441-5. [doi: 10.1093/gerona/55.8.m441](https://doi.org/10.1093/gerona/55.8.m441).
- [16] Jonsson E, Henriksson M, Hirschfeld H. Does the functional reach test reflect stability limits in elderly people? *J Rehabil Med*. 2003 Jan;35(1):26-30. [doi: 10.1080/16501970306099](https://doi.org/10.1080/16501970306099).
- [17] Newton RA. Validity of the multi-directional reach test: a practical measure for limits of stability in older adults. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*. 2001 Apr;56(4):M248-52. [doi: 10.1093/gerona/56.4.m248](https://doi.org/10.1093/gerona/56.4.m248).
- [18] Ferreira S, Raimundo A, Marmeleira J. Test-retest reliability of the functional reach test and the hand grip strength test in older adults using nursing home services. *Irish Journal of Medical Science (1971-)*. 2021 Nov; 190(4):1625-32.
- [19] Laddhiperla S, Telang V. Relationship of Age, Gender & Anthropometric Factors on Forward and Lateral Functional Reach in Standing in Normal Indian Adults. Website: www.ijpot.com. 2015 Oct; 9(4):92. doi.org/10.5958/0973-5674.2015.00152.5
- [20] Pandian JS, Minaz SUK, Johney A. Normative data for Functional Reach Test in Indian Children. Effectiveness of Multiple Plane Relaxed Passive Movements given along with Conventional Treatment in Cervical. 2011 Apr;5(2):72.
- [21] Moriyama Y, Yamada T, Shimamura R, Ohmi T, Hirosawa M, Yamauchi T, et al. Movement patterns of the functional reach test do not reflect physical function in healthy young and older participants. *PLoS One*. 2022 Mar; 17(3): e0266195. [doi: 10.1371/journal.pone.0266195](https://doi.org/10.1371/journal.pone.0266195).
- [22] Takahashi T, Ishida K, Yamamoto H, Takata J, Nishinaga M, Doi Y, et al. Modification of the functional reach test: analysis of lateral and anterior functional reach in community-dwelling older people. *Arch Gerontol Geriatr*. 2006 Mar-Apr; 42(2):167-73. [doi: 10.1016/j.archger.2005.06.010](https://doi.org/10.1016/j.archger.2005.06.010).



Original Article

Exercise Echocardiography and Dobutamine Stress Echocardiography in The Assessment of Suspected or Known Coronary Artery Disease

Muhammad Rahman Khalid¹, Irfan Ali², Irfan Ali Arbab³, Iftikhar Ahmed⁴, Bilal Akhtar⁵, Masroor H. Sharfi⁶

¹Department of Cardiology, Liaquat University of Medical and Health Sciences Jamshoro

²NICVD, Karachi, Pakistan

³Interventional Cardiology Unit Liaquat University Hospital, Hyderabad, Pakistan

⁴NICVD, Hyderabad, Pakistan

⁵NICVD, Lyari Karachi, Pakistan

⁶Pediatric Cardiology Department, King Faisal Specialist Hospital and RC, Jeddah, Saudi Arabia

ARTICLE INFO

Key Words:

Dobutamine stress echocardiography, Exercise echocardiography, coronary artery disease

How to Cite:

Rahman Khalid, M. ., Ali, I. ., Ali Arbab, I. ., Ahmed, I. ., Akhtar, B. ., & Sharfi, M. H. . (2022). Exercise Echocardiography and Dobutamine Stress Echocardiography in The Assessment of Suspected or Known Coronary Artery Disease: Exercise Echocardiography and Dobutamine Stress Echocardiography. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.517>

***Corresponding Author:**

Muhammad Rahman Khalid
 Department of Cardiology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
rahmankhalid@gmail.com

Received Date: 2nd June, 2022

Acceptance Date: 20th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Exercise echocardiography has become a significant tool of non-invasive valuation of coronary artery disease (CAD). The Exercise echocardiography and dobutamine stress echocardiography are widely applied methods with different clinical procedures and indications. **Objective:** The study was aimed for the Assessment of Suspected or Known Coronary Artery Disease in Assessment of Suspected or Known Coronary Artery Disease. **Methods:** Total 260 consecutive patients endured Stress Echocardiography in the Cardiology department of NICVD Karachi for one-year duration from January 2021 to December 2021. The treadmill was used for Exercise echocardiography applying the Bruce protocol. The standard method was applied for dobutamine stress echocardiography. The Stress Echocardiography was taken as positive on the basis of the appearance of worsening or new wall motion abnormalities. **Results:** Exercise echocardiography performed by 160 patients and DSE in 100 subjects with mean age of 47.21 and 53.10 years, correspondingly. Males were dominated in both groups. The both groups have similar risk factors. In the diagnosis of CAD, Exercise echocardiography was used more often than dobutamine stress echocardiography (61.5% vs 38.5%). The Viability tests have been carried out exclusively by DSE. The frequency of adverse events was 29% in dobutamine stress echocardiography and no one has side-effects in exercise echocardiography. Stress-related dysfunction of left ventricle was much communal in dobutamine stress echocardiography. **Conclusions:** Exercise Echocardiography is a better and safer non-invasive imaging method among subjects who can execute exercise, but DSE is further beneficial for pre-operative evaluation, viability and patients who are disabled physically for ergometer and treadmill exercise test.

INTRODUCTION

Exercise echocardiography (SE) is an extremely useful, modern, non-invasive tool of diagnosis for the valuation of suspected or diagnosed coronary artery disease (CAD patients)1-2. The most common types of SE used in clinical practice are treadmill echocardiography, exercise echocardiography, and dobutamine stress echocardiography (DSE)3-4. The indications and techniques differ in both tests. Published data on SE are scarce in our country, and no comparative study of these two sister modalities has ever been reported in Pakistan5-

6. In this descriptive study, we will look at the indications, applicability, results and clinical applications of these two tests.

METHODS

260 consecutive patients endured Stress Echocardiography in the Cardiology department of NICVD Karachi for one-year duration from January 2021 to December 2021. Inclusion criteria were all patients referred for evaluation of known or suspected ischemic heart

disease. Dobutamine stress echocardiography was accomplished in subjects with physical disabilities or unable to exercise. All other patients were included in the echocardiographic examination on the treadmill. The exclusion criterion was patients having contraindication to dobutamine and exercise echocardiography. Patients advised to do an overnight fast or at least 2½ hours fasting prior to stress echocardiography. In stable patients, medication was withdrawn 48 hours prior to the study, while unstable patients were assessed with continuing treatment. Clinical data on risk factors, pre-existing ischemic heart disease, revascularization, and cardiac medications were recorded on pre-designed forms. A history and a brief physical examination were performed to rule out any known contraindications for exercise / dobutamine SE.

Equipment: The tests were conducted using echocardiography machine and the integrated operating system for stress testing and a multi-frequency probe (2.5, 3.7 and 5 MHz). Studies recorded simultaneously on magnetic optical disk (MOD's), video tapes and a hard disk. In order to facilitate imaging from the apex of the heart, an echocardiographic bed with cut-out window was used. The 12-lead ECG is recorded at rest, at the end of each phase, and during recovery. A downward or flat depression of the ST segment 1mm from the J point is considered positive for stress induced ischemia. The rhythm was continuously monitored for any arrhythmias. Dobutamine infusion given with an automatic infusion pump. Blood pressure and heart rate are recorded at each stage. During the examination, a fully equipped resuscitation trolley was located at the patient's bedside. The ETT was performed on a standard treadmill. The authors himself performed all echocardiographic examinations and their interpretation. A trained charge nurse took the pulse and blood pressure. An ECG technician recorded a 12-lead ECG and operated the monitoring system. Clinical data collected by a trained computer assistant.

Exercise Treadmill Echo: The Resting images taken from the standard digitized technique and stored. The chest electrodes have been used in a modified way to facilitate the visualization of the apex and the parasternal space, i.e., one intercostal space above for V2, V3 and one space below for V4, V5, V6. The Bruce protocol was adopted in most patients and a minority of patients exercised according to the modified Bruce protocol. The exercise was carried out in accordance with the proposed criteria. The patient was placed on the imaging bed in the left lateral decubitus position immediately later to the finish of exercise (without a cooling-down period). Post-stress imaging is performed in 60-90 seconds. The stress and rest images are demonstrated side by side on quad screen format in cine

loop. Work saved on the MODS and hard drive for future use.

Dobutamine Stress Echo: Resting images of echocardiography taken from the apical and parasternal windows. 4 typical images were obtained, 1 = parasternal short axis, 2 = parasternal long axis, 3 = apical 4-chambers, 4 = apical 2-chambers were obtained. In addition, images of the apical short and long axis were frequently recorded. Images captured at the end of each stage (resting, low, average and peak dose). All images were digitized online and demonstrated side by side for comparing still images in a continuous film loop. Four independent quad screens were used, 1 quad screen for all 2-chamber apical view, 1 for all 4-chambers apical views, etc. The upper left quadrant of each quad screen showed baseline images, lower left quadrant for mid dose, lower right quadrant for peak dose images and the upper right quadrant for low dose.

Echocardiographic interpretation: The 16-segment model suggested by the American Society of Echocardiography was used for analysis, and each segment was assessed on the basis of its systolic thickening and motion. 1 will be normal 2 will be hypokinetic 3 will be akinetic 4 will be bedyskinetic 5 have aneurysm. The Wall Motion Score index was determined by dividing the sum of the scores by the total numeral of segments displayed. WMSI comes from both rest and stress. A positive test result was determined when there is new abnormal motion in wall or when an existing abnormality worsened (from hypokinesia to akinesia). The lack of a hyperdynamic response to an appropriate stress level was also considered hypokinesia. In the case of viability, the biphasic response (improved at low dose and worsened at high dose) was found to be the most powerful indicator. However, sustained improvement in regional function up to the maximum dose for viable myocardium or cardiomyopathy has also been considered. Overall LV function was assessed by end systolic volume (ESV) and EF. Usually, during stress, EF increases and ESV decreases; otherwise, the test is considered positive for exercise-induced LV dysfunction.

RESULTS

Exercise echocardiography performed by 160 patients and DSE in 100 patients with mean age of 47.21 and 53.10 years, correspondingly. Males were dominated in both groups. The both groups have similar risk factors with the exception of hypertension and smoking, which are more common in men (Table 1).

	Ex.E	DSE
Males	102	70
Mean age	47.21	53
Hypertension	51.9%	36%
Diabetes Mellitus	28.8%	25%
Hypercholesteremia	21.2%	23%
Smoking	35.4%	20%

Evaluation of known CAD	40.4%	37%
Diagnostic of chest pain, LV dysfunction or dyspnea	57.7%	23%
Follow up after CABG	5.8%	4%
Assessment of viable myocardium	3.8%	24%
Preoperative assessment for non-cardiac surgery	1.25%	4%
Follow up after atherectomy/ angioplasty	3.2%	2%
Rehab study after MI	0.6%	0
No of patients	160	100

Table 1: patient characteristics

In the diagnosis of CAD, Exercise echocardiography was used more often than dobutamine stress echocardiography (61.5% vs 38.5%). The frequency of adverse events was 29% in dobutamine stress echocardiography and no one has side-effects in exercise echocardiography. Stress-related dysfunction of left ventricle was much communal in dobutamine stress echocardiography. (Table 2)

Side-effects	Percentage
Palpitations	16
headaches	5
Lightedness	39
Tremors or chills	8
others	6
Complications	
Sustained V- tachycardia	3

Table 2: Side-effects in DSE

Most of the patients in both groups had satisfactory image quality, with the exception of 10% who had poor images after exercise in exercise echocardiography. The mean maximum heart rate was higher in exercise echocardiography than in DSE (148 Vs 102 mmHg). The maximum mean systolic blood pressure was almost the same (145 Vs 140 mmHg).

Vessel	Lesions detected by SE	Lesions detected by Coronary angiography
RCA	13	13
LAD	12	11
Lcx	10	12
Total	35	36

Table 3: Correlation with Coronary Angiography

The increase in end systolic volume (ESV) after stress and the decrease in EF occurred more frequently in DSE than in exercise echocardiography. Coronary angiograms of 16 patients were available for comparison. There was a 100% correlation with SE. LAD lesions were detected equally in both modes where RCA and LCx disease were diagnosed much higher in DSE than exercise echocardiography. (Table 4)

No of lesions detected by	LAD	RCA	Lcx
Ex.E	12	13	3
DSE	10	8	10
P-value	0.11	0.02	0.008

Table 4: Comparison of detection of lesions by Ex. E and DSE

DISCUSSION

Out of the studied cohort of 260 patients, Exercise echocardiography performed by 160 patients and dobutamine stress echocardiography in 100 patients. Patients undergoing DSE were elder and much frequently had a past of bypass surgery and myocardial infarction, more cardiac risk factors (hypertension, hyperlipidaemia, diabetes, family history of early coronary disease, smoking, higher peak WMSI, abnormal ECGs more frequent at rest, poorer LV systolic function, and therefore coronary angiography is not advised in these subjects⁵⁻⁶. With limited resources, a test with high predictive value is very useful in reducing costly invasive procedures such as coronary angiography. The diagnostic accuracy and predictive value of DSE is sophisticated than that of simple exercise ECG. Exercise echocardiography is superior to DSE because it is more physiological, has a better homodynamic profile, restores symptoms, and has fewer side effects⁷⁻⁸. In the current study, 29% of patients experienced some type of side effect with DSE, while none with Ex.E⁹⁻¹⁰. However, the exercise echo is technically more difficult due to hyperventilation, excessive movement of the chest wall, and tachycardia¹¹⁻¹². DSE is less demanding because the patient is comfortable in a good position for ultrasound imaging without hyperventilation or significant tachycardia, and has ample time for imaging. In contrast, a positive exercise echocardiogram and the extent of regional wall motion disorders are directly related to an increased risk of an event¹³⁻¹⁴. There was a 100% correlation between the exercise echo and coronary angiograms, and the distribution of the coronary vessels was almost identical to that found in the exercise echo in the ADA and RCA regions; however, left side circumference disease is relatively underdiagnosed and is consistent with many studies. However, DSE was superior to Ex.E in the diagnosis of left hand circumflex disease (p-value 0.009)¹⁵⁻¹⁶. In our series, which was reported as 20% in some studies, no patient developed hypotension from dobutamine stress. This may be due to the relatively low dose of dobutamine administered in our series and the very limited use of atropine (only in 7 patients)¹⁷⁻¹⁸. Only 3% of patients developed ventricular arrhythmias in DSE and these are not uncommon, 9% of patients developed premature atrial or ventricular ectopy, and 5% had serial SVT or VT. Data on several studies have revealed MI or ventricular fibrillation in 1 in 2,000 patients¹⁹⁻²⁰. These arrhythmias are usually seen in patients with impaired wall motion at rest or with a history of arrhythmias²¹⁻²². One of our patients developed ventricular fibrillation and was able to successfully perform

CPR. He suffered a myocardial infarction in the anterior wall.

CONCLUSION

Out of the studied cohort of 260 patients, Exercise echocardiography performed by 160 patients and dobutamine stress echocardiography in 100 patients. Patients undergoing DSE were elder and much frequently had a past of bypass surgery and myocardial infarction, more cardiac risk factors (hypertension, hyperlipidaemia, diabetes, family history of early coronary disease, smoking, higher peak WMSI, abnormal ECGs more frequent at rest, poorer LV systolic function, and therefore coronary angiography is not advised in these subjects⁵⁻⁶. With limited resources, a test with high predictive value is very useful in reducing costly invasive procedures such as coronary angiography. The diagnostic accuracy and predictive value of DSE is sophisticated than that of simple exercise ECG. Exercise echocardiography is superior to DSE because it is more physiological, has a better hemodynamic profile, restores symptoms, and has fewer side effects⁷⁻⁸. In the current study, 29% of patients experienced some type of side effect with DSE, while none with Ex.E⁹⁻¹⁰. However, the exercise echo is technically more difficult due to hyperventilation, excessive movement of the chest wall, and tachycardia¹¹⁻¹². DSE is less demanding because the patient is comfortable in a good position for ultrasound imaging without hyperventilation or significant tachycardia, and has ample time for imaging. In contrast, a positive exercise echocardiogram and the extent of regional wall motion disorders are directly related to an increased risk of an event¹³⁻¹⁴. There was a 100% correlation between the exercise echo and coronary angiograms, and the distribution of the coronary vessels was almost identical to that found in the exercise echo in the ADA and RCA regions; however, left side circumference disease is relatively underdiagnosed and is consistent with many studies. However, DSE was superior to Ex.E in the diagnosis of left hand circumflex disease (p -value 0.009)¹⁵⁻¹⁶. In our series, which was reported as 20% in some studies, no patient developed hypotension from dobutamine stress. This may be due to the relatively low dose of dobutamine administered in our series and the very limited use of atropine (only in 7 patients)¹⁷⁻¹⁸. Only 3% of patients developed ventricular arrhythmias in DSE and these are not uncommon, 9% of patients developed premature atrial or ventricular ectopy, and 5% had serial SVT or VT. Data on several studies have revealed MI or ventricular fibrillation in 1 in 2,000 patients¹⁹⁻²⁰. These arrhythmias are usually seen in patients with impaired wall motion at rest or with a history of arrhythmias²¹⁻²². One of our patients developed

ventricular fibrillation and was able to successfully perform CPR. He suffered a myocardial infarction in the anterior wall.history of arrhythmias²¹⁻²². One of our patients developed ventricular fibrillation and was able to successfully perform CPR. He suffered a myocardial infarction in the anterior wall.

REFERENCES

- [1] Al-Lamee RK, Shun-Shin MJ, Howard JP, Nowbar AN, Rajkumar C, Thompson D, Sen S, Nijjer S, Petraco R, Davies J, Keeble T. Dobutamine Stress Echocardiography Ischemia as a Predictor of the Placebo-Controlled Efficacy of Percutaneous Coronary Intervention in Stable Coronary Artery Disease: The Stress Echocardiography-Stratified Analysis of ORBITA. *Circulation*. 2019 Dec 10;140(24):1971-80.
- [2] Zacharias K, Ahmed A, Shah BN, Gurunathan S, Young G, Acosta D, Senior R. Relative clinical and economic impact of exercise echocardiography vs. exercise electrocardiography, as first line investigation in patients without known coronary artery disease and new stable angina: a randomized prospective study. *European Heart Journal-Cardiovascular Imaging*. 2017 Feb 1;18(2):195-202.
- [3] Sicari R, Cortigiani L. The clinical use of stress echocardiography in ischemic heart disease. *Cardiovascular Ultrasound*. 2017 Dec;15(1):1-6.
- [4] Mordi IR, Badar AA, Irving RJ, Weir-McCall JR, Houston JG, Lang CC. Efficacy of noninvasive cardiac imaging tests in diagnosis and management of stable coronary artery disease. *Vascular health and risk management*. 2017;13:427.
- [5] Lancellotti P, Dulgheru R, Go YY, Sugimoto T, Marchetta S, Oury C, Garbi M. Stress echocardiography in patients with native valvular heart disease. *Heart*. 2018 May 1;104(10):807-13.
- [6] Moss AJ, Williams MC, Newby DE, Nicol ED. The updated NICE guidelines: cardiac CT as the first-line test for coronary artery disease. *Current cardiovascular imaging reports*. 2017 May;10(5):1-7.
- [7] Ciampi Q, Zagatina A, Cortigiani L, Gaibazzi N, Borguezan Daros C, Zhuravskaya N, Wierzbowska-Drabik K, Kasprzak JD, de Castro e Silva Pretto JL, D'Andrea A, Djordjevic-Dikic A. Functional, anatomical, and prognostic correlates of coronary flow velocity reserve during stress echocardiography. *Journal of the American College of Cardiology*. 2019 Nov 5;74(18):2278-91.
- [8] Pellikka PA, Arruda-Olson A, Chaudhry FA, Chen MH, Marshall JE, Porter TR, Sawada SG. Guidelines for performance, interpretation, and application of

- stress echocardiography in ischemic heart disease: from the American Society of Echocardiography. *Journal of the American Society of Echocardiography*. 2020 Jan 1;33(1):1-41.
- [9] Gurunathan S, Senior R. Stress echocardiography in stable coronary artery disease. *Current Cardiology Reports*. 2017 Dec;19(12):1-9.
- [10] Mattoso AA, Tsutsui JM, Kowatsch I, Cruz VY, Sbrano JC, Ribeiro HB, Kalil Filho R, Porter TR, Mathias Jr W. Prognostic value of dobutamine stress myocardial perfusion echocardiography in patients with known or suspected coronary artery disease and normal left ventricular function. *PLoS one*. 2017 Feb 24;12(2):e0172280.
- [11] Cortigiani L, Huqi A, Ciampi Q, Bombardini T, Bovenzi F, Picano E. Integration of wall motion, coronary flow velocity, and left ventricular contractile reserve in a single test: prognostic value of vasodilator stress echocardiography in patients with diabetes. *Journal of the American Society of Echocardiography*. 2018 Jun 1;31(6):692-701.
- [12] Picano E, Ciampi Q, Citro R, D'Andrea A, Scali MC, Cortigiani L, Olivetto I, Mori F, Galderisi M, Costantino MF, Pratali L. Stress echo 2020: the international stress echo study in ischemic and non-ischemic heart disease. *Cardiovascular ultrasound*. 2017 Dec;15(1):1-21.
- [13] Mangla A, Oliveros E, Williams Sr KA, Kalra DK. Cardiac imaging in the diagnosis of coronary artery disease. *Current problems in cardiology*. 2017 Oct 1;42(10):316-66.
- [14] Płońska-Gościński E, Kukulski T, Hryniewiecki T, Kasprzak JD, Kosmala W, Olszowska M, Mizia-Stec K, Pysz P, Zaborska B, Stokłosa P, Gąsior Z. Clinical application of stress echocardiography in valvular heart disease: an expert consensus of the Working Group on Valvular Heart Disease of the Polish Cardiac Society. *Kardiologia Polska (Polish Heart Journal)*. 2020;78(6):632-41.
- [15] McLeod G, Shum K, Gupta T, Chakravorty S, Kachur S, Bienvenu L, White M, Shah SB. Echocardiography in congenital heart disease. *Progress in Cardiovascular Diseases*. 2018 Nov 1;61(5-6):468-75.
- [16] Siontis GC, Mavridis D, Greenwood JP, Coles B, Nikolakopoulou A, Jüni P, Salanti G, Windecker S. Outcomes of non-invasive diagnostic modalities for the detection of coronary artery disease: network meta-analysis of diagnostic randomised controlled trials. *bmj*. 2018 Feb 21;360.
- [17] Ahres A, Jablonkai B, Oze A, Ruboczky G, Nagybaczoni B, Szigeti ZS, Kenessey A, Balogh ZS, Szilveszter B, Kolossvary M, Maurovich-Horvat P. P5619 Correlation between dobutamine stress echocardiography and invasive fractional flow reserve in patients with known moderate coronary artery stenosis. *European Heart Journal*. 2018 Aug 1;39(suppl_1):ehy566-P5619.
- [18] Gentry III JL, Phelan D, Desai MY, Griffin BP. The role of stress echocardiography in valvular heart disease: a current appraisal. *Cardiology*. 2017;137(3):137-50.
- [19] Samiei N, Parsaee M, Pourafkari L, Tajlil A, Pasbani Y, Rafati A, Nader ND. The value of negative stress echocardiography in predicting cardiovascular events among adults with no known coronary disease. *Journal of Cardiovascular and Thoracic Research*. 2019;11(2):85.
- [20] Zareba KM, Raman SV. Exercise and Dobutamine Stress CMR. In *Cardiovascular Magnetic Resonance Imaging 2019* (pp. 175-184). Springer, New York, NY.
- [21] Doherty JU, Kort S, Mehran R, Schoenhagen P, Soman P. ACC/AATS/AHA/ASE/ASNC/HRS/SCAI/SCCT/SCMR/STS 2017 appropriate use criteria for multimodality imaging in valvular heart disease: a report of the American college of cardiology appropriate use criteria task force, American association for thoracic surgery, American heart association, American society of echocardiography, American society of nuclear cardiology, heart rhythm society, society for cardiovascular angiography and interventions, society of cardiovascular computed tomography, society for *Journal of the American College of Cardiology*. 2017 Sep 26;70(13):1647-72.
- [22] Ntoskas T, Ahmad F, Woodmansey P. Safety and efficacy of physiologist-led dobutamine stress echocardiography: experience from a tertiary cardiac centre. *Echo research and practice*. 2018 Sep 1;5(3):105-12.



Original Article

Factors Associated with Vesicovaginal Fistula Their Treatment and Outcome

Saira Dars¹, Saifullah Brohi², Aisha Masroor Bhatti³, Rabail Bashir Keerio⁴, Farah Liaquat⁵, Kouser Karim⁶¹Dept. of Gynecology & Obstetrics, Liaquat University of Medical & Health Sciences, Jamshoro²Bilawal Medical College, Liaquat University of Medical & Health Sciences, Jamshoro³General Surgery, Liaquat University of Medical & Health Sciences, Jamshoro⁴Department of Surgery Baqai Medical University⁵Dept. of Gynecology & Obstetrics Baqai Medical University, Karachi⁶Gynecologist and Maternal Fetal Medicine Specialist

ARTICLE INFO

Key Words:

Factors Associated with Vesicovaginal Fistula Their Treatment and Outcome

How to Cite:

Dars, S., Brohi, S., Masroor Bhatti, A., Bashir Keerio, R., Liaquat, F., & Karim, K. (2022). Factors Associated with Vesicovaginal Fistula and Their Treatment Outcome : Factors Associated with Vesicovaginal Fistula Their Treatment and Outcome. *Pakistan BioMedical Journal*, 5(6), 70-74. <https://doi.org/10.54393/pbmj.v5i6.516>

*Corresponding Author:

Bushra Mubarak
 University Institute of Medical Laboratory Sciences,
 The University of Lahore, Pakistan
 Bushra.mubarik@yahoo.com

Received Date: 2nd June, 2022

Acceptance Date: 20th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Introduction: Vesicovaginal fistulas (VVF) also known as vesicovaginal fistula, have become a growing public health concern especially of developing countries. The most cited reason in literature of VVF is by prolonged and obstructed labor. With improvement in quality care delivery in health around the globe, the etiology of VVF too evolving in the country. **Objective:** This study was done to find out the factors associated with vesicovaginal fistula and to determine the success rate of operative procedure for treatment of vesicovaginal fistula. **Method:** This cross sectional study was carried out in Department of Gynaecology and Obstetrics in Liaquat University Hospital, Hyderabad from January 2021 to December 2021 among 60 women at different ages suffering from vesicovaginal fistula due to gynaecological or obstetrical causes or malignancy. **Result:** Majority of the patients were "young primipara with short stature and malnourished, coming from lower socioeconomic condition of rural areas. Prolonged labor 24 (40%) was the most common cause of vesicovaginal fistula, followed by gynaecological surgeries mainly hysterectomies 18(30%) and malignancy 4 (6.6%) rare cause. The success rate of repair following first and second attempt was 92% and 8% respectively. Overall success rate was 48(96%) and functionally failed with a failure in 2(4%) cases. This study showed main cause for developing fistula showing prolonged labor and majority of patient were treated pervaginally. Most of the cases(96%) had successful repair which is very encouraging and correlates well with recently published series. **Conclusion:** Fistula can be totally preventable by proper antenatal care identification of high risk cases, timely referral, proper intranatal, postnatal care, and proper training. So improvement of health care services and dedication will prevent this type of morbidity. The best results are obtained when repair of vesicovaginal fistulae is carried out under optimal conditions".

INTRODUCTION

An abnormal communication between "urinary and genital tract is termed vesicovaginal fistula. The commonest type of genitourinary fistula is vesicovaginal fistula. Vesicovaginal fistula is an abnormal fistulous communication tract between vagina and urinary bladder, which leads to continuous involuntary passage of urine into vagina. Genitourinary fistula is a major problem in many developing countries especially the vesicovaginal fistula commonly caused by prolonged and obstructed labor is

one of the worst complication of child birth [1,2] Genitourinary fistula is a devastating condition affecting the physical and psychological health of women. With advance obstetric care these fistula are rare in industrialized world. Globally about 3.5 million women are living with genitourinary fistula, a miserable condition [3]. An incidence of 12 per 1000 deliveries has estimated worldwide, with an annual incidence of up to 50,000 to 100,000 [4]. In Bangladesh 1.9 percent women are suffering

from Vesicovaginal fistula (BIRRERTH) [5]. According to UNFPA & Engender Health, the number of women living with fistula is estimated to be 1.69 per 1000 ever married women [6]. Vesicovaginal fistulas result from mainly obstetrical and gynaecological cause. In the developing countries, 80-90 percent vesicovaginal fistulas are of obstetrical origin [7]. Lacks of privacy in hospital, objection from families, indifferent attitude of husband leads to prolong labor, encourage obstructed labor. Recently the incidence of genitourinary fistula following gynecological surgery, especially hysterectomy has increased [8]. Repair of the vesicovaginal fistula is a challenging task for the fistula surgeons worldwide. The outcome of vesicovaginal fistula repair depends on many factors like site, size and number of fistula, urethral length, bladder capacity and amount of scarring etc [9,10]. This study was designed to find out the factors associated with vesicovaginal fistula and to determine the success rate of operative procedure for treatment of vesicovaginal fistula at Liaquat University Hospital, Hyderabad.

METHODS

The study was cross sectional study in nature & was done at Department of Gyneacology and Obstetrics of Liaquat University Hospital, Hyderabad from January 2021 to December 2021 among 60 women suffering from vesicovaginal fistula. After admission all eligible patients were informed and written consent was obtained. Patient admitted with signs of dribbling of urine due to history of previous operative procedure and obstructed or prolonged labor or malignancy were included in the study while patients also having rectovaginal fistula or complete perineal tear were exclusion from the study. A detailed history has taken to pin point the casual factor. This included respondent's personal information, socio economic condition, past obstetrical and medical history, pattern of medical care and problem faced by the women suffering from vesicovaginal fistula. Each woman was evaluated with a detailed history as regards age, parity, antecedent event leading to fistula e.g., obstetric or gynecological. Obstetrical events including duration of labor, place, type of delivery, pregnancy outcome, and duration of fistula were detailed. The assessment included the women's general physical condition, size, site and number of fistula, amount of scarring of fistulous, margins or stenosis of the vagina. Detailed examination were done including examination under anesthesia. After the assessment of the patient appropriate operative measure were taken. All the result were noted in predesigned history sheet. Surgery was considered to be successful if patient can hold urine and there is no leakage of urine in between

the act of voiding after removal of catheter and before discharge from the hospital. After collection of data, analysis was done by computer aided statistical software SPSS v. 21. Data were presented in the form of tables and graphs. Data were analyzed with descriptive statistics. The level of significance of 0.05 were used for this study.

RESULTS

During a period of one year, 60 women that satisfied the inclusion criteria were prospectively evaluated & the results were analyzed. Among 14776 patients admitted in department of Gyneacology and Obstetrics of Liaquat University Hospital, Hyderabad, there were 60 vesicovaginal fistula, yielding a frequency to be 0.4%, and among total Gynae patients of 3832 yielding a frequency to be 1.5%. Age distribution of patients (60)- Majority [22 (36%)] patients belongs to age group 21-30 years, second commonest age was 31-40 years about 16(27%). Most of the patients [26 (43.3%)] in this study were young primipara, next [18(30.0%)] were para (4, 7%) and 6(10%) of them were grand multipara.

Causative Factors		No. of Patients	%
A.	Obstetrical Prolonged	40	66.66%
	Prolonged Labor (Vaginal Delivery)	26	43.33%
	Obstructed Labor (Caesarean Section)	14	23.33%
B.	Gynaecological Causes	20	33.33%
	Total Abdominal Hysterectomy	18	30.00%
	Malignancy	2	33.33%

Table 1: Aetiology Based Distribution (n=60)

Distribution of cases according to aetiology of fistula (Table 1): (A) Obstetrical causes 40 (66.66%) patients, among them prolonged labor (vaginal delivery) 26(43.33%), obstructed labor (caesarean. section) 14 (23.33%) - (B) Gynaecological causes 20 (33.33%) patients, among them total abdominal hysterectomy 18 (30.00%), malignancy 2 (33.33%).

Distribution of Cases according to Types (n=60)		
Types of Fistula	No. of Patients	%
Vesico-vaginal	36	60%
Vesico-cervical	6	10%
Uretero-vaginal	18	30%

Table 2: Distribution of Cases according to Types (n=60)

Table 2 shows distribution of cases according to types of fistula (n=60). Vesicovaginal fistula was the commonest and constituted 60%.

Types of Fistula	No. of Patients	%
Small (up to 2 cm)	32	53.3%
Medium (2.1-3 cm)	18	30%
Large (>3 cm.)	10	16%

Table 3: Distribution of Cases according to Size (n=60)

In this study 53.3% of patients had small size fistula (commonest) which is shown in Table III. Out of 60 patients with vesicovaginal fistulae, 4 patients with small fistulae healed conservatively with continuous catheter drainage where one patient could not be operated upon because they suffered from carcinoma cervix in terminal stages. 4 patients were advised to come after 3 months because of presence of unhealthy granulation tissues around the fistulae. Therefore, 50 patients underwent surgery. The commonest approach used was transvaginal 34 (68%) and 16 patients (32%) were repaired through abdominal procedure with layer closure.

Number of Previous Attempt	No. of Patients	%
No Attempt	42	84%
One Attempt	26	12%
Two Attempt	2	4%

Table 4: Patient distribution as per previous attempt of repair (n=50)

Majority (84%) patients in this series had no history of previous attempts of repair. 12% patients had single attempt. Table IV shows previous attempts of repair.

Types of Fistula	No. of Patients	%	P-value
Conservative Management	10	16.67%	<0.001
Surgical Management	50	83.33%	
Cured	48	96%	
Failure	1	4%	

Table 4: Outcome of the Study (n=60)

Among 50 patients cure rate was 96% (n=50). In this study failure rate was 4% (Table-V). P value was <0.001 the test is significant. Repair of fistula was difficult due to associated additional cofactor - vaginal stenosis [4 (8.8%)], attachment to pubic bone [4 (8.8%)], associated hydronephrosis [8 (16%)]. Post-operative problems among patients were retention of urine due to catheter blockage [4 - (8%)], urethral leakage [2 (4%)], UTI [8 (16%)]. In 8% patients' catheter needed to be changed due to catheter block.

DISCUSSION

Obstetric fistula has gained international attention in the last 10-15 years. The condition has been researched mostly in developing countries like Nigeria, Ethiopia, Niger and Tanzania. Most studies of obstetric fistula uses observational, analytical study designs, mainly cross sectional studies. The research conducted are typically hospital based retrospective analysis of case records/patient records. Case control studies are not commonly used. The true incidence of vesicovaginal fistula is unknown as many women do not reach hospital and continue to be neglected by their husbands and ostracized

from society. Overall prevalence has been estimated at 0.2 to 2% in different societies. Its occurrence reflects the level of maternity care in a community and most are a consequence of mismanaged labor, a sequelae to obstructed labor [9]. In my study period the frequency of vesicovaginal fistula among all admitted patients of Obstetric and Gynae Department was 0.40% and among Gynae patients the frequency was 1.5%. The highest prevalence is in poor communities of Africa and Asia and constitute 0.5-1.7% of gynaecological admission in teaching hospital [10]. Only three studies were identified using a case control design and that was one study in Nigeria, and a recent study in Zambia and in north eastern Nigeria [11-13]. There is a shared view that the main cause of obstetric fistula is prolonged labor and that the major outcome is stillbirths [14]. Research uncovers that many women are in labor for several days, often in the presence of a traditional birth attendant and little or no access to emergency obstetric care [15]. The majority of research highlights the following predispositions: low reproductive age, biological factors such as short stature and incomplete pelvis growth [16,17]. Cultural aspects such as female genital mutilation and socioeconomic aspects such as low education and poverty. Many studies found malnutrition to be a risk factor, however some claimed that this needs to be further researched. Many studies found that VVFs occurred mostly in first pregnancies [18]. However some studies did not agree with this. The success rate of obstetric fistula repair is in general in between 80 to 90 percentile [19]. Success rate is generally lower for completely cured patients, sometimes as low as 60% [20]. One main predictor of surgery outcome is identified in some studies to be the amount of vaginal scarring [21]. The majority of iatrogenic fistulas develop subsequent to caesarean section. In our study the incidence of urological fistula arising out of obstetrical complication was 66.66% (40/60). In one study obstetrical complications were responsible for 88% cases and gynecological surgeries for 9% cases. One study conducted in Pakistan revealed a total number of 287 patients with genitourinary fistula. The mean age of patients with urinary fistula was 31.5 + 7.5 years, parity was 4.2 ± 2.8, and duration of labor was 38.4 ± 6.5 hours. The most common type of urinary fistula was vesico vaginal fistula [250 (89.9%)]. A total of 268 patients underwent surgery. The success rate following first, second and third attempt was 85%, 91% and 96% respectively. In our study, 50 patients underwent surgery among 30 patients. In our study prolonged labor with spontaneous delivery was responsible for 43.3% cases and obstructed labor with surgical interference was responsible for another 23.3%. So the study demonstrates

the high rate of successful closure of the fistula in a specialized fistula unit, but highlights the problems of persistent urinary incontinence following closure [22]. There were some limitations in this study: period of study was insufficient to conduct a quality study, sample size was small that was not correlated with sample size calculation, it was a hospital based study, not representing the community population, this study was conducted in a single hospital which may not be the representative for the whole country.

CONCLUSION

It was found that fistulas occurred mainly due to prolonged and obstructed labour, which can be totally preventable by proper antenatal care, identification of high risk cases, timely referral, proper intra natal and postnatal care. Iatrogenic fistula can be prevented by proper training. Repair of genito urinary fistula in appropriate time and in appropriate route by an expert surgeon can minimize failure rate".

REFERENCES

- [1] Nahar S, SARKAR M, DASC KP, AKTAR N. Iatrogenic Genitourinary Fistulae: A Survey in Khulna Medical College. *Journal of Bangladesh College of Physicians and Surgeons*. 2005 May;23(2):68.
- [2] Fatema MK, Saha E, Begum F, Lucky SN, Rahman F. Causal factors and treatment outcome of genitourinary fistula in a teaching hospital. *Bangladesh Medical Journal Khulna*. 2017;50(1-2):18-21. doi.10.3329/bmj.v50i1-2.35837
- [3] Uprety DK, Budhathoki B, Subedi S, Regmi MC. Vesicovaginal fistula at tertiary care center in eastern Nepal. *Journal of Nepal Medical Association*. 2008 Jul 1;47(171). doi.10.31729/jnma.305
- [4] Singh V, Sinha RJ, Mehrotra S, Sankhwar SN, Bhatt S. Repair of vesicovaginal fistula by the transabdominal route: outcome at a north Indian tertiary hospital. *Int Urogynecol J*. 2012 Apr;23(4):411-6. doi: 10.1007/s00192-011-1544-7.
- [5] Fatema MK, Saha E, Begum F, Lucky SN, Rahman F. Causal factors and treatment outcome of genitourinary fistula in a teaching hospital. *Bangladesh Medical Journal Khulna*. 2017;50(1-2):18-21.
- [6] Begum B, Khandakar S, Rahman F. A Study on Outcome of VVF Repair at Kumudini Women's Medical College Hospital. *Bangladesh Medical Journal*. 2011;40(3):18-20.
- [7] Konar H. DC Dutta's Textbook of Gynecology Including Contraception. Jaypee Brothers Medical Publishers; 2013.
- [8] Sachdev PS, Hassan N, Abbasi RM, Das CM. Genitourinary fistula: a major morbidity in developing countries. *Journal of Ayub Medical College Abbottabad*. 2009 Jun 1;21(2):8-11.
- [9] Begum B, Khandakar S, Rahman F. A Study on Outcome of VVF Repair at Kumudini Women's Medical College Hospital. *Bangladesh Medical Journal*. 2011;40(3):18-20. doi.10.3329/bmj.v40i3.18652
- [10] Vyas N, Nandi PR, Mahmood M, Tandon V, Dwivedi US, Singh PB. Bladder mucosal autografts for repair of vesicovaginal fistula. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2005 Jan;112(1):112-4.-4. doi.10.1111/j.1471-0528.2004.00316.x
- [11] Ezegwui HU, Nwogu-Ikojo EE. Vesico-vaginal fistula in Eastern Nigeria. *Journal of obstetrics and gynaecology*. 2005 Jan 1;25(6):589-91. doi.o10.1080/01443610500239479
- [12] Porcaro AB, Zicari M, Antonioli SZ, Pianon R, Monaco C, Migliorini F, Longo M, Comunale L. Vesicouterine fistulas following cesarean section Report on a case, review and update of the literature. *International urology and nephrology*. 2002 Sep;34(3):335-44. doi.10.1023/A:1024443822378.
- [13] Melah GS, Massa AA, Yahaya UR, Bukar M, Kizaya DD, El-Nafaty AU. Risk factors for obstetric fistulae in north-eastern Nigeria. *Journal of Obstetrics and Gynaecology*. 2007 Jan 1;27(8):819-23. doi.10.1080/01443610701709825
- [14] Modinos G, Vercammen A, Mechelli A, Knegeting H, McGuire PK, Aleman A. Structural covariance in the hallucinating brain: a voxel-based morphometry study. *Journal of Psychiatry and Neuroscience*. 2009 Nov 1;34(6):465-9. doi./10.1016/S1701-2163(16)32305-2
- [15] Wall LL. Obstetric vesicovaginal fistula as an international public-health problem. *The Lancet*. 2006 Sep 30;368(9542):1201-9. doi.10.1016/S0140-6736(06)69476-2
- [16] Wall LL, Karshima JA, Kirschner C, Arrowsmith SD. The obstetric vesicovaginal fistula: characteristics of 899 patients from Jos, Nigeria. *American journal of obstetrics and gynecology*. 2004 Apr 1;190(4):1011-6. /doi./10.1016/j.ajog.2004.02.007.
- [17] Holme A, Breen M, MacArthur C. Obstetric fistulae: a study of women managed at the Monze Mission Hospital, Zambia. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2007 Aug;114(8):1010-7. doi.10.1111/j.1471-0528.2007.01353.x
- [18] Shumaker SA, Wyman JF, Uebersax JS, McClish D, Fantl JA. Health-related quality of life measures for

- women with urinary incontinence: the Incontinence Impact Questionnaire and the Urogenital Distress Inventory. *Quality of life Research*. 1994 Oct;3(5):291-306. doi.10.1007/BF00451721
- [19] Barber M, Walters MD, Bump RC. Short forms of two condition-specific quality-of-life questionnaires for women with pelvic floor disorders (PFDI-20 and PFIQ-7). *American journal of obstetrics and gynecology*. 2005 Jul 1;193(1):103-13. doi.10.1016/j.ajog.2004.12.025
- [20] Cohen BL, Gousse AE. Current techniques for vesicovaginal fistula repair: surgical pearls to optimize cure rate. *Current urology reports*. 2007 Sep;8(5):413-8. doi.10.1007/s11934-007-0040-6
- [21] Frajzyngier V, Ruminjo J, Asiimwe F, Barry TH, Bello A, Danladi D, Ganda SO, Idris S, Inoussa M, Lynch M, Mussell F. Factors influencing choice of surgical route of repair of genitourinary fistula, and the influence of route of repair on surgical outcomes: findings from a prospective cohort study. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2012 Oct;119(11):1344-53. doi.10.1111/j.1471-0528.2012.03461.x
- [22] Nardos R, Browning A, Chen CC. Risk factors that predict failure after vaginal repair of obstetric vesicovaginal fistulae. *American journal of obstetrics and gynecology*. 2009 May 1;200(5):578-e1. /doi./10.1016/j.ajog.2008.12.008



Original Article

Frequency of Depression Among Chronic Hepatitis C Patients Visiting Haji Abdul Qayyum Hospital Sahiwal

Hira Iftikhar¹, Zahra Iftikhar², Noman Qutab³, Rana Aamir Diwan¹, Tayyaba Ayub^{4*}, Tallat Anwar Faridi⁴

¹Department of Community Medicine, Sahiwal Medical College, Sahiwal, Pakistan

²Brentwood Resource Centre, Brentwood, England

³Basic Health Unit (BHU), Dadra Bala, Punjab, Pakistan

⁴University Institute of Public Health, The University of Lahore, Lahore, Pakistan

ARTICLE INFO

Key Words:

Cirrhosis, Hepatitis C, Depression

How to Cite:

Iftikhar, H. ., Iftikhar, Z., Qutab, N. ., Aamir Diwan, R. ., Ayub, T. ., & Anwar Faridi, T. . (2022). Frequency of Depression Among Chronic Hepatitis C Patients Visiting Haji Abdul Qayyum Hospital Sahiwal: Frequency of Depression Among Chronic Hepatitis C Patients. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.521>

***Corresponding Author:**

Tayyaba Ayub
 University Institute of Public Health, The University of Lahore, Lahore, Pakistan
tayyabaayub123@gmail.com

Received Date: 4th Jun, 2022

Acceptance Date: 20th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Hepatitis C is prominently a hepatic disease whose infection ranges in severity from a mild illness to serious lifelong complications. Multiple organ systems in the body may get affected. Depression is an important complication in almost 70% of HCV patients. **Objectives:** To find out the frequency of depression in chronic hepatitis C infected population of District Sahiwal. **Methods:** Descriptive cross-sectional study was performed at Gastroenterology Clinic, Haji Abdul Qayyum Hospital, Sahiwal during nine months from September 2020 to June 2021. Total 350 patients were selected by non - probability purposive sampling on the basis of preset inclusion and exclusion criteria. Beck's Depression Inventory Scale was utilized to assess the patients for depression and correlate it with level of education and occupation. **Results:** Out of 350 patients of CHC, 56.6% were male and 43.4% were female. 4.3% patients were suffering from borderline depression; 42.3% were suffering from moderate depression; 46.3% were suffering from severe depression and 2.3 % were suffering from extreme depression. Association of depression with household income ($p = 0.044$) and duration of disease ($p = 0.00$) were significant while association of depression with level of education ($p = 0.655$) and occupation ($p = 0.219$) were not significant. **Conclusion:** Level of depression in patients of CHC is dangerously high. Level of depression in patients of CHC is strongly dependent on household income and duration of disease and independent of level of education and occupation.

INTRODUCTION

Hepatitis C is a worldwide disease and it's estimated that almost 185 million people have been infected with this disease. Out of 185 million people, 2.9% are diagnosed in Africa, 1.3% in Americas, in Asia 64 %, and in Australia 75% [1]. In Pakistan, the prevalence of Chronic Hepatitis C (CHC) is 6 % [2]. It has been observed that every year almost 3 to 4 million cases of CHC appear because of the non-availability of CHC vaccination and these numbers are continuously rising. Modes of transmission are through exposure to various body fluids including serum, semen and saliva. This may happen through intravenous drug abuse, unsafe

injection practices, un-safe health care practices, transfusion of unscreened blood and blood products, dialysis, unprotected sexual encounters, post-transplant transmission (in 16% of the cases), perinatal or vertical transmission. Very high burden of chronic HCV infection has been observed to be reported in intravenous drug abusers, men who have sexual encounters with men, and individuals in jails or prisons. Many cases of acute HCV infection have also been reported. Usually these cases are being reported among HIV-infected individuals due to the similarity of risk factors and mode of transmission in both

of these viruses. Hepatitis C virus can also get transmitted vertically. Although the rate of vertical transmission is quite low (0.2% to 0.4%) [2], but this matter still needs attention. The symptoms which occur initially after inoculation with Hepatitis C virus include general systemic symptoms. Then 0.0 – 0.6% of the patients, suicidal ideation in 3.5 – 10% of the patients, and suicidal attempt is present in 0.0 – 0.2% of the patients [7]. Psychiatric disturbances cause 44% of the patients to leave the medication of CHC [8]. Depression is a leading cause of disability worldwide. Major depression is a serious side effect of interferon- α (IFN- α), which is used in the treatment therapy of CHC [9]. In a study by Sarwar S et al., the prevalence of depression in CHC was 56% in 2017 [10]. Rahman AS et al., showed that the prevalence of depression in CHC was 87% in 2017 [11]. In a study by Bhutto et al., in Karachi, the frequency of depression in CHC was 72.3% [12]. Another study in Karachi showed 59% rate of depression in patients of CHC [13]. Adrees et al., performed a study in Faisalabad, in which the prevalence was 48% [14]. In multiple international studies, the rate of developing depression in CHC was quite high but these rates were comparatively lower than the rates in Pakistan. Abbas et al., performed a study in Egypt in which the frequency of depression in CHC was 29% [15]. In a study by Egmond et al., performed in Brazil, frequency of major depression was 37.9% and other types of depressive disorders were found in 46.3% of the participants [16]. A developing country like Pakistan which has scarce health sector resources, has limited data related to this topic. This study had been directed to estimate the frequency and level of depression in CHC patients of Sahiwal. This study was a great source of knowledge in identifying the frequency of depression in CHC patients which is essential in preventing the mental health problems of the patients in Sahiwal. It was also helpful in creating general awareness regarding the associated risk factors in depression. Study results are also beneficial for clinician's counselors and health professionals in developing strategies and interventions that could be given to patients along with the treatment of this chronic disease. This local estimate may be utilized to assess and compare the prevalence the disease directs itself to hepatic manifestations. In later stages of life, it progresses to liver cirrhosis within 20-30 years after infection [3]. 1 – 4 % of individuals develop hepatocellular carcinoma every year [4]. There is an intricate correlation among mental health disorders and CHC. Rates of psychiatric problems are significantly higher in CHC as compared to rates of psychiatric problems in general population [5]. Depression is present in 30 – 70% of the patients of CHC [6], irritability in 17 – 67% of the patients [6],

schizophrenia in 3.9% of the patients [6], bipolar disorder in 2.6% of the patients [7], anxiety in 11 – 45% of the patients [7], fatigue in 39 – 80% of the patients, sleep disturbance in 18 – 45% of the patients, mania in 0.0 – 3.2% of the patients, psychosis in on district level or provincial level or more extensively on national level. This can help the policy makers to constitute mental health strategies to match the international standards of health care.

METHODS

Total 350 patients were selected by non- probability Purposive sampling. Sample comprised of male and female patients having age between 15 – 70yrs who, were positive for anti – HCV antibodies by ELISA or positive for HCV RNA by PCR for HCV. Patients of all genotypes were included. Patients having previous history of or undergoing any treatment for previous psychiatric / psychological / psychotic / epileptic / neural disease were excluded from the study. Patients with history of death of any family member in past six months, patients of any disabling or disfiguring disease, ladies during pregnancy or puerperium, lactating mothers, patients taking oral hormonal therapies, patients of endocrine disorders, immuno-compromised patients, organ transplant patients and patients having Hepatitis C for less than 6 months' duration were also excluded from the study. Beck's Depression Inventory Scale (BDI) was used to measure depression. This scale has 21 items with minimum and maximum scores as 0, 1, 2, 3. Depression was labeled if score was greater than 17. Patients scoring between 17 and 20 on the scale had borderline depression. Patients scoring between 21 and 30 on the scale had moderate depression. Patients scoring between 31 and 40 on the scale had severe depression. Patients scoring more than 40 on the scale had extreme depression. CHC (chronic hepatitis C) was labeled based on the detection of HCV RNA by PCR or anti-HCV antibodies by ELISA for more than six months' duration. Data were collected after approval from Institutional Review Board IRB (Letter no 1) Ethical Review Board of University of Lahore. Questionnaires were filled by interview method. Data were analyzed by utilizing SPSS version 21.0. For categorical data i.e., BDI score for depression and age, crosstab was utilized. Post – stratification Chi square test was used for association of socio demographical factors. p-value of less than or equal to 0.05 ($p \leq 0.05$) was considered as significant.

RESULTS

Out of 350, 17 participants were not suffering from depression, 15 participants were suffering from borderline depression, 148 participants were suffering from moderate

depression, 162 participants were suffering from severe depression and 8 participants were suffering from extreme depression, Figure 1.

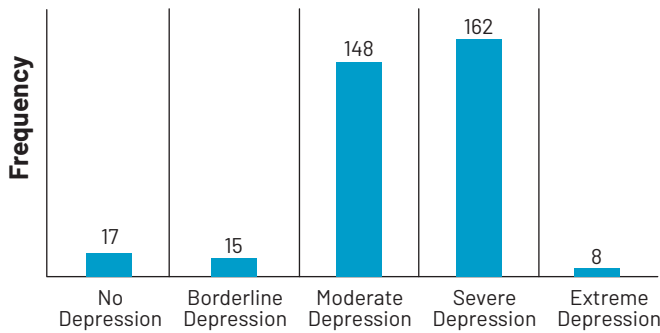


Figure 1: Frequency of Depression (n=350)

There was statistically significant association between disease duration and depression because probability of error was $p = 0.01$ ($p < 0.05$) with degree of freedom (df) = 8. Out of 2.3% participants who were having extreme depression, 25% patients had CHC for < 5 years, 12.5% patients had CHC for 5 to 10 years and 62.5% patients had CHC for > 10 years. (Table 1)

Duration of Disease	Level of depression					Total	df	P
	No Depression	Borderline Depression	Moderate Depression	Severe Depression	Extreme Depression			
less than 5 years	16 (94.1%)	14 (93.3%)	3 (2.0%)	4 (2.5%)	2 (25.0%)	39 (11.1%)	8	0.01
5 - 10 years	1 (5.9%)	0 (0.0%)	56 (37.8%)	63 (38.9%)	1 (12.5%)	121 (34.6%)		
more than 10 years	0 (0.0%)	1 (6.7%)	89 (60.1%)	95 (58.6%)	5 (62.5%)	190 (54.3%)		
Total	0 (0.0%)	1 (6.7%)	89 (60.1%)	95 (58.6%)	5 (62.5%)	190 (54.3%)		

Table 1: Crosstab for Duration of disease (n=350)

The association between household income and depression was statistically significant because probability of error was (p) = 0.044 ($p < 0.05$) with degree of freedom (df) = 12. Out of 2.3% participants who were having extreme depression, 50% patients were having household income less than 20,000 Rs. and 50% patients were having household income between 20,000 Rs. and 40,000 Rs. (Table 2). The association between occupation and depression wasn't statistically significant because probability value (p) = 0.219 ($p > 0.05$) with degree of freedom (df) = 8. Out of 46.3% participants who were having severe depression, 2.5% patients were unemployed, 55.6% patients were skilled workers and 42% patients were professionals. Out of 2.3% participants who were having extreme depression, 50% patients were skilled workers and 50% patients were professionals. The association between level of education and depression was not statistically significant because probability value (p) = 0.655 ($p > 0.05$) with degree of freedom (df) = 16. Out of 46.3% participants who were having severe depression,

13.6% patients were uneducated, 33.3% patients had completed matriculation level, 42% patients had completed intermediate level and 11.1% patients had completed bachelors' level. Out of 2.3% participants who were having extreme depression, 12.5% patients were uneducated, 37.5% patients had completed matriculation level and 50% patients had completed intermediate level.

House hold Income	Level of depression					Total n=350	df	P
	No Depression	Borderline Depression	Moderate Depression	Severe Depression	Extreme Depression			
less than 20,000	8 (47.1%)	8 (53.3%)	76 (51.4%)	58 (35.8%)	4 (50.0%)	154 (44.0%)	12	0.044
20- 40 thousand	8 (47.1%)	7 (46.7%)	60 (40.5%)	86 (53.1%)	4 (50.0%)	165 (47.1%)		
40-60 thousand	1 (5.9%)	0 (0.0%)	9 (6.1%)	13 (8.0%)	0 (0.0%)	23 (6.6%)		
More than 60 thousand	0 (0.0%)	0 (0.0%)	3 (2.0%)	5 (3.1%)	0 (0.0%)	8 (2.3%)		
Total	17 (4.9%)	15 (4.3%)	148 (42.3%)	162 (46.3%)	8 (2.3%)	350 (100.0%)		

Table 2: Crosstab for household income (n=350)

DISCUSSION

In present study, the rate of depression in patients of CHC was alarmingly high 95.2%. This is very much higher than majority of the studies from Pakistan. In a study by Waseem T et al., the prevalence of depression in CHC was 64% [17]. In a study by Aslam MN et al. the prevalence of depression was 29% [18]. In a study by Sarwar S et al., the prevalence of depression in CHC was 56% in 2017 [10]. In a study by Fatima K et al., the prevalence of depression in CHC was 90.6% [19]. In a study by Rahman AS et al., the prevalence of depression in CHC was 87% in 2017 [11]. In a study by Bhutto et al., in Karachi, the frequency of depression in CHC was 72.3% [12]. Another study in Karachi showed 59% rate of depression in patients of CHC [13]. Adrees et al., performed a study in Faisalabad, in which the prevalence was 48% [14]. In multiple international studies, the rate of developing depression in CHC was quite high but these rates were comparatively lower than the rates in Pakistan. Abbas et al., performed a study in Egypt in which the frequency of depression in CHC was 29% [15]. In a study by Egmond et al., performed in Brazil, major depression was 37.9% and other types of depressive disorders were found in 46.3% of the participants [16]. In present study, level of depression in patients of CHC had strong statistical significance with duration of disease (p value = 0.00). Out of all depressed patients, 54.3% patients were having CHC for more than 10 years, 34.6% patients were having CHC for 5 to 10 years and 11.1% patients were having CHC for less than 5 years. Similar results were shown in the studies by Memon et al [12]. Fatima. K et al., [14] and Abbas et al., [19]. In present study, out of all depressed patients, 91% had household income < 40,000 and association of income and depression was statistically significant because p value = 0.044 ($p < 0.05$)

with $df = 12$. Similar results were shown in a study performed by Sarwar S et al., [13]. Abbas. SM et al., conducted a study in 2017 in which lower socioeconomic status, un-employment and illiteracy were important risk factors in developing depression in CHC [19]. In a study by Nagi et al., in Shalimar hospital Lahore, 53% patients of chronic liver Disease were suffering from depression [20].

CONCLUSION

Level of depression in patients of CHC is independent of level of education and occupation but strongly dependent on household income and duration of disease.

REFERENCES

- [1] Martínez I, Ryan P, Valencia J, Resino S. The challenging road to hepatitis C virus eradication. *Journal of Clinical Medicine*. 2021 Jan;10(4):611. doi: [10.3390/jcm10040611](https://doi.org/10.3390/jcm10040611)
- [2] Qamar Z, Anwar F, Ahmad R, Haq I, Khan AM, Hussain R, et al. Prevalence of Hepatitis C virus and determination of its genotypes in subjects of Tehsil Daggar District Buner, KP, Pakistan. *Clinical Epidemiology and Global Health*. 2021 Oct 1; 12:100809. doi: [10.1016/j.cegh.2021.100809](https://doi.org/10.1016/j.cegh.2021.100809)
- [3] Wang JH, Hung SJ. Lichen planus associated with hepatitis B, hepatitis C, and liver cirrhosis in a nationwide cohort study. *J Am Acad Dermatol*. 2021 Apr;84(4):1085-1086. doi: [10.1016/j.jaad.2020.07.073](https://doi.org/10.1016/j.jaad.2020.07.073).
- [4] Roche B, Coilly A, Duclos-Vallee JC, Samuel D. The impact of treatment of hepatitis C with DAAs on the occurrence of HCC. *Liver Int*. 2018 Feb;38 Suppl 1:139-145. doi: [10.1111/liv.13659](https://doi.org/10.1111/liv.13659).
- [5] Chong LW, Hsu CC, Lee CY, Chou RH, Lin CL, Chang KH, et al. Association of viral hepatitis and bipolar disorder: a nationwide population-based study. *J Transl Med*. 2018 Jun 22;16(1):173. doi: [10.1186/s12967-018-1542-3](https://doi.org/10.1186/s12967-018-1542-3).
- [6] Najaf HN, Kadhim DJ, Alkofee AJ, Al-Mashhadani DA. Depression, Anxiety and Stress Among a Sample of Chronic Hepatitis C Patients in AL-Najaf Province/Iraq. *International Journal of Research in Pharmaceutical Sciences*. 2019;10(4): 3170-7. doi: [10.26452/ijrps.v10i4.1616](https://doi.org/10.26452/ijrps.v10i4.1616)
- [7] Siddique S, Aaraj S, Haider I. Frequency of Depressive Disorders in Patients of Hepatitis C. *Age (years)*. 2018 Jan 1;21(35):45.
- [8] Janda M, Mergenhagen KA. The Effect of Psychosocial Factors on Success Rates of Hepatitis C Treatment. *Psychosomatics*. 2017 Nov-Dec;58(6):624-632. doi: [10.1016/j.psym.2017.07.003](https://doi.org/10.1016/j.psym.2017.07.003).
- [9] Hoyo-Becerra C, Liu Z, Yao J, Kaltwasser B, Gerken G, Hermann DM, Schlaak JF. Rapid Regulation of Depression-Associated Genes in a New Mouse Model Mimicking Interferon- α -Related Depression in Hepatitis C Virus Infection. *Mol Neurobiol*. 2015 Aug;52(1):318-29. doi: [10.1007/s12035-014-8861-z](https://doi.org/10.1007/s12035-014-8861-z).
- [10] Sarwar S, Babur W, Mahwish S, Anwar I. Prevalence of depression among Hepatitis-C patients in tertiary care hospital. *Pak J Surg*. 2018;34(2):140-3.
- [11] Rahman AS, et al. Prevalence of depression after treatment with conventional interferon's and ribavirin therapy in patients with hepatitis C using PHQ-9. *Am J Res Med Sci*, 2019;5(1). doi: [10.5455/ajrms.20181102081059](https://doi.org/10.5455/ajrms.20181102081059)
- [12] Bhutto AR, Jat MI, Rafi S, Amar W. Frequency of Anxiety and Depression in Chronic Hepatitis C Patients Visiting a Tertiary Care Hospi-Tal at Gadap Town, Karachi. *Journal of Postgraduate Medical Institute*. 2019;33(2):125-9.
- [13] Memon SA, Zuberi BF, Ashfaq MN, Kiran Z, Qadeer R, Memon AR, et al. Frequency of depression in chronic Hepatitis C naïve patients. *Pak J Med Sci*. 2011 Jul 1; 27:780-3.
- [14] Adrees M, Athar HM, Riaz MZ, Noor A, Noor M. Frequency of Depression in patients with HCV On Interferon Alfa Therapy. *Annals of Punjab Medical College(APMC)*. 2018;12(4).
- [15] Abbas SM, Salama HM, Nour-Eldein H. Depression among adults with chronic hepatitis C on antiviral treatment in Port-Said, Egypt. *Journal of Public Health*. 2018 Dec;26(6):679-86. doi: [10.1007/s10389-018-0907-7](https://doi.org/10.1007/s10389-018-0907-7)
- [16] Egmond E, Mariño Z, Navines R, Oriolo G, Pla A, Bartres C, et al. Incidence of depression in patients with hepatitis C treated with direct-acting antivirals. *Braz J Psychiatry*. 2020 Jan-Feb;42(1):72-76. doi: [10.1590/1516-4446-2018-0336](https://doi.org/10.1590/1516-4446-2018-0336).
- [17] Waseem T. Prevalence of Depression in patients of Chronic Hepatitis B & C Presenting to Mayo Hospital Lahore. *Methods*. 2015 Feb.
- [18] Aslam MN, Qureshi UF, Nadeem M. Anxiety and Depression: Prevalence in Chronic Hepatitis C Patients. *The Professional Medical Journal*. 2016 Mar 10;23(03):36-38. doi: [10.29309/TPMJ/2016.23.03.1484](https://doi.org/10.29309/TPMJ/2016.23.03.1484)
- [19] Fatima K, Ghani MU, Ali M, Bano K, Fatima B, Shahzad A. Frequency and severity of depression in patients with Hepatitis C. *Rawal Medical Journal*. 2019;44 (2):255-8.
- [20] Nagi ML, Manan S, Shaheen A, Amjad M, Farooq M, Kazmi ST. Depression; frequency of depression among patients of chronic liver disease attending a

tertiary care private hospital of Lahore. Professional Medical Journal. 2018 Nov 10;25(11):1701-6. DOI: 10.29309/TPMJ/18.4824



Original Article

Frequency of Voice Changes during Covid-19 Infections: A Retrospective Study

Janet Shanem¹, Muhammad Sikander Ghayas Khan¹, Muhammad Azzam Khan², Aayeshah Firdous³, Sadaf Hameed³, Arooba Asmat⁴, Shabana Majid⁵, Sabahat Khan⁶ and Tallat Anwar Faridi⁷.

¹Department of Health Professional Technologies, University of Lahore, Pakistan

²Department Rehabilitation Sciences, University of Lahore, Pakistan

³Department of Allied Health Sciences, Rashid Latif Khan University, Lahore, Pakistan

⁴Department of Speech and Language Pathology, Sikandar Medical, Gujranwala, Pakistan

⁵Department of Speech and Language Therapy, Hameed Latif Hospital, Lahore, Pakistan

⁶Rashid Latif Khan University, Lahore, Pakistan

⁷University Institute of Public Health, University of Lahore, Pakistan

ARTICLE INFO

Key Words:

Voice changes, Covid-19, weak voice

How to Cite:

Shanem, J. ., Sikander Ghayas Khan, M. ., Azzam Khan, M. ., Firdous, A., Hameed Sial, S., Asmat, A. ., Majid, S. ., Khan, S. ., & Anwar Faridi, T. . (2022). Frequency of Voice Changes during Covid-19 Infections: A Retrospective Study: Frequency of Voice Changes during Covid-19 Infections: A Retrospective Study. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.525>

*Corresponding Author:

Janet Shanem

Department of Health Professional Technologies,
University of Lahore. Pakistan

Received Date: 7th June, 2022

Acceptance Date: 22nd June, 2022

Published Date: 30th June, 2022

ABSTRACT

Communication is defined as the phenomenon found specifically in animal species. It was however refined and modified only by the human species. Language and speech are two basic areas that fall under the umbrella of communication. With these processes also comes the impending danger of abnormal speech and language, leading to the development of their disorders. **Objectives:** Reporting the frequency changes in the voice of patients who are positive of covid-19. **Methods:** Application of cross-section study type of retrospective nature was steered. Details were extracted from 2 trust hospitals of Lahore, UOL Teaching Hospital and Arif Memorial Hospital. Convenient based sample accumulation technique was applied for data assembly from subjects. The Voice Handicap Index (VHI), was used for the evaluation of patient perceived voice changes. **Results:** Data of 379 patients of Covid-19 infection was compiled. Shaky and weak voice, unclear voice and change in voice observed at the end of the day were all highlighted as voice changes in subjects. Out of 379, 263 experience shaky and weak voice to some extent which meant 69.4% of the participants experienced this. 241 out of 379 experienced problems with voice clarity and complained about not being able to speak clearly, meaning 63.6% faced this issue. 242 experienced change of voice over the passage of time in entire day, indicating 63.9% experienced this. **Conclusion:** Weak voice or having a shaky voice, having voice that was not clear enough to be understood by others, and feeling a change in voice quality over the day were considered as pointers of voice change. collecting and analyzing the data, the investigation concluded that voice changes were observed in individuals during Covid-19 infection.

INTRODUCTION

Communication is defined as the process in which exchange of information in the terms of thoughts, notions, moods and emotions between living beings takes place. This spectacle is not only classified to humans, animals also use this to interact. Communication in humans has 2 basic components, language and speech. Speech is the neuromuscular process that results in the production of appropriate sounds from the vocal tract. Speech occurs when individuals make meaningful sounds with the help of

the articulators that are set in motion when instructed. The components of speech include, voice, fluency in speaking and articulation of an individual. All these components need to be existing in an individual to achieve decent speech in order to communicate. A problem in any one of the components can lead to abnormalities of the vocal tract and thus disrupt production of proper speech for communication. The properties of these components varies from individual to individual however there is a set

standard even still in order to have appropriate voice, proper articulation and effortless fluency [1,2]. Voice is the sound produced at the level of the vocal cords when they vibrate. It is the raw material for our speech. The process of voice manufacture involves the lungs, bronchi, trachea, larynx and specifically the vocal cord movement. The pulmonary air departing the lungs, comes in contact with the glottis, the opening of the vocal cords in the larynx, leading to the vibration of the vocal cords production of sound. Phonation and thus voice is an important aspect of speech. This sound then acts as a raw material which then passes through the various cavities of the pharynx, mouth and nose to shape and transform into various speech sounds humans produce so effortlessly. Voice can only be produced if the air that exits the lungs and lower respiratory tract and interacts in the glottis region if the timings of the air expulsion or vocal cord opening are altered, this process may not even occur subsequently [3]. Production of voice mechanically involves multifaceted adduction of cords of voice and how it is controlled by the muscles present in larynx. It is significant in a research related to voice to determine a theory that links voice function and structure to how the speaker uses and controls his/her voice for communicating personal details and sense [4,5]. Loudness or vibratory amplitude is characterized as the highest or maximum movement of the vocal cords from resting position while a person phonates. The higher the amplitude of the vocal cord vibration, the louder the sound. Pitch or the frequency of the voice can be defined as the number of cycles of vocal cord vibration per unit time. When the length of the vocal cords is increased the number of cycles of vocal cord vibration decreases, decreasing the pitch of one's voice and vice versa [6,7]. Voice quality inevitably with voice pitch as they both are related with the physics of vocal cords: pitch is estimated by the speed of vibration, type of phonation is judged by the degree of closure and opening of the glottis. The quality of voice can be elucidated as that aspect of voice that makes the voice of every human being sound different from the others. Fluency is defined as one's ability to produce smoothly flowing speech sounds and words while communicating. These include, the rate of speech, the complexity of the words that a person produces in his/her speech and the mean length of utterance. Therefore, problems due to one factor can lead to problems of fluency and thus affect the overall speech of an individual [8,9]. There are 5 normal physiological processes that are contributing to the production of speech. These are, respiration, phonation, resonance, articulation and prosody. Of all these processes, the respiration is of the utmost importance a prerequisite to respiration and its control is appropriate respiration for good production speech; individuals who

have poor control of their respiration are found to have, weak speech. Respiration is one of the most important parts of speech, as it provides the air tides for voice phonation. It supplies the larynx with pulmonic air which is then used to create "phonation" [10,11]. There can be various causes and reasons that the voice is impaired, and due to this the disorders of voice are classified into 3 types on the basis of cause. These types are, structural voice disorders, neurogenic voice disorders. Structural voice disorders are those that occur due to a physical alteration or damage of a structure involved in voice production. The second type of voice disorder is the neurogenic voice disorder. This type of voice disorder occurs as result of nerve damage or impairment of the central nervous system which in turn affects the muscles innervating the larynx for voice production. The third type of voice disorder is the functional voice disorder [12,13]. A study carried out in the USA in 2020 by Ismail and colleagues, hypothesized that COVID-19 signs might be observed through the examination of vocal cord vibration. Results showed that COVID-19 had lead to vocal cord disruption during voice production, and also caused asymmetrical movements of the vocal cords which were then used to spot COVID-19 [14]. As the respiratory system plays an important role in voice and thus speech production, impairment of the system or any of its structure can lead to weakened production of voice. Disorders of the respiratory system affect the voice production. One of such disorders is the pandemic of COVID-19. Which not solely impacted our breathing or respiratory system but it has also led to impact the voice. The voice quality is greatly impacted by the method of human breathing while speaking, by speed and extent of exhalation (in relation with the quantity of words present in the sentences), and by variations and force of being rushed through the larynx. It has been established that COVID-19 impacts the respiratory system and tends to infect the lower respiratory tract. There is a high likelihood that condition may then lead to problems in the upper respiratory tract. Infection of the lower tract can cause the vocal cords and the larynx to work inefficiently leading to an improper voice production for speech tasks. [15-19]. A study was carried out in Germany by Bartl-Pokorny and colleagues in 2020 which also aimed at studying changes in voice using acoustic analysis. The study highlighted that the means of segment length of voice and the frequency of voiced segments produces the most imperative alterations among all the vowels demonstrating gaps and breaks in the airstream pathway during voice production in Covid-19 infected individuals [20]. A study by Pinkas and colleagues was carried out in 2020 The researchers hypothesized that use of an electronic application could be used to diagnose COVID-19 and help identify the presence

of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The patients went through swab testing and were grouped into COVID-19 positive patients, the COVID-19 negative individuals were included in the control group for the study [21]. A study was carried out in 2018, highlighting how an upper respiratory tract infection can lead to a direct impact on the larynx and especially the vocal cords. A person is diagnosed with unilateral and idiopathic vocal cord paralysis if the vocal cord paralysis occurs without any proper cause or reason. The mentioned research was aimed to scrutinize cases of idiopathic vocal cord paralysis that were reported in institutions and also to shed light on whether there is an association between the upper respiratory tract and its infections and the occurrence of idiopathic paralysis of the vocal folds [22].

METHODS

Investigation was carried out from June 2020 to January 2021. A cross-sectional natured design was decided for the study and was used to compile data retrospectively from two private trust hospitals of Lahore. Approval from the Internal Review Board (IRB) of the University of Lahore was first obtained. After this, the specimens were ruled to be accumulated through convenient non-probability selection procedure or sampling method with ages between 20 and 50 years who had tested positive in Covid-19 Polymerase Chain Reaction (PCR) tests. 379 were chosen to participate in the research after the sample sizes of the previous research studies related to voice were studied. Those subjects were included who had the infection a month ago or less. Individuals who had co-morbid breathing or voice problems or hormonal diseases that could influence the results were not included. An informed consent in written manner was attained from the subjects, specimens were collected through the Voice Handicap Index (VHI) questionnaire, used in many researches after proper validation of the tool. The questionnaire consists of 30 questions that help record various voice concerns patients had suffered from and also help to recognize and identify the presence of any voice changes. Demographic related details and information pertaining to gender, occupation, duration of infection, duration of voice problems was amassed from each subject. The speech and language pathologist/therapist entered the data in the questionnaire related to the voice changes, issues and symptoms experienced by the patients. Data were analyzed using SPSS 22.0 to determine the how frequent were voice changes and issues experienced by the diagnosed population. Demographic related variables were designated out by descriptive statistics. Frequencies, percentages and quantities were scrutinized using categorical type of data.

RESULTS

Table 1. Provides general information regarding the 379 participants, age range was divided into 3 categories, gender was divided into 2 categories and occupations of the subjects were divided into 3 categories. The results indicate that most participants fell between 20 to 30 years' age. Data was compiled more from females than males. 64.4 % of the subjects were between ages 20 to 30 years. 55.7% of the population was female in the study. 68.9 % individuals were found to fall in the professional category.

Demographics	Frequency	Percentage	
Age	20-30 years	244	64.4
	31-40 years	39	10.3
	41-50 years	96	25.3
Gender	Male	168	44.3
	Female	211	55.7
Occupation	Student	66	17.4
	Professional	251	68.9
	Unemployed	52	13.7

Table 1: Demographics related to the participants

Table 2 was made to divide the observed voice changes into 3 basic groupings. Weak and shaky voice, unclear voice and voice changes noticed after an entire day of speaking were noted as 3 distinct traits related to voice change. The table provides the evidence that voice changes were found to be present in majority of the subjects involved in this research.

Voice changes observed	Frequency	Percentage	
Shaky and weak sounding voice	Never	64	16.9
	Almost Never	52	13.7
	Sometimes	151	39.8
	Almost Always	67	17.7
	Always	45	11.9
Voice was not clear during speech	Never	83	21.9
	Almost Never	55	14.5
	Sometimes	118	31.1
	Almost Always	61	16.1
	Always	62	16.4

Table 2: Indicating specific voice changes observed and recorded

Voice changed after using it entire day	Frequency	Percentage
Never	90	23.7
Almost Never	47	12.4
Sometimes	118	31.1
Almost Always	94	24.8
Always	30	7.9

Table 3: frequencies

DISCUSSION

This research is meant to help aid Covid-19 diagnosis by the presence of voice changes in infected individuals. The voice changes were noted through the use of a questionnaire. This helped the infected people choose

from a given number of options the option that suited them the most regarding their voice during their quarantine period. Another research that aimed at using sounds to diagnose Covid-19 was carried out by Brown and colleagues. In this research sounds of cough and breathing were compared between the Covid-19 positive. In this investigation, more females participated in data collection whereas in the study by Brown and colleagues, more data was collected by males than females. The age group from which data was mostly collected was 20-30 years, whereas more people from 30-39 age group participated in the other study [25, 26]. An article was published by Almada and Maranhao which highlighted voice symptoms in relation with a Covid-19 infection similar to the essence and theme of my research study. Their study aims to promote more voice-based research in correlation with Covid-19 which was performed in my study. They argue that voice change has been a symptom of infections of the respiratory tract and asthma and that its application in this area may lead to a new approach to the Covid-19 infection which is similar to the objective of the existing study. The current investigation was intended to deliver evidence that voice changes can occur during Covid-19 which has been the notion behind the article written by Almada and Maranhao as well [26]. The study by Asiaee and colleagues used the probability sampling technique for employing healthy individuals and used non-probability sampling technique, convenient sampling for data collection of infected patients. This is similar to present research since it also uses the non-probability type, convenient sampling for data collection. The data in their study was collected from a hospital which matches with this study as data was collected from two hospitals. Some of the infected participants chosen in their study passed away during the data collection procedure due to complications of the Covid-19 infection. The present study collected data from individuals who recovered from Covid-19 and are alive and well [27]. The study carried out by Deshmukh and colleagues was a comparative study between infected and healthy individuals whereas my study was completely on Covid-19 positive individuals. This study was a cross-sectional study, the data was collected during the time the individuals were infected whereas my study was a retrospective study and the data was collected after the recovery of the Covid-19 patients. The results of the study carried out by Deshmukh and colleagues indicated that voice flow changes were observed in infected patients which is similar to the results of my study as well, that showed that voice changes were observed in infected patients most of the time during the infection [28]

CONCLUSION

The presence of a shaky and weak voice also indicates that

participants' voices went through a change and had become relatively weaker and shakier than their normal healthy voice. It was also proved that voice change after its use for the entire day was also commonly noted issue in the subjects involved. The voice sounded unclear to the listeners when the participants talked indicating that due to Covid-19 infection their voices changed and had become difficult to be understood by the listeners on the phone or through a barrier placed between the subjects and the family members for isolation. These voice changes observed in the patients are unavoidable, as Covid-19 infection is a respiratory tract infection. The respiratory tract is important for the production of a normal voice. It is highly unlikely for a compromised respiratory tract to produce a normal healthy voice. The respiratory tract's function becomes restricted and therefore leads to changes in the voice. This study highlighted the presence of voice changes and how they were identified through the experiences of Covid-19 patients.

REFERENCES

- [1] Sillars AL, Vangelisti AL. Communication: Basic properties and their relevance to relationship research.
- [2] Speaks CE. Introduction to sound: acoustics for the hearing and speech sciences. Plural Publishing; 2017 Dec 29.
- [3] Zhang Y, Zheng X, Xue Q. A Deep Neural Network Based Glottal Flow Model for Predicting Fluid-Structure Interactions during Voice Production. *Appl Sci (Basel)*. 2020 Jan 2;10(2):705. doi: 10.3390/app10020705
- [4] Zhang Z. Mechanics of human voice production and control. *J Acoust Soc Am*. 2016 Oct;140(4):2614. doi: 10.1121/1.4964509
- [5] Six elements of Vocal Variety and how to master them part 1- volume [Internet]. Inter-activ.co.uk. 2017 [cited 2021 Mar 31]. Available from: <https://www.inter-activ.co.uk/presentation-skills/six-elements-of-vocal-variety-and-how-to-master-them-part-1-volume/>
- [6] Harger D. The Effects of Sleep Deprivation on the Acoustic and Perceptual Characteristics of Voice (Doctoral dissertation, University of Colorado at Boulder).
- [7] Johnson J, Puts DA. Voice pitch. *Encyclopedia of evolutionary psychological science*. 2021:8461-3. doi:10.1007/978-3-319-16999-6_1414-2
- [8] Penttilä N, Korpijaakko-Huuhka AM, Kent RD. Auditory-Perceptual Assessment of Fluency in Typical and Neurologically Disordered Speech. *J Speech Lang Hear Res*. 2018 May 17;61(5):1086-1103.

- doi:10.1044/2018_JSLHR-S-17-0326
- [9] Penttilä N, Korpijaakko-Huuhka AM, Kent RD. Auditory-Perceptual Assessment of Fluency in Typical and Neurologically Disordered Speech. *J Speech Lang Hear Res.* 2018 May 17;61(5):1086-1103. doi:10.1044/2018_JSLHR-S-17-0326.
- [10] Schölderle T, Haas E, Baumeister S, Ziegler W. Intelligibility, Articulation Rate, Fluency, and Communicative Efficiency in Typically Developing Children. *J Speech Lang Hear Res.* 2021 Jul 16;64(7):2575-2585. doi: 10.1044/2021_JSLHR-20-00640
- [11] Blumberg MI. Respiration and speech in the cerebral palsied child. *AMA Am J Dis Child.* 1955 Jan;89(1):48-53. doi:10.1001/archpedi.1955.02050110064009
- [12] Lee SJ, Choi HS, Kim H. A Comparison of Voice Activity and Participation Profiles Among Etiological Groups. *J Voice.* 2019 Sep;33(5):804.e5-804.e12. doi:10.1016/j.jvoice.2018.04.016.
- [13] Singh U, Kumar SS. Perception of Stuttering in Individuals With Stuttering. *Indian Journal of Otolaryngology and Head & Neck Surgery.* 2021 Jan 21:1-1. doi.10.1007/s12070-020-02344-4
- [14] Al Ismail M, Deshmukh S, Singh R. Detection of COVID-19 through the analysis of vocal fold oscillations. InICASSP 2021-2021 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP) 2021 Jun 6(pp. 1035-1039). IEEE. doi.10.1109/ICASSP39728.2021.9414201
- [15] Hixon TJ. *Respiratory function in speech and song.* College-Hill; 1987.
- [16] Zhang Z. Mechanics of human voice production and control. *J Acoust Soc Am.* 2016 Oct;140(4):2614. doi:10.1121/1.4964509.
- [17] Gramming P, Sundberg J, Ternström S, Leanderson R, Perkins WH. Relationship between changes in voice pitch and loudness. *Journal of voice.* 1988 Jan 1;2(2):118-26. doi.10.1016/S0892-1997(88)80067-5
- [18] Quatieri TF, Talkar T, Palmer JS. A Framework for Biomarkers of COVID-19 Based on Coordination of Speech-Production Subsystems. *IEEE Open J Eng Med Biol.* 2020 May 29;1:203-206. doi: 10.1109/OJEMB.2020.2998051
- [19] Emerich Gordon K, Reed O. The Role of the Pelvic Floor in Respiration: A Multidisciplinary Literature Review. *J Voice.* 2020 Mar;34(2):243-249. doi: 10.1016/j.jvoice.2018.09.024.
- [20] Bartl-Pokorny KD, Pokorny FB, Batliner A, Amiriparian S, Semertzidou A, Eyben F, et al. The voice of COVID-19: Acoustic correlates of infection in sustained vowels. *J Acoust Soc Am.* 2021 Jun; 149(6):4377. doi:10.1121/10.0005194
- [21] Pinkas G, Karny Y, Malachi A, Barkai G, Bachar G, Aharonson V. SARS-CoV-2 Detection From Voice. *IEEE Open J Eng Med Biol.* 2020 Sep 24;1:268-274. doi:10.1109/OJEMB.2020.3026468.
- [22] Bhatt NK, Pipkorn P, Paniello RC. Association between Upper Respiratory Infection and Idiopathic Unilateral Vocal Fold Paralysis. *Ann Otol Rhinol Laryngol.* 2018 Oct;127(10):667-671. doi: 10.1177/0003489418787542.
- [23] Jacobson BH, Johnson A, Grywalski C, Silbergleit A, Jacobson G, Benninger MS, et al. The voice handicap index (VHI) development and validation. *American journal of speech-language pathology.* 1997 Aug;6(3):66-70. doi.10.1044/1058-0360.0603.66
- [24] Cantarella G, Aldè M, Consonni D, Zuccotti G, Bernardino FD, Barozzi S, et al. Prevalence of Dysphonia in Non hospitalized Patients with COVID-19 in Lombardy, the Italian Epicenter of the Pandemic. *J Voice.* 2021 Mar 14:S0892-1997(21)00108-9. doi:10.1016/j.jvoice.2021.03.009.
- [25] Han J, Brown C, Chauhan J, Grammenos A, Hasthanasombat A, Spathis D, Xia T, et al. Exploring automatic COVID-19 diagnosis via voice and symptoms from crowdsourced data. InICASSP 2021-2021 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP) 2021 Jun 6 (pp.83288332).IEEE. doi.10.1109/ICASSP39728.2021.9414576
- [26] Almada M, Maranhão J. Voice-based diagnosis of covid-19: ethical and legal challenges. *International DataPrivacyLaw.* 2021Feb;11(1):6375. doi.10.1093/idpl/ipab004
- [27] Asiaee M, Vahedian-Azimi A, Atashi SS, Keramatfar A, Nourbakhsh M. Voice Quality Evaluation in Patients With COVID-19: An Acoustic Analysis. *J Voice.* 2020 Oct1:S08921997(20)303684. doi:10.1016/j.jvoice.2020.09.024.
- [28] Khoudja MA, Fareh M, Bouarfa H. Ontology matching using neural networks: survey and analysis. In2018 international conference on applied smart systems (ICASS)2018Nov24(pp.16).IEEE. doi.10.1109/ICASSP39728.2021.9414530



Original Article

Importance of Iron Deficiency in Patients with Recurrent Aphthous Stomatitis

Mehmil Aslam¹, Arfat Bashir², Zafar Abbas^{3*}, Muhammad Saad Ul Hassan⁴, Amna Afridi⁴, Syed Akbar Abbas Zaidi⁵¹Hamdard University, Karachi, Pakistan²Oral and maxillofacial surgery department, Jinnah Sindh Medical University, Karachi, Pakistan³Dow International dental college, Karachi, Pakistan⁴Liaquat College of Medicine and Dentistry, Karachi, Pakistan⁵Dental Education Department, Bahria University of Health Sciences, Karachi, Pakistan

ARTICLE INFO

Key Words:

Iron, Ferritin, Hemoglobin

How to Cite:

Aslam, M. ., Bashir, A. ., Abbas, Z., Saad Ul Hassan, M. ., Afridi, A. . & Abbas Zaidi, S. A. (2022). Importance Of Iron Deficiency in Patients with Recurrent Aphthous Stomatitis: Iron Deficiency in Patients with Recurrent Aphthous Stomatitis. Pakistan BioMedical Journal, 5(6).<https://doi.org/10.54393/pbmj.v5i6.528>

*Corresponding Author:

Zafar Abbas

Dow International dental college, Karachi, Pakistan

Drzafarabbas10@gmail.com

Received Date: 8th June, 2022

Acceptance Date: 22nd June, 2022

Published Date: 30th June, 2022

ABSTRACT

Aphtha is a Greek word for ulceration which is a common problem in dentistry for diagnosis and treatment. **Objective:** To assess serum levels of iron among patients with RAS and its comparison with the control group. **Methods:** The analysis involved 150 subjects alienated into 2 groups as a group with recurrence of aphthous ulcer and a control group. The 75 patients were encompassed in the control group and 70 in the aphthous ulcer matched for age and sex. Based on the history and clinical examination, the diagnosis of RAS was made. By ELISA test and ELX 800 Absorbance Microplate Reader tool, Serum ferritin was measured, while micro-lab 300 was used to evaluate serum hemoglobin and iron levels. **Results:** Grounded on standard values of laboratory investigations, serum levels of iron were suggestively lower in patients of RAS in comparison to the control group. Minor RAS type was observed in 71 patients (94.7%), while major RAS was reported in 4 patients (5.3%). Out of 75, 20% had multiple ulcers and 80% had a single ulcer. While RAS was localized in non-keratinized mucous membrane in 64 patients (85.3%), in 6 patients (8%); RAS was located in keratinized mucous membrane and both non-keratinized and keratinized mucosa were seen in 5 subjects (6.7%). **Conclusion:** The presence of iron deficiency has been linked to recurrent aphthous stomatitis.

INTRODUCTION

Aphtha is a Greek word for ulceration which is a common problem in dentistry for diagnosis and treatment [1-2]. A feature of RAS is erythematous ulcers of the oral mucosa, which might be multiple or single, with a history of shallow necrotic center surrounded by raised margins and recurrence, with erythematous halo and gray-yellow pseudo-membrane. A patient with RAS will experience pain in the mouth, ranging from simple discomfort to soreness with normal oral functions such as chewing and swallowing [3-4]. Children are apparently up to 39% more affected, and patients who have positive family history are most likely to progress towards RAS than without family history [5]. These recurrent ulcers are classified by size, type, healing time as large or minor RAS, and herpetic ulcers and

numbers of RAS. The maximum communal type is minor one, accounting for 82% of all types [6-7]. This disease is of unknown etiology and multifactorial. The utmost probable triggers are localized injury, stress and genetic predisposition. The nutritional deficiencies, systemic diseases, endocrine disorders, food allergies and cessation of smoking might also be taken as related factors [8]. It is assumed that the contributory agents cause oxidative stress, but the particular reason of RAS is still not clear. The exact pathogenesis and etiology of RAS has not been recognized. Hematological deficits also suggested to be a possible etiological factor, but the data presented are still contradictory, possibly due to ethnic, geographical and dietary differences [9-10]. Since oral epithelium may thin

out and atrophy in the absenteeism of blood cells, RAS may be due to anemia in the absence of any complications. Oral epithelial atrophy makes it more susceptible to injury and creates a favorable environment for the penetration of the bacterial antigen, one of the reasons tangled in the RAS pathogenesis. In Pakistan, hematological abnormalities are common in 19% to 29% of the over-all population, and about 1.4% of individuals suffer from anemia [11]. This morbidity is instigated by iron deficiency and can be detected by non-invasive approaches such as serum ferritin (SFer), serum iron (SI) and hemoglobin (Hgb) [12]. This study was designed to assess serum levels of iron among patients with RAS and its comparison with the control group.

METHODS

This case-control study was held in the dental outpatient department (OPD) of Hamdard University, Karachi for six-months duration from July 2021 to December 2021. Formal approval of the Ethics Review Committee was obtained prior to the start of the research. Total 150 subjects were included using a non-probability technique of sampling, and after meeting the inclusion and exclusion criteria, they were alienated into 2 groups: patients with RAS from group I (75) and controls from group II (75). The criteria of selection for group I were subjects of all ages and sexes with an active aphthous lesion with a history of recurrent attacks of mouth ulcers at least three times a year. Healthy subjects with no history of any systemic disease and aphthous stomatitis were encompassed in control group. Recurrent aphthous ulcer was identified on the base of clinical examination and history. The criteria of exclusion was aphthous ulcers in the last 2 months, lactation, pregnancy, alcohol use, smoking and any oral lesions other than iron supplementation, use of immunomodulatory agents, taken any therapeutic regimen, multivitamins and steroids. Demographic information, namely gender, age, history of systemic diseases and occupation was recorded. The oral mucosa was carefully examined for the size, type, location and number of the ulcers. Venous blood was collected from study participants and submitted to a laboratory for evaluation. By ELISA test and ELX 800 Absorbance Microplate Reader tool, Serum ferritin was measured, while micro-lab 300 was used to evaluate serum hemoglobin and iron levels. The collected data was entered into the SPSS 21.0 for analysis. Gender is articulated as frequency and percentage and arithmetic variables such as ferritin, age, iron and Hb levels are stated as standard and mean deviation. The significant difference was determined with an independent t-test in means amid patients and controls. P values less than or equal to 0.05 were measured significant with the confidence interval of 5%.

RESULTS

In RAS group I; there were 50 women (66.7%) and 25 men (33.3%), while in control group II; there were 43 women (57.3%) and 32 men (42.7%). The RAS group mean age was (29.02±8.95)years, and that of the control group was (31.11±7.2)years. The mean ages comparison among the RAS and the control group was not significant ($p > 0.05$).

Demographic Features	Group I (RAS) n = (75)	Group II (Control) n = (75)
Age(years)10-20 years	13(17.3%)	10 (14.2%)
21-30 years	39 (52%)	32 (45.7%)
31-40 years	23 (30.7%)	28 (40%)
Gender		
Male	25 (33.3%)	32 (42.7%)
Female	50 (66.7%)	43 (57.3%)

Table 1: Demographic Features of Patients and Control Group

The features of patients in group I and II by age and sex is presented in Table 1. It was found that the change in the level of ferritin among the control and RAS group was significant in the 21-30 years and 30-40 years age group ($p < 0.005$). When comparing the gender, a significant difference was found at $p < 0.05$ for women, Table 2.

Demographic Features	Group I (RAS) n = (75)	Group II (Control) n = (75)	p-value
Age (years)	Ferritin (ng/ml) Mean±SD	Ferritin (ng/ml) Mean±SD	
10-20 years	28.01±11.2	35.64± 20.1	0.39
21-30 years	24.10±13	36.0± 14	0.003
31-40 years	24.2±11	36.20± 16	0.003
Gender			
Male	37.9±15.9	42.31± 10.1	0.43
Female	28.2±14.8	41.02± 18.2	0.00

Table 2: Demographic Features Conferring to The Patient's and Control's Serum Ferritin Levels

Mean hemoglobin levels in the 21-30 and 31-40 age-group in the RAS group were significantly lower than the control group ($p < 0.05$) (Table 3).

Demographic Features	Group I (RAS) n = (75)	Group II (Control) n = (75)	p-value
Age (years)	Hemoglobin (g/dl) Mean±SD	Hemoglobin (g/dl) Mean±SD	
10-20 years	12.1±1.3	12.9±2.4	0.11
21-30 years	11.8±1.9	15.1±1.8	0.01
31-40 years	13.1±1.5	14.8±1.2	0.01
Gender			
Male	15.1±1.2	14.9±0.9	0.10
Female	12.9±2.3	15.1±1.1	0.01

Table 3: Demographic Features Conferring to The Patient's and Control's Serum Hemoglobin Levels

Minor RAS type was observed in 71 patients (94.7%), while major RAS was reported in 4 patients (5.3%). Out of 75, 20% had multiple ulcers and 80% had a single ulcer. While RAS was localized in non-keratinized mucous membrane in 64 patients (85.3%), in 6 patients (8%); RAS was located in

keratinized mucous membrane and both non-keratinized and keratinized mucosa were seen in 5 subjects (6.7%).

Age (years)	(n=75) Group I (RAS)	(n = 75) Group II (Control)	p-value
	(g/dl) iron Mean±SD	(g/dl) iron Mean±SD	
10-20 years	12.1±1.3	12.9±2.4	0.11
21-30 years	11.8±1.9	15.1±1.8	0.01
31-40 years	13.1±1.5	14.8±1.2	0.01
Gender			
Male	15.1±1.2	14.9±0.9	0.10
Female	12.9±2.3	15.1±1.1	0.01

Table 4: Demographic Features Conferring to The Patient's and Control's

DISCUSSION

Many aspects institute to play a part in the pathogenesis of aphthous stomatitis. It is suggested that the hematological parameters are the most important influences in recurrent aphthous stomatitis. So, in this analysis, hematological parameters were determined among these patients [13]. The present research discovered that 28.76 years is the mean age of patients with RAS, which means they are in their third decade of life. The same situation is reported in the literature. In this study, women are more affected by RAS than men unlike other studies [14]. This may be because women are more prone to endocrine fluctuations and gestation, and are extra predisposed to mental stress. In this analysis, according to other studies, most RAS appear to be of a minor type. We also found that most ulcers are found in non-keratinized mucosa as it is mobile and therefore more susceptible to injuries that predispose to ulcer development. These results are in line with the Islamabad Dental Hospital study. Hematological failure was observed more frequently in patients with RAS in comparison to the group of control [15]. In one study, it is reported that 59% of RAS patients with hematological deficiencies improved after using replacement treatment, while 29% exhibited significant development [16-17]. This study found lower levels of ferritin and hemoglobin in the RAS group in comparison to the control group. These conclusions are reinforced by additional analyses. Due to the decrease level of Hb, the oxygen carrying capacity is reduced in anemic patients, ultimately causing the oral mucosa to atrophy and thus ulcerate [18]. Similarly, iron is necessary for the correct growth and function of oral epithelial cells. It is also a necessary component of the cytochrome oxidase enzyme, which is required for normal epithelial maturation. When there is iron deficiency, levels of cytochrome oxidase fall and ultimately cause atrophy of epithelium, putting the oral mucosa at danger of ulceration. In addition, iron deficiency causes abnormal formation of vascular channels, ensuing in atrophy and reduced blood flow [19-20]. The shortcomings of the study,

in the inadequate sample size and study design, i.e., a cross-sectional study, but believe that this may be useful in signifying a causal association between hematological parameters and RAS. In order to create new treatment options and prophylaxis in patients with RAS, a larger trial of prospective stomatitis studies should be carried out.

CONCLUSION

patients with RAS have higher levels of iron deficiency than the control group, it was concluded that iron deficit was linked to recurrent aphthous stomatitis.

REFERENCES

- [1] Ślebioda Z, Krawiecka E, Szponar E, Dorocka-Bobkowska B. Haematinic deficiencies and patient clinical profiles in Polish patients with RAS(RAS). *Journal of Oral Pathology & Medicine*. 2018 May; 47(5):531-537. doi: 10.1111/jop.12703.
- [2] Lin HP, Wu YH, Wang YP, Wu YC, Chang JY, Sun A. Anemia and hematinic deficiencies in anti-gastric parietal cell antibody-positive or all autoantibodies-negative RASpatients. *Journal of the Formosan Medical Association*. 2017 Feb; 116(2):99-106. doi: 10.1016/j.jfma.2016.10.006.
- [3] Al-Amad SH, Hasan H. Vitamin D and hematinic deficiencies in patients with recurrent aphthous stomatitis. *Clinical Oral Investigation*. 2020 Jul; 24(7):2427-2432. doi: 10.1007/s00784-019-03102-9.
- [4] Chiang CP, Yu-Fong Chang J, Wang YP, Wu YH, Wu YC, Sun A. RAS- Etiology, serum autoantibodies, anemia, hematinic deficiencies, and management. *Journal of the Formosan Medical Association*. 2019 Sep; 118(9):1279-1289. doi: 10.1016/j.jfma.2018.10.023.
- [5] Wu YC, Wu YH, Wang YP, Chang JY, Chen HM, Sun A. Antigastric parietal cell and antithyroid autoantibodies in patients with recurrent aphthous stomatitis. *Journal of the Formosan Medical Association*. 2017 Jan; 116(1):4-9. doi: 10.1016/j.jfma.2016.09.008.
- [6] Gülseren D, Hapa A, Ersoy-Evans S, Elçin G, Karaduman A. Is there a role of food additives in recurrent aphthous stomatitis? A prospective study with patch testing. *International Journal of Dermatology*. 2017 Mar; 56(3):302-306. doi: 10.1111/ijd.13515.
- [7] Nurdiana N, Astari P. Relationship between Recurrent Aphthous Stomatitis with Iron Deficiency Anemia: Hubungan Antara Stomatitis Aftosa Rekuren Dengan Anemia Defisiensi Besi. *Dentika Dental Journal*. 2018 Dec; 21(2):41-6.
- [8] Lin KC, Tsai LL, Ko EC, Sheng-Po Yuan K, Wu SY. Comorbidity profiles among patients with recurrent

- aphthous stomatitis: A case-control study. *Journal of the Formosan Medical Association*. 2019 Mar; 118(3):664-670. doi: 10.1016/j.jfma.2018.10.002.
- [9] Rodriguez-Archilla A, Brykova M. Relevance of hematological parameters in patients with recurrent aphthous stomatitis. *Dentistry and Medical Research*. 2019 Jul;7(2):35.
- [10] Ślebioda Z, Krawiecka E, Szponar E, Dorocka-Bobkowska B. Evaluation of serum zinc levels in patients with RAS(RAS). *BMC Oral Health*. 2017 Dec; 17(1):158. doi: 10.1186/s12903-017-0450-x.
- [11] Al-Amad SH. Helicobacter pylori and gastric hyperacidity, and their association with recurrent aphthous stomatitis. *International Journal of Oral and Maxillofacial Surgery*. 2020 Dec; 49(12):1599-1604. doi: 10.1016/j.ijom.2020.05.013.
- [12] Kareem AH, Al-Emaam MK, Jasim ER. Evaluation of Serum B12, Folic Acid, Iron, Ferritin, Total Iron Binding Capacity and Unsaturated Iron Binding Capacity in Patients with RASin Sulaimani City. *Indian Journal of Public Health Research & Development*. 2020 May; 11(5).
- [13] Tidgundi MS, Moinuddin K, Baig MS. Ferritin and vitamin B12 levels in patients with recurrent aphthous ulcers. *Age*. 2017;39(7.56):37-7. DOI: 10.18231/2394-6377.2017.0032
- [14] Namrata M, Abilasha R. Recurrent aphthous stomatitis. *International journal of orofacial biology*. 2017 Jul; 1(2):43. DOI: 10.4103/ijofb.ijofb_14_17
- [15] Tamer F, Avci E. Decreased serum ferritin and vitamin D levels in patients with recurrent aphthous stomatitis. *Our Dermatology Online Journal*. 2019 Mar; 10(3). doi.org/10.7241/ourd.20193.1
- [16] Chiang CP, Wu YH, Yu-Fong Chang J, Wang YP, Chen HM, Sun A. Serum thyroid autoantibodies are not associated with anemia, hematinic deficiencies, and hyperhomocysteinemia in patients with Behcet's disease. *Journal of Dental Sciences*. 2018 Sep;13(3):256-262. doi: 10.1016/j.jds.2018.05.001.
- [17] Kadir AK, Islam AH, Ruhan M, Mowla A, Nipun JN, Phil M. Recurrent aphthous stomatitis: An overview. *International Journal of Oral Health Dentistry*. 2020; 4:6-11. DOI: 10.18231/2395-499X.2018.0002
- [18] Nalbantoğlu B, Nalbantoğlu A. Vitamin D Levels in Children with Recurrent Aphthous Stomatitis. *Ear, Nose and Throat Journal*. 2020 Aug; 99(7):460-463. doi: 10.1177/0145561319882783.
- [19] Ślebioda Z, Dorocka-Bobkowska B. Systemic and environmental risk factors for RASin a Polish cohort of patients. *Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii*. 2019 Apr; 36(2):196-201. doi: 10.5114/ada.2018.74638.
- [20] Rasi A, Zamanian A, Mehran G, Ezati A, Rastin V, Karimi S. Comparing the effect of injectable vitamin B with conventional oral treatment on aphthous stomatitis. *Journal of Skin and Stem Cell*. 2018 Jun 30;5(1-2). DOI: 10.5812/jssc.69052



Original Article

Incidence of Impacted Canine in Patients Visiting Tertiary Care Hospital of Peshawar, Pakistan

 Neelofar Nausheen¹, Pashmina Nisar¹, Muhammad Saroosh Jamil², Ambereen Humayun³, Muhammad Atae Mustafa Mahayyudin⁴, Ulfat Shehzadi⁵ and Maryam Aslam⁵
¹ Department of Oral Biology, Sardar Begum Dental College, Gandhara University, Peshawar, Pakistan

² Department of Pathology, Rahbar Medical and Dental College, Lahore, Pakistan

³ Department of Anatomy, Peshawar Dental College, Peshawar, Pakistan

⁴ Dalian Medical University, University In Dalian, China

⁵ Department of Life Sciences, School of Science, University of Management and Technology, Lahore, Pakistan

ARTICLE INFO

Key Words:

tooth impaction, Canine, Tooth eruption, egregious imposition, orthomograph (OPG).

How to Cite:

 Nausheen, N. ., Nisar, P. ., Saroosh Jamil, M. ., Humayun, A. ., Atae Mustafa Mahayyudin, M. ., Shehzadi, U. ., & Aslam, M. . (2022). Incidence of Impacted Canine in Patients Visiting Tertiary Care Hospital of Peshawar, Pakistan: Impacted Canine in Patients Visiting Tertiary Care Hospital of Peshawar, Pakistan. *Pakistan BioMedical Journal*, 5(6), 89-92. <https://doi.org/10.54393/pbmj.v5i6.587>

*Corresponding Author:

 Neelofar Nausheen
 Department of Oral Biology, Sardar Begum Dental College, Gandhara University, Peshawar
neelofarnaushen@hotmail.com

Received Date: 22nd June, 2022

Acceptance Date: 27th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Among all the dental problems, tooth impaction is one of the leading dental problems these days. It is stated as the improper infusion when the tooth has erupted at the predicted time. Canine impaction is the most egregious imposition and leads to frequent dental complications.

Objective: To estimate the incidence of impacted canine in patients visiting tertiary care hospital of Peshawar, Pakistan **Methods:** This retrospective study was conducted at Peshawar Dental College from 2018 to 2021. A total of 1326 patients visited the dental health care center during this period **Results:** Out of total 1326 patients, only 64 (4.8%) cases of affected canines were found with the orthomograph (OPG). Furthermore, these 64 individuals had affected canines in various sites, including the mandible, maxillary, left side and right side. Among total 64 patients, 153 impacted teeth were found on different locations. In these 153 impacted teeth, 37(24.2%) incidents of affected canines were recorded on the top right, whereas 49(32%) were documented on the other side. However, 58(37.9%) cases of impacted maxillary canine and only 9 cases (5.9%) of mandibular impacted canine were reported. **Conclusion:** Early diagnosis and treatment processes should be required to prevent different problems of canine impaction. Moreover, proper awareness and treatment approaches should be used in order to eradicate the after-effects of canine impaction.

INTRODUCTION

These days' dental issues are spread frequently around the world [1]. Impactions refer to a pathological condition in which the teeth are unable to grow for a certain time [2]. These conditions also disturb the normal process of eruption. Among all the teeth the canines require a longer period to develop. Due to its complex occlusion route, it is now one of the third most common impactions which occur next to maxillary third molars and mandibular teeth [3]. The impaction of canines varies from one population to another. It is also estimated that about 12 to 15% of people

are generally affected by it [2]. The occurrence of tooth impaction in tribal populations was 5.6 to 18.8% [4-6]. In a study conducted in 2019, 1593 patients OPG's were evaluated to estimate the frequencies of canine anomalies. Impacted canines were found in 22 patients and hence the prevalence was 1.38%, maxillary canine had 0.93%, mandibular canine has 0.37%, canine agenesis in 0.06%, transmigration in 0.12%, canine transposition in 0.18% and ectopic canine in 5.5% patients. No gender difference was observed [7]. Shapira Chaushu and Becker

(2000) observed the rate of impaction in the general population which is 1 to 3% [8]. In Budapest Hungary, a ten-year study has been conducted and it was deduced that the impaction of maxillary canines has a prevalence rate of 5.4% [9]. Many theories have been associated with the impact of canines such as genetic theory and guidance theory. The genetic theory describes that the impaction can be occurred by certain anomalies like missing incisors or small size of incisors. The latter one depicted that the lateral incisors serve as a guide which result allows the growth of canines on the lateral roots of incisors [10, 11]. Moreover, the impaction of canines can be diagnosed by radiographic and clinical examinations. That's why the dental experts examine the condition of impaction based on following parameters; 1) absence of pertaining growth of canines towards the lip region 2) occurrence of palatal bulge in the region of canine. 3) slow growth of permanent canines or growth of deciduous canine in the late age of 14-15 years. 4) splaying of permanent incisors of the lateral region, and prolonged erupting time. 5) the increased All the general parameters for impacted teeth can be omitted but due to the vitality of canine teeth in the person's oral cavity, a little omission can't be afforded. However, the improper treatment of impacted canines, leads towards several complications. Some of them are listed below; 1) formation of dentigerous cyst 2) prevalence of infection due to partial erupting of teeth. 3) impacted tooth promotes the resorption of external roots. 4) the neighboring teeth began to migrate and the length of arch is lost 5) resorption towards internal region 6) occurrence of lingual /labial misplacement due to impaction of canines. 7) severe pain and combined symptoms that have been mentioned above [12]. Moreover, as the canine teeth are the longest among all, any kind of impaction in it can affect the other teeth too which in result affecting the person's aesthetic smile [13]. The occurrence of this impaction varies from one population to another. Due to these variations, an appropriate method for early detection should be eagerly needed for delivering the suitable treatment. In order to guide and erupt the canine teeth in a proper position the early diagnosis of proper orthodontic and surgical examination approaches is useful. The immediate intermediation is required that will prevent the certain complications arising from canine impaction including pathological, aesthetic, and functional. The current study aims to find the canine impaction prevalence in the Pakistani Population

METHODS

The retrospective study was conducted at the Peshawar Dental College from 2018 to 2021. In this three-year study, 1326 patients visited the dental health care center. This particular area considers the ideal setting for the study.

Furthermore, records were appraised from the Radiology Department of this hospital. In general, the members in this the research comprised of both genders between the ages of 13 and 50 years. In this study, those patients were included who had missing permanent canines including mandibular and maxillary on side of the right and left. Nevertheless, those patients were excluded from a study that have any abnormality including pathological conditions for example a tumor, palate, cleft on lip, cyst, as well as odontoma respectively. The collection of data was initiated after obtaining approval by the hospital administration's responsible authority. Orthopantomogram is considered the key method for the data collection which is also called orthomograph (OPG) or panotomograph. Furthermore, a panoramic image representation radiograph of the molars and jaw is used in this instrument, as well as a patient's maxilla. In addition, a questionnaire as a guide was also used in the study which has the information on the demographic profile of a patient. All the information was collected by analyzing the 1326 patient record files. This information was obtained with the assistance of the hospital radiology department. Data was coded for analysis and entry using the SPSS "statistical software tool" (version 21). Descriptive statistics were used for data presented in terms of percentages or frequencies. The percentage however was obtained by multiplying by 100 the probabilities (f) for each of the alternatives divided by the population's number (N). $P = f/N \times 100$ where P is the percentage, f is the frequency of each option, and N is the total population.

RESULTS

Out of total 1326 patients, 556 (41.9%) were males and 770 (58.1%) were females, the age ranging from 13 to 50. Only 64 (4.8%) impacted maxillary canines were founded, in which 29 (45.3%) were males and 35 (54.7%) were females. The most cases 40 (62.5%) were present between aged 13- 25 years' age as compared to ages between 26 to 50 years. Furthermore, these 64 individuals had affected canines in various sites, including the mandible, maxillary, left side and right side. Among total 64 patients, 153 impacted teeth were found on different locations. In these 153 impacted teeth, 37 (24.2%) incidents of affected canines were recorded on the top right, whereas 49 (32%) were documented on the other side. However, 58 (37.9%) cases of impacted maxillary canine and only 9 cases (5.9%) of mandibular impacted canine were reported.

DISCUSSION

In this current study, 4.8% patients were identified with canine impaction who pursue dental health in Hospital. The incidence rate of impacted canines is about 4.8% in present study. The previous research was carried out in

2019, where 22 impacted canine individuals out of 1593 subjects were therefore identified via OPG with 1.38 % of impacted canines. Similarly, 82 canine impacted patients out of 2200 subjects were then identified in 2015 with a prevalence rate of 3.7%. Furthermore, this retrospective analysis depicted that the canine impaction is prevalent at the rate of 1.7% and out of 1593 patients this rate was 1.38 % [14]. A similar study in 2015 conducted by Abu-Hussein and his colleagues, described that females with canine impaction have a high percentage as compared to men with 55.1% and 43.9% respectively. In addition, there was only a 1.7% prevalence of impacted canines out of 8243 patients reviewed via radiograph [15]. Moreover, another cross-sectional retrospective study explained that 146 cases were affected by impacted canines out of 8243 cases of radiographs [16]. According to a current study, the percentage of gender is almost the same. However, in some rare cases, the percentages of affected men compared to women, canine obstruction is marginally greater. Therefore, the percentage of male affected with canine impaction was 51.1% while the percentage of female affected with canine impaction were 48.9% [17] and another study describes that 77 % of men were affected by canine impaction and 23% were women. However, females with impacted canine teeth had a higher percentage (56.1%) in comparison to males (43.9%) observed in 2014 as well [18]. Moreover, the most impacted teeth are canine in the maxillary as well as the maxillary left molar is more likely to be impacted, and affected teeth in the maxilla occur more than twice as common as impacted teeth in the mandible. Moreover, on the upper edge, impacted canines were found in much more than a half of the cases, but on the other side, more than one among the cases had affected teeth. Between September 2013 and December 2018, a retrospective cross-sectional study was conducted, half of the patients had canine impaction on the other side. But more over a third of individuals experienced a canine effect on their right side [19]. A study conducted in 2019 shows no gender difference was found. Furthermore, the highest recorded cases of maxillary canine impaction were found in the recent study. Moreover, a retrospective and cross-sectional study was done in Saudi Arabia, where researchers concluded that canine obstruction in the maxilla is more frequent than tooth impaction in the mandible. Generally, the clinical study that was accompanied in "2016" described that the percentage of maxillary impacted canines is less than one percent (0.93%)[20]. In the current study, the most severe cases of canine impaction received by Mandibular canine impaction with only 3.7% between the patients. On the contrary, there was only 0.37% of cases were recorded with mandibular impacted canine between 22 patients having canine

impaction.

CONCLUSIONS

Several approaches are needed for considering the complexities the canine teeth. Early detection and early treatment methods play a significant role among affected individuals with impacted canines that prevent different problems. Inside the study limitations, the prevalence of canine impaction in this study was 5.9% among participants. Proper and early diagnostic tests, as well as various treatment methods, are required to avoid sequelae occurring because of canine impaction. Finally, preventive methods should be implemented to inhibit the impaction of canines that is also significant. Orthodontists and dentists must work efficiently with patients for improving dental as well as oral health.

REFERENCES

- [1] Litsas G, Acar A. A review of early displaced maxillary canines: etiology, diagnosis and interceptive treatment. *Open Dent J.* 2011 Mar 16;5:39-47. doi: 10.2174/1874210601105010039.
- [2] American Dental Association (2020) Canine Impaction. <https://www.ada.org/en/search-results?q=canine%20impaction&t=all&sort=relevance>
- [3] Watted N. and Abu-Hussein M. Prevalence of Impacted Canines in Arab Population in Israel. *International Journal of Public Health Research*, 2014. 6, 71-77.
- [4] Delli K, Livas C. and Bornstein, M.M. (2013) Lateral Incisor Agenesis, Canine Impaction and Characteristics of Supernumerary Teeth in a South European Male Population. *European Journal of Dentistry*, 7, 278. doi:10.4103/1305-7456.115410
- [5] Thilander B, Myrberg N. The prevalence of malocclusion in Swedish schoolchildren. *Scand J Dent Res.* 1973;81(1):12-21. doi: 10.1111/j.1600-0722.1973.tb01489.x.
- [6] Shah, R.M., Rm, S., Ma, B. and Tf, V. (1978) Studies of Permanent Tooth Anomalies in 7,886 Canadian Individuals. II. Congenitally Missing, Supernumerary and Peg Teeth.
- [7] Jain S, Debbarma S. Patterns and prevalence of canine anomalies in orthodontic patients. *Med Pharm Rep.* 2019 Jan;92(1):72-78. doi: 10.15386/cjmed-907.
- [8] Shapira J, Chaushu S, Becker A. Prevalence of tooth transposition, third molar agenesis, and maxillary canine impaction in individuals with Down syndrome. *Angle Orthod.* 2000 Aug;70(4):290-6. doi: 10.1043/0003-3219(2000)070<0290
- [9] Al-Zoubi H., Alharbi AA, Ferguson DJ and Zafar MS.

- Frequency of Impacted Teeth and Categorization of Impacted Canines: A Retrospective Radiographic Study Using Orthopantomograms. *European Journal of Dentistry*, 2017. 11, 1171-121. doi:10.4103/ejd.ejd_308_16
- [10] Celikoglu M., Kamak H and Oktay H. Investigation of Transmigrated and Impacted Maxillary and Mandibular Canine Teeth in an Orthodontic Patient Population. *Journal of Oral and Maxillofacial Surgery*, 2010. 68, 1001-1006. doi:10.1016/j.joms.2009.09.006
- [11] Mann, R, Gandikota C, Juvvadi SR, Rama HRM and Anche S. Impacted Canines: Etiology, Diagnosis, and Orthodontic Management. *Journal of Pharmacy & Bioallied Sciences*, 2012. 4, S234-S238. <https://doi.org/10.4103/0975-7406.100216>
- [12] Garib DG, Alencar BM, Lauris JRP and Baccetti T. Agenesis of Maxillary Lateral Incisors and Associated Dental Anomalies. *American Journal of Orthodontics and Dentofacial Orthopedics*, 2010. 137, 732-e1. doi:10.1016/j.ajodo.2009.12.024
- [13] Shafer WG, Hine MK and Levy BM. *A Textbook of Oral Pathology*. 1963. 2nd Edition, WB Saunders, Philadelphia, 2-75.
- [14] Abutayyem H. Prevalence of Impacted Maxillary Canines and Its Associated Anomalies among a Dental College Patients. *EC Dental Science*, 2019. 18, 2048-2058.
- [15] Abu-Hussein M, Watted N, Azzaldeen A, Yehia M, Awadi O and Abu-Hussein Y. Prevalence of Malocclusion and Impacted Canine in Arab Israelian Population (Arab48). *International Journal of Public Health Research*, 2015. 3, 180-191.
- [16] Manne R, Gandikota S, Juvvadi SR, Reddy H, Rama M, Anche S. Impacted canines: Etiology, diagnosis, and orthodontic management. *J Pharm Bioallied Sci*. 2012 Aug; 4(Suppl 2): S234-S238. doi: 10.4103/0975-7406.100216.
- [17] Mercuri E, Cassetta M, Cavallini C, Vicari D, Leonardi R, Barbato E. Dental anomalies and clinical features in patients with maxillary canine impaction: A retrospective study. *Med Oral Patol Oral Cir Bucal*. 2013 Jul; 18(4):e597-e602. doi:10.4317/medoral.18746
- [18] Arandi, N., Rabi, T. and Mustafa, S. The Prevalence of Impacted Maxillary Canines in a Palestinian Population: A Retrospective Study. *Open Journal of Stomatology*, 2017. 7, 283-290.
- [19] Kumar S, Mehrotra P, Bhagchandani J, Singh A, Garg A, Kumar S et al. Localization of Impacted Canines. *J Clin Diagn Res*. 2015 Jan; 9(1): ZE11-ZE14. doi: 10.7860/JCDR/2015/10529.5480
- [20] Alyami B, Braimah R, Alharieth S. Prevalence and pattern of impacted canines in Najran, South Western Saudi Arabian population. *Saudi Dent J*. 2020 Sep; 32(6):300-305. doi:10.1016/j.sdentj.2019.10.002.



Original Article

Knowledge, Attitude and Practices about Vitamin D among Females suffering from vitamin D deficiency

Marwa Zulfiqar¹, Raima Mariam¹, Barira Waseem¹, Ayesha Zafar¹, Fatima Sheraz¹, Amsa Fatima¹, Misbah Arshad¹¹The University of Lahore, Lahore, Pakistan

ARTICLE INFO

Key Words:

Knowledge, Attitude, Vitamin D, Females, Deficiency, Foods

How to Cite:

Zulfiqar, M. ., Mariam, R. ., Waseem, B. ., Zafar, A., Sheraz, F. ., Fatima, A. ., & Arshad, M. . (2022). Knowledge, Attitude and Practices about Vitamin D among Females suffering from vitamin D deficiency : Vitamin D among Females suffering from vitamin D deficiency. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.508>

*Corresponding Author:

Misbah Arshad

The University of Lahore, Lahore, Pakistan

Fatimamisbah10@gmail.com

Received Date: 26th May, 2022

Acceptance Date: 20th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Vitamin D is essential for supporting women's health throughout their lifespan. A fundamental function of Vitamin D is to regulate the metabolism and absorption of our bone health. Vitamin D deficiency can occur in young women, especially those who are pregnant, and the risk of this increases with age. **Objective:** To highlight the growing preponderance, attitude and beliefs of women regarding Vitamin D. **Methods:** At the Jinnah Hospital in Lahore a comparative cross-sectional study was conducted. A non-probability convenient sampling strategy was used to select 100 ladies. A pre-tested questionnaire was used to evaluate the participants. The data were analyzed using SPSS version 20.0. All females aged between 20 to 90 years suffering from Vitamin D deficiency admitted in Jinnah Hospital, Lahore were included. **Results:** Out of 100 patients 56 of them answered that they were consuming vitamin D supplements <1- 2 times in a month, 33 of them said 2-3 times in a month while the remaining 11 said 4-6 times in a month. **Conclusions:** Women were greatly affected by the it's deficiency. Vitamin D deficiency was more prevalent in early ages as in the older age. The women significantly lacked knowledge about the foods to be consumed and the right nutrition intake for Vitamin d deficiency.

INTRODUCTION

Vitamin D is essential for supporting women's health throughout their lifespan. A fundamental function of Vitamin d is to regulate the metabolism and absorption of our bone health. Vitamin D deficiency can occur in young women, especially those who are pregnant, and the risk of this increases with age [1]. Vitamin D is naturally present in food sources which include mackerel, salmon and sardines, egg yolk, liver, red meat, and fortified foods such as cereals and margarine are naturally rich food origins of vitamin D [2,3]. Vitamin D is noticed to play a combination of roles in the development of bone. It is also known to be linked to various diseases and mortality [4]. Its drawback in girls will cause growth retardation [5]. During pregnancy, the placenta becomes the main site for extrarenal

activation of vitamins. Pregnant women particularly need to secure their requirement for vitamin D is encountered and that their baby is born with adequate vitamin D for timely infancy [6,7]. The primary origin of vitamin D is sunlight but various women around the world are vitamin D deficient due to the lack of acknowledgment to sunlight [8]. Pregnant women and breastfeeding mothers require 400 mcg per day [9]. The same amount of vitamin D is recommended for women older than 60 years and those who spend more time indoors instead of taking it from the sun. It has been detected that women who have PCOS possess a low level of vitamin D [10]. Women with poor vitamin D grades are more inclined to endure postpartum depression. Despite having abundant sunshine, many

pregnant women have low vitamin D serum levels [11]. This deficiency can lead to low estrogen levels and osteoporosis. Further, 85% of women aged 60 years or older retained low to deficient levels of Vitamin D as of due to this, it lessened their trait of life and gained the hazard of acquiring a disease called Alzheimer's disease and dementia [12-15]. Vitamin D deficiency in women can be inspected using the 25-hydroxyvitamin D radioimmunoassay in guidance of the accurate clinical approach [16]. This particular nutrient can lead us to range the impact of major health problems that affect women, extra than men [17,19]. This study was aimed to highlight the growing preponderance of Vitamin D and educate the women about the significance of Vitamin D in the area of Lahore. This also highlights the attitude and beliefs of women regarding Vitamin D.

METHODS

At the Jinnah Hospital in Lahore a comparative cross-sectional study was conducted. A non-probability convenient sampling strategy was used to select 100 ladies. A pre-tested questionnaire was used to evaluate the participants. The data were analyzed using SPSS version 20.0. Females who did not have Vitamin D deficiency were excluded and if they were under the age of 20 or over the age of 90. In inclusion criteria, all females aged between 20 to 90 years suffering from Vitamin D deficiency admitted in Jinnah Hospital, Lahore were selected.

RESULTS

Out of 100 people, 40 people were below 30 years of age, 39 people were between 30-50 years, 14 people were between 51-70 years of age whereas 7 fell between 71-90 years of age. One was underweight according to the BMI. 65 people maintained healthy body BMI. 24 people were falling in the category of overweight while 10 were obese according to their BMI. Out of 100 people, 36 people were single, 45 people were married. Out of 100 people, 19 people belonged to the lower middle class, 61 people were from middle class and 20 people belonged to Upper class families. When talking about the residential location, 78 people out of 100 lived in urban areas while 22 people came from rural areas, Table 1.

Sr No.	Age				
	<30	30-50	51-70	71-90	Total
1	40	39	14	7	100
	BMI				
	Underweight	Healthy Weight	Overweight	Obese	Total
2	1	65	24	10	100
	Marital Status				
	Single	Married	Widowed	Total	
3	36	45	19	100	

Sr No.	Socio-economic Status			Total
	Lower Middle Class	Middle Class	Upper Class	
4	19	61	20	100
	Residential Location			
	Urban	Rural	Total	
5	78	22	100	

Table 1: Demographic Data

Table 2 shows participant's knowledge about Vitamin D and its deficiency

Sr No.	Heard of vitamin D			Total
	Yes	No		
1.	80	20		100
	Any source of vitamin D			
	Yes	No	Total	
2.	77	23		100
	Vitamin D good for bone health			
	Yes	No	Total	
3.	72	28		100
	Sunlight can give vitamin D			
	Yes	No	Total	
4.	70	30		100
	More than recommendation vitamin D is harmful			
	Yes	No	I don't know	Total
5.	53	24	23	100
	Elderly people are at high risk of vitamin D deficiency			
	Yes	No	I don't know	Total
6.	64	15	21	100
	Inappropriate dietary intakes are related to vitamin D deficiency			
	Yes	No	I don't know	Total
7.	45	32	23	100
	Required vitamin D is produced with direct contact with the sun			
	Yes	No	I don't know	Total
8.	47	27	26	100
	Vitamin D deficiency most important health issue			
	Yes	No	I don't know	Total
9.	42	23	35	100
	Bone pain and fatigue are among the vitamin D deficiency symptoms.			
	Yes	No	I don't know	Total
10.	42	23	35	100

Table 2: Knowledge regarding Vitamin D and its deficiency

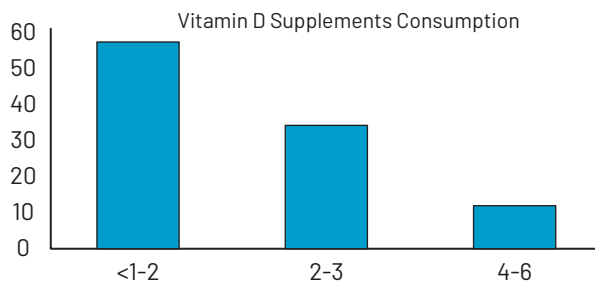
Out of 100 participants 3 of them strongly disagreed with urbanization, 1 with shortage of public place, 1 with full time indoor occupation, 1 with inefficient education, 1 with supplement intake, 1 with recommended by physician and 2 with unwillingness to take vitamin D test, Table 3.

Attitude towards	Attitude					Total
	Strongly agree	Agree	No idea	Disagree	Strongly Disagree	
Urbanization	38	34	21	4	3	100
Shortage of public places	24	39	31	5	1	100
Full time indoor occupation	26	36	29	8	1	100
Inefficient education	22	43	21	13	1	100

Attitude towards	Attitude					Total
	Strongly agree	Agree	No idea	Disagree	Strongly Disagree	
Supplement intake	19	26	37	17	1	100
Recommended by physician	18	27	28	24	3	100
Unwillingness to take vitamin D	31	40	19	8	2	100

Table 3: Attitude regarding Vitamin D deficiency

Out of 100 patients 56 of them answered that they were consuming vitamin D supplements <1- 2 times in a month, 33 of them said 2-3 times in a month while the remaining 11 said 4-6 times in a month, Figure 1.



DISCUSSION

A study was conducted to find out Vitamin D deficiency in the females. The patients were selected through non-probability convenient sampling technique. 80 out of 100 people heard of vitamin D before while 20 people were those who never heard of vitamin D tests before. Amina et al., (2020) conducted a similar study in which 72% participants have never been tested for vitamin D deficiency [20]. Participants had limited knowledge about vitamin D, despite being identified as high-risk population. Another study was conducted by Haq et al., 2017 in which Vitamin D and its effects on the body were well-understood by 72% of those polled. In our study, 66 persons had direct sun exposure on a daily basis, while 34 people did not have direct sun contact on a daily basis. In a similar study, Haq et al., (2017) found that students' attitudes toward sunlight exposure were poor, with 65.2% of students avoiding being in the sun, 62.5% believing that sunlight exposure was harmful to skin, and 65.4% assuming that their Vitamin D levels were sufficient without having their laboratory tests done. When it comes to home location, 78 out of 100 respondents in our research resided in cities, while 22 lived in rural areas. Haq et al., 2017 conducted a similar survey in which the bulk of the respondents, 73 (70.2%), lived in rural areas while only 31 (29.8%) lived in urban areas [21].

CONCLUSION

The study concluded that vitamin D is an essential nutrient

for the proper functioning of body. Women are greatly affected by the its deficiency. Vitamin D deficiency was more prevalent in early ages as in the older age. The women significantly lacked knowledge about the foods to be consumed and the right nutrition intake for Vitamin D deficiency.

REFERENCES

- [1] Prentice A. Vitamin D deficiency: a global perspective. *Nutrition reviews*. 2008 Oct 1;66 (suppl_2): S153-64. doi.org/10.1111/j.1753-4887.2008.00100.x
- [2] Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. *The American journal of clinical nutrition*. 2008 Apr 1;87(4):1080S-6S. doi.org/10.1093/ajcn/87.4.1080S
- [3] Zemb P, Bergman P, Camargo CA, Cavalier E, Cormier C, Courbebaisse M, et al. Vitamin D deficiency and the COVID-19 pandemic. *J Glob Antimicrob Resist*. 2020 Sep 1; 22: 133-4. doi.org/10.1016/j.jgar.2020.05.006
- [4] Lips P DT, Oleksik A, Black D, Cummings S, Cox D, Nickelsen T. A global study of vitamin D status and parathyroid function in postmenopausal women with osteoporosis: baseline data from the multiple outcomes of raloxifene evaluation clinical trial. *The Journal of Clinical Endocrinology & Metabolism* 2001 Mar; 86(3): 1212. doi.org/10.1210/jcem.86.3.7327
- [5] Anagnostis P, Karras S, Goulis DG. Vitamin D in human reproduction: a narrative review. *International journal of clinical practice* 2013 Mar; 67(3): 225-35. doi.org/10.1111/ijcp.12031
- [6] Lips P. Vitamin D deficiency and secondary hyperparathyroidism in the elderly: consequences for bone loss and fractures and therapeutic implications. *Endocrine reviews* 2001 Aug; 22(4): 477-501. doi.org/10.1210/edrv.22.4.0437
- [7] Baker S, Devine A, Miller M, Dare J. A multiliteracies approach to adolescent nutrition education. *Asia Pac Food Nutr Collab Behav Nutr Newsletter* 2017 May; 4 (1): 1-2.
- [8] Health Nif, Excellence C. Vitamin D: supplement use in specific population groups: National Institute for Health and Care Excellence NICE. 2017; 2(1): 3-7.
- [9] Holick MF. Resurrection of vitamin D deficiency and rickets. *The Journal of clinical investigation* 2006 Aug; 116(8): 62-72. doi.org/10.1172/JCI29449
- [10] Bischoff-Ferrari HA, Willett WC, Wong JB, Stuck AE, Staehelin HB, Orav EJ, et al. Prevention of nonvertebral fractures with oral vitamin D and dose dependency: a meta-analysis of randomized

- controlled trials. Archives of internal medicine 2009 Mar; 169(6): 551-61. doi.org/10.1001/archinternmed.2008.600
- [11] Holick MF. The vitamin D deficiency pandemic: a forgotten hormone important for health. Public health reviews 2010 Jun; 32(1): 267-83. doi.org/10.1007/BF03391602
- [12] Ahmed F, Khosravi-Boroujeni H, Khan MR, Roy AK, Raqib R. Prevalence and Predictors of Vitamin D Deficiency and Insufficiency among Pregnant Rural Women in Bangladesh. Nutrients. 2021 Feb;13(2):449. doi.org/10.3390/nu13020449
- [13] Elsammak MY, Al-Wossaibi AA, Al-Howeish A, Alsaeed J. High prevalence of vitamin D deficiency in the sunny Eastern region of Saudi Arabia: a hospital-based study. East Mediterr Health J. 2011 Apr;17(4):317-22. doi.org/10.26719/2011.17.4.317
- [14] Moy FM, Hoe VC, Hairi NN, Vethakkan SR, Bulgiba A. Vitamin D deficiency and depression among women from an urban community in a tropical country. Public health nutrition 2017 Jul; 20(10): 44-50. doi.org/10.1017/S1368980016000811
- [15] O'Connor C, Glatt D, White L, Revuelta Iniesta R. Knowledge, attitudes and perceptions towards vitamin D in a UK adult population: a cross-sectional study. International journal of environmental research and public health 2018 Nov; 15(11): 23- 87. doi.org/10.3390/ijerph15112387
- [16] Shamsi U, Azam I, Shamsi A, Shamsi D, Callen D. Frequency and determinants of vitamin D deficiency among premenopausal and postmenopausal women in Karachi Pakistan. BMC women's health 2021 Dec; 21(1): 1-8. doi.org/10.1186/s12905-021-01339-9
- [17] Mustafa G, Asadi MA, Iqbal I, Bashir N. Low vitamin D status in nursing Pakistani mothers in an environment of ample sunshine: a cross-sectional study. BMC pregnancy and childbirth 2018 Dec; 18(1): 1-7. doi.org/10.1186/s12884-018-2062-0
- [18] Özdemir AA, Gündemir YE, Küçük M, Sarıcı DY, Elgörmüş Y, Çağ Y, et al. Vitamin D deficiency in pregnant women and their infants. Journal of clinical research in pediatric endocrinology 2018 Mar; 10(1): 40-44. doi.org/10.4274/jcrpe.4706
- [19] Jarvis G, Geraghty S. Importance of vitamin D during the antenatal period for maternal well-being. British Journal of Midwifery 2020 Jun; 28(6): 8-253. doi.org/10.12968/bjom.2020.28.6.353
- [20] Tariq A, Khan SR, Basharat A. Assessment of knowledge, attitudes and practice towards Vitamin D among university students in Pakistan. BMC public health 2020 Dec; 20(1): 1-10. doi.org/10.1186/s12889-020-8453-y
- [21] Haq F, Khan R, Mustehsan ZH. Assessment of knowledge, attitude and practices regarding vitamin D among students of Saidu medical college, Swat. Pakistan Journal of Public Health 2017 Jun; 7(1): 1-4. doi.org/10.32413/pjph.v7i1.17



Original Article

Long-Term Outcomes of Ventriculoperitoneal Shunt Surgery in Patients with Hydrocephalus

Naeem UI Haq¹, Inayat Shah¹, Musawer Khan¹¹Department of Neurosurgery, MTI Mardan Medical Complex, Bacha Khan Medical Collage, Mardan, KPK, Pakistan

ARTICLE INFO

Key Words:

VP Shunt, Cerebrospinal Fluid, Hydrocephalus, Peritoneum, Shunt Replacement

How to Cite:

Haq, N. U. ., Shah, I. ., & Khan, M. . (2022). Long-term outcomes of Ventriculoperitoneal Shunt Surgery in Patients with Hydrocephalus: Ventriculoperitoneal Shunt Surgery in Hydrocephalus Patients . Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.509>

*Corresponding Author:

Inayat Shah
 Department of Neurosurgery, MTI Mardan Medical Complex, Bacha Khan Medical Collage, Mardan, KPK, Pakistan
dr.inayatshahgmail.com

Received Date: 27th May, 2022

Acceptance Date: 16th June, 2022

Published Date: 30th June, 2022

ABSTRACT

For the treatment of hydrocephalus, VP shunt surgery is considered the most appropriate method of treatment, but this treatment has a number of complications, it needs to be replaced after the failure of the previous shunt. **Objective:** To evaluate the different regulatory factors involved in the failure of Shunt surgery, the initiation point of shunt failure, and the number of shunt surgeries required after first shunt treatment. The time duration required for shunt failure was also considered to evaluate the lifelong experience with this VP shunt surgery. **Methods:** It is a retrospective study with a statistical approach. This study was conducted in Neurosurgery unit, Mardan medical complex / Bacha khan medical college, Mardan for the Duration of One year August 2020 to July 2021. Patients suffering from hydrocephalus undergoing shunt surgery visited the neurosurgery unit of Mardan Medical complex, Bacha Khan Medical College were included in the study. Complete information related to the etiology, imaging results, demographic distribution, surgery reports, and medical follow-ups were analyzed thoroughly. **Results:** About 25 patients having VP shunt surgery were selected; their average age was above 60 years. The median mean of the follow-ups were 6 and 9 respectively. Patients with having age of more than 18 years are considered adult patients and constituted of the 70 % of the total. The rate of shunt failure was estimated, it was about 46.2 %. The pediatric patients are more prone to shunt failure than the adult ones. Different factors are involved in shunt replacement but age and sex have a major role. Shunt replacement time is quite low in young patients. While in case of age, male patients have a greater number of shunt replacements within their lifespan. **Conclusion:** The results inferred that age has a particular role in the triggering of shunt failure, many other factors are also associated independently to increase the rate of shunt failure. There is a need for controlled studies to understand the link between risk factors and shunt failure rate.

INTRODUCTION

The primary treatment for the patients suffering from hydrocephalus is the bypassing of CSF (cerebrospinal fluid) from the ventricles to the peritoneum and this method is thought to be the more effective method for the treatment. In this disease, fluid initiate to build inside the cavities within the brain, Due to excess amount of fluid, the size of ventricles is enhanced and pressurized the cavity inside the brain [1,2]. If the patient does not recover, then secondary treatments are provided to initiate the recovery process. The third method of treatment is ventriculostomy. The first method of treatment is effective by bypassing spinal fluid required a number of surgeries and revisions of

these surgeries, this thing makes it quite complicated and expensive. This method also creates a number of other complications and put pressure on social and medical budgets. The failure of different surgeries also took place in distal and proximal regions [3-5]. Apart from all adverse effects of primary treatment of the disease, a number of other methods are also used for the treatment of the disease such as neurosurgery. The primary method of treatment by bypassing the cerebrospinal fluid has been proved useless in a number of patients, there is a need to replace and regularly monitor the shunt. But previous studies support this method of VP shunt, this method

improves neurological outputs. A number of risk factors play their role in the failure of the shunt treatment such as demographic distribution of patients, etiology, and type of disorder. A number of other regulatory factors play their role in the failure of the VP shunt method [6]. A few recent studies suggest that the etiology of this disease, sex, and age of the patient have no significant effect on the incidence of failure of this shunt treatment, but other factors play their role in the initiation of failure of the disease. However, if a patient has some kind of tumor in some cranial tissues along with hydrocephalus disease, this tumor independently induces the initiation of failure of the VP shunt surgery, and it triggers the need for a new bypass for the Cerebrospinal fluid. About 25 patients with this VP shunt surgery were tested for the failure of surgery and all the factors related to the failure were considered [7-9].

METHODS

This study was conducted in Neurosurgery unit, Mardan medical complex / Bacha khan medical college, Mardan for the Duration of One year August 2020 to July 2021. The selection of patients was already defined within the introduction, demographic distribution, etiology, age, and sex are all considered. By using different databases, patients were diagnosed with hydrocephalus and were previously treated with VP shunt treatment. Patients were selected from December 2020 to December 2021 for the study of VP shunt failure [10]. Patients having VP shunt surgery were completely assessed by using medical charts for their symptom analysis, results of imaging by ultrasonography, reports of their surgery, and follow-up. The protocol of this surgery was also analyzed to find whether it is approved by CDC (Center for disease control) or not. For more accuracy, the authenticity of the results was also confirmed. Information related to the different factors involved in the failure of shunt treatment, date of treatment initiation, date of replacement of shunt, date of all revisions, and malfunctioning zone and failure were also analyzed [11]. The primary purpose of this research work was to find the number of revisions required after first shunt surgery, the rate of shunt replacement, and all the linked factors involved in the initiation of failure of shunt surgery. Shunt replacement or revision means replacing it with a new shunt or bypass after the first insertion within the patient. When patients were diagnosed, about eight different groups of etiology were observed [12-13]. These etiology groups were idiopathic, cysts, hemorrhage in the cerebral, dysraphism of the spinal, post-traumatic, post-craniotomy, and congenital. Some other etiologies were also observed such as stenosis of an aqueduct, meningitis, and many more [14]. For the comparison of shunt failure

rates in different groups, the Fisher test was used. The group that has a variable shunt failure rate and is not comparable to the Fisher test, was analyzed by the Wilcoxon test. A regression test was used to find out the shunt revisions. Kaplan Meier test was used for survival prediction of the shunt in different time durations. When the probability value of a particular test came out less than 0.05, it was considered significant statistically [15].

RESULTS

The study had 25 patients that participated and VP shunt surgery was carried out on them. At the time of the surgery the median age in the studied patients was 42 and range was from 0-90. Of the 25 patients that were selected 8 (30%) were patients having pediatric problems. These patients had age less than 17 years. The 17 (70%) of the patients were adults at the time of shunt surgery placement. The highly observed conditions were tumor and cyst in 24% of the patients. 19% had cerebral hemorrhage, 19% were with idiopathic issues, and 10% and 8% had congenital and posttraumatic illness respectively. Among all the types of hydrocephalus that was observed, obstructive hydrocephalus was found in 50% of the patients. There were 28% cases of communicating hydrocephalus and 12% cases of normal pressure hydrocephalus found among the patients. The other types represented 8% of the participants of this study (Table 1).

Variable	Number of participants (n=25)	Patients with revisions (n=10)	p-value
Sex	12 (49%)	4 (48%)	<0.01
Male	12 (49%)	5 (48%)	
Female	13 (51%)	4 (44%)	
Ethnicity			<0.01
White	15 (62%)	4 (41%)	
Black	9 (36%)	5 (50%)	
Other	1 (1%)		
Age group			<0.01
Pediatric less than 17 years	8 (30%)	7 (70%)	
Greater than 17 years age	17 (69)	3 (30%)	
Process before insertion of shunt			<0.01
Yes	4 (17%)	3 (30%)	
No	20 (83%)	6 (60%)	
hydrocephalus etiology			<0.01
Tumor	6 (24%)	2 (2%)	
Cerebral hemorrhage	5 (20%)	6 (60%)	
Idiopathic	5 (20%)	2 (20%)	
Congenital	2.5 (10%)	8 (80%)	
Posttraumatic	2 (8%)	4 (40%)	
Spinal dysraphism	2 (8%)	5 (50%)	
Postcraniotomy	1 (4%)	1 (10%)	
Other	2 (8%)	5 (50%)	
Hydrocephalus type			<0.01

Obstructive	12 (25%)	5 (50%)	
Communicative	7 (28%)	4 (40%)	
Normal pressure hydrocephalus	3 (12%)	1 (10%)	
Other	2 (8%)	7 (70%)	

Table 1: Patients Demographics and Rate of Shunt Revisions

Off the 25 patients that were 4 (17%) had already procedures done before the VP shunt surgery. The follow up time means of the included patients, after the initial surgery was calculated as 9 years (Table 2).

Shunt revisions	Pediatric patients	adults	Total
Total patients	8	17	25
Shunt revisions	5 (70%)	6 (40%)	
Mean number of revisions per patient	2	0.6	

Table 2: Patients suffering from Hydrocephalus

DISCUSSION

Although there are advances in the CSF diversionary treatments, improved shunt hardware and endoscopic techniques still the treatment of hydrocephalus is one of the biggest challenges that scientist face right now. Especially because shunting comes with many shunting failures that's why it's malfunctioning provides the scientists with great challenge while designing its treatment [16]. Most of the patients with shunt treatment face this problem in their life that their shunt stops working and it results in failure. Then they had to carry out shunt revisions. As most of the invasive treatment s involve risks and complications it is very important to identify the risk factors that can adversely affect the treatment procedure. Therefore, here a long term analysis was carried out to look for perioperative complications for shunt survival in a small group of patients [17]. One of the limitation is its retrospective study designs. Retrospective study design make the study biased in a randomized controlled trait. Also the diagnostic and the procedure of treatment has no predefined scheme which makes the interpretation biased. Analyzed way cannot be used to study the factors included in present study [18]. The studies revealed that the occurrence rate of shunt revisions in participated patients is 46%. Infants had a greater rate of shunt revisions as compared to adult patients. (78% vs 32%). The incident rates of shunt revisions that we got in our studies matched with the previous reports. The complication rate of shunt treatment in adults with hydrocephalus was obtained as 20%. Berry et al., reported that in a 5-year duration, the infant patients received 24 shunt revisions. Other studies have shown that 14% of the infant patients experienced shunt blockage just in the first month of their treatment. And 40-50% of the patients had reported the shunt failure after the surgery. The shunt complication if take place early prove to be very problematic for patients.

There is need of close monitoring that is required especially during the early few months of the treatment [19]. Studies have reported that type of hydrocephalus, age, etiology, all these factors play important role in causing risk in early shunt failures. Other studies also support these findings that shunt revisions are linked to age, etiological factors, and type of hydrocephalus. Our findings also showed that the age at which the shunt treatment is carried out plays important role in deciding the shunt revisions in multicenter study carried out by Shah et al., it was found that the infants have greatest chances of shunt revisions and the rate of shunt failures increases with each shunt revision. Another study carried out by Tuli et al., demonstrated that the age at which the first shunt is inserted into the patient is most important factor and it plays role in further shunt revisions [20]. Therefore, the multiple shunt revisions need more aggressive clinical follow-up as the shunt failure risk is greater now. However, there are many other risk factors also that plays important role in shunt revisions of the patient. The studies indicate that the complication of shunt revision after the application of initial shunt surgery as well as successive shunt surgeries is time dependent aspect. The Kaplan – Meier survival curve that is drawn to show initial deep slope then it is followed by a steady and balanced slope with the passage of time, which shows that in case of most of the shunt revisions, the revision take place whether it was subsequent or initial shunt surgery [21]. Normally the first steep slope shows the complications that are linked to air-borne contaminations produced during the surgery. Whereas the next slope tells us about the risk and complications those come with the shunt itself. All these studies further support that the deeper steep slope was observed in case of pediatric patients as compared to the non-pediatric patients. Therefore, we can say that these findings show that the shunt revisions percentage incidence is much elevated in infant patients as compared to the adults just after the procedure of initial shunt surgery [22]. In this study we found that the shunt revisions and the associated factors with the failure of shunt procedure in small population. There were multiple risks that were involved in shunt treatment and there were many risks involved after initial shunt application.

CONCLUSION

The retrospective study was carried out top look for the shunt revision rates and the factors that were linked with the failure of suing shunt treatment. There were multiple factors that contributed and it was found that there exists a strong link between the risk factors and shunt survival. Therefore, these complications contribute to decide the shunt survival rates. VP shunt is an effective treatment for

hydrocephalus however it is associated with infection blockage.

REFERENCES

- [1] Paff M, Alexandru-Abrams D, Muhonen M, Loudon W. Ventriculoperitoneal shunt complications: a review. *Interdisciplinary Neurosurgery*. 2018 Sep; 13:66-70. doi.org/10.1016/j.inat.2018.04.004.
- [2] Broggi M, Zattra CM, Schiariti M, Acerbi F, Tringali G, Falco J et al. Diagnosis of Ventriculoperitoneal Shunt Malfunction: A Practical Algorithm. *World Neurosurgery*. 2020 May; 137:e479-e486. doi: 10.1016/j.wneu.2020.02.003.
- [3] Anderson IA, Saukila LF, Robins JMW, Akhunbay-Fudge CY, Goodden JR, Tyagi AK et al. Factors associated with 30-day ventriculoperitoneal shunt failure in pediatric and adult patients. *Journal of Neurosurgery*. 2018 Mar; 130(1):145-153. doi: 10.3171/2017.8.JNS17399.
- [4] Liptak GS, McDonald JV. Ventriculoperitoneal shunts in children: factors affecting shunt survival. *Pediatr Neurosci*. 1985;12(6):289-93. doi: 10.1159/000120268.
- [5] Mallucci CL, Jenkinson MD, Conroy EJ, Hartley JC, Brown M, Dalton J et al. Antibiotic or silver versus standard ventriculoperitoneal shunts (BASICS): a multicentre, single-blinded, randomised trial and economic evaluation. *Lancet*. 2019 Oct; 394(10208):1530-1539. doi: 10.1016/S0140-6736(19)31603-4.
- [6] Azad TD, Zhang Y, Varshneya K, Veeravagu A, Ratliff JK, Li G. Lumboperitoneal and Ventriculoperitoneal Shunting for Idiopathic Intracranial Hypertension Demonstrate Comparable Failure and Complication Rates. *Neurosurgery*. 2020 Feb; 86(2):272-280. doi: 10.1093/neuros/nyz080.
- [7] Lund-Johansen M, Svendsen F, Wester K. Shunt failures and complications in adults as related to shunt type, diagnosis, and the experience of the surgeon. *Neurosurgery*. 1994 Nov; 35(5):839-44; discussion 844. doi: 10.1227/00006123-199411000-00006.
- [8] McGirt MJ, Leveque JC, Wellons JC, Villavicencio AT, Hopkins JS, Fuchs HE et al. Cerebrospinal fluid shunt survival and etiology of failures: a seven-year institutional experience. *Pediatric Neurosurgery*. 2002 May; 36(5):248-55. doi: 10.1159/000058428.
- [9] Mohanty A, Biswas A, Satish S, Vollmer DG. Efficacy of endoscopic third ventriculostomy in fourth ventricular outlet obstruction. *Neurosurgery*. 2008 Nov; 63(5):905-13; discussion 913-4. doi: 10.1227/01.NEU.0000333262.38548.E1.
- [10] Patwardhan RV, Nanda A. Implanted ventricular shunts in the United States: the billion-dollar-a-year cost of hydrocephalus treatment. *Neurosurgery*. 2005 Jan; 56(1):139-44; discussion 144-5. doi: 10.1227/01.neu.0000146206.40375.41.
- [11] Piatt JH Jr, Carlson CV. A search for determinants of cerebrospinal fluid shunt survival: retrospective analysis of a 14-year institutional experience. *Pediatric Neurosurgery*. 1993 Sep-Oct; 19(5):233-41; discussion 242. doi: 10.1159/000120738.
- [12] Piatt JH Jr, Garton HJ. Clinical diagnosis of ventriculoperitoneal shunt failure among children with hydrocephalus. *Pediatric Emergency Care*. 2008 Apr; 24(4):20110. doi:10.1097/PEC.0b013e31816a8d43.
- [13] Prusseit J, Simon M, von der Brelie C, Heep A, Molitor E, Volz S et al. Epidemiology, prevention and management of ventriculoperitoneal shunt infections in children. *Pediatric Neurosurgery*. 2009;45(5):325-36. doi: 10.1159/000257520.
- [14] Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Infection Control & Hospital Epidemiology*. 1999 Apr; 27(2):97-132.
- [15] Puca A, Anile C, Maira G, Rossi G. Cerebrospinal fluid shunting for hydrocephalus in the adult: factors related to shunt revision. *Neurosurgery*. 1991 Dec; 29(6):822-6. doi: 10.1097/00006123-199112000-00003.
- [16] Reddy GK, Bollam P, Caldito G. Ventriculoperitoneal shunt surgery and the risk of shunt infection in patients with hydrocephalus: long-term single institution experience. *World Neurosurgery*. 2012 Jul; 78(1-2):155-63. doi: 10.1016/j.wneu.2011.10.034.
- [17] Reddy GK, Bollam P, Caldito G, Willis B, Guthikonda B, Nanda A. Ventriculoperitoneal shunt complications in hydrocephalus patients with intracranial tumors: an analysis of relevant risk factors. *Journal of neuro-oncology*. 2011 Jun; 103(2):333-42. doi: 10.1007/s11060-010-0393-4.
- [18] Berry JG, Hall MA, Sharma V, Goumnerova L, Slonim AD, Shah SS. A multi-institutional, 5-year analysis of initial and multiple ventricular shunt revisions in children. *Neurosurgery*. 2008 Feb; 62(2):445-53; discussion 453-4. doi:10.1227/01.neu.0000316012.20797.04.
- [19] Bhasin RR, Chen MK, Pincus DW. Salvaging the "lost peritoneum" after ventriculoatrial shunt failures. *Child's Nervous System*. 2007 May; 23(5):483-6. doi.org/10.1007/s00381-006-0292-3.
- [20] Reddy GK, Bollam P, Caldito G. Long-term outcomes of ventriculoperitoneal shunt surgery in patients with hydrocephalus. *World Neurosurgery*. 2014 Feb;

- 81(2):404-10. doi:10.1016/j.wneu.2013.01.096.
- [22] Dobran M, Nasi D, Mancini F, Gladi M, Polonara G, Marini A et al. Relationship between the location of the ventricular catheter tip and the ventriculoperitoneal shunt malfunction. *Clinical neurology and neurosurgery*. 2018 Dec; 175:50-53. doi: 10.1016/j.clineuro.2018.10.006.
- [21] Paudel P, Bista P, Pahari DP, Sharma GR. Ventriculoperitoneal Shunt Complication in Pediatric Hydrocephalus: Risk Factor Analysis from a Single Institution in Nepal. *Asian Journal of Neurosurgery*. 2020 Feb; 15(1):83-87. doi: 10.4103/ajns.AJNS_216_19.



Original Article

Normal Doppler Ultrasonography Indices of Bilateral Common and Internal Carotid Arteries". A Cross Sectional Study

 Qurat ul Ain¹, Shazia Rehma², Furozan Baig¹, Arifa Mobeen¹, Sania Maqbool¹, Mohsina Nasim¹, Amtullah Ansari¹, and Sara Fatima¹
¹ University of Management Sciences & Technology, Lahore, Pakistan² Imperial College of Business Studies, Lahore, Pakistan

ARTICLE INFO

Key Words:

Doppler Ultrasonography, Internal carotid artery (ICD)

How to Cite:

 Ain , Q. ul ., Rehma , S. ., Baig , F. ., Mobeen, A. ., Maqbool, S. ., Nasim, M. ., Ansari , A. ., & Fatima, S. . . (2022). Normal Doppler Ultrasonography Indices of Bilateral Common and Internal Carotid Arteries". A Cross Sectional Study: Normal Doppler U/S Indices of Carotid Arteries. Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.566>

*Corresponding Author:

 Sania Maqbool
 University of Management Sciences and Technology
 Lahore, Pakistan
saniamaqbool28@gmail.com

Received Date: 16th June, 2022

Acceptance Date: 23rd June, 2022

Published Date: 30th June, 2022

ABSTRACT

Carotid Arterial Intima Media Thickness (CA-IMT) is taken as an important indicator of atherosclerosis with increasing age and long term exposure to particulate air pollution associated diseases like hypertension, diabetes, obesity, cigarette smoking, alcohol usage, drugs, deranged lipid profile and high cholesterol, high salt and fatty diet **Objective:** To evaluate the Doppler ultrasonography indices of common and internal carotid arteries on both sides in normal individuals. **Methods:** A prospective comparative cross sectional study was conducted at Imperial Diagnostic and Research Centre, Imperial College of Business Studies, Lahore, Pakistan for a period of four months after the approval of synopsis. Convenient sampling technique was used and all patients visiting us during study interval of and fulfilling the inclusion criteria were included. A total of 50 participants age range from 15 to 68 years, were included. Aloka Prosound α 5 SV, equipped with linear array probe with frequency of 6-9MHz, was used. All the participants, who were normal volunteers, were subjected to B-mode imaging and color-coded Doppler ultrasonography of their common carotid arteries and internal carotid artery in supine position. Baseline investigation was taken for blood pressure (BP) during resting phase. Participant's age, weight and height were also assessed and recorded on questionnaire forms. MedCalc was then used to apply relevant tests for statistical analysis. Repeated Measures ANOVA was performed to see the difference between the values taken during supine and standing position on each side. **Results:** The IMT showed significant positive correlation with the age in both right and left CCA and ICAs. EDV values of right CCA showed significant positive correlation and RI and PI showed significant negative correlation with age. PSV and SD values of left CCA and PSV of right ICA showed significant negative correlation with age. Left ICA diameter and PSV showed the significant positive correlation with age. **Conclusion:** The study provides the information about normal Doppler indices which might be useful in the evaluation of cases of carotid artery diseases. These figures can be used to gain a better understanding of the aetiology of ischemic strokes in the brain.

INTRODUCTION

Intima media thickness (IMT) of carotid artery is caused by fat deposition in the artery can lead to blockage of supply to the brain and lead to stroke. Stroke will lead to deprivation of brain cells from oxygen, as a consequence the brain cells die causing permanent disability [1,2]. Ultrasound imaging or carotid duplex is a safe, painless and widely used method to produce the pictures inside body by using ultrasound waves [3]. Conventional ultrasound uses a high frequency transducer for ultrasound scanning. Doppler ultrasound on the other hand evaluates the blood flow velocity and

direction across a vessel. Carotid duplex uses a combination of conventional ultrasound and Doppler ultrasound for the assessment of carotid arteries blood flow, speed and direction of blood flow in the arteries and measuring the diameter of blood vessel and degree of obstruction if present [4]. Thickness of carotid artery is measured by using ultrasound pictures of intima and media thickness of a carotid artery the two most inner layers of carotid artery. And any abnormality in the thickness of the inner most layers of carotid arteries identify the

cardiovascular disease [5]. Predictive value of carotid artery test is increased when carotid artery media thickness is measured at multiple extra cranial sites. Normal IMT in healthy young people is <0.8mm and value at or above 1mm is an indicator of atherosclerosis or any cardiovascular disease in any age group. Adults less than 30 years of age have a thickness of 0.73mm and <0.7mm respectively [6]. Focal areas of vessel stenosis have little effect on total flow in a vessel until a critical narrowing is reached. Generally about 70% reduction in area or a 50% reduction in diameter beyond this value blood flow rapidly decreases as the pressure drop across the narrowing increases [7]. Embryologic vascular system develops at 19th day before the appearance of somites. Primitive mesenchyme and mesoderm forms vascular channels within embryonic disc that coalesce into blood vessel. First three arches formed at 28th day of pregnancy and these arches involute at the formation of 5th, 6th and 7th arches. This pattern of formation and regression is considered as normal anatomical pattern of variations in great vessels [8]. The carotid vessel turns superiorly to emerge from carotid canal at the foramen lecerum. The carotid artery then runs medially, anteriorly and laterally to the sella turcica into the cavernous sinus. And it then enters into the subarachnoid space by turning upward and medial to the anterior clinoid process and pierces the dura into arachnoid [9]. Right common carotid artery takes its origin from brachiocephalic trunk at the base of neck. Left common carotid artery is the 2nd branch of aortic arch which takes its origin from highest part of aortic arch. Left common carotid artery is located posterior laterally to the brachiocephalic trunk in the superior media sternum and ascends antero-laterally to trachea to enter into the neck posterior to the left sternoclavicular joint [10]. The common carotid arteries and internal carotid artery peak systolic ratio lies within range of 0.3 to 1.0 in normal individuals. These velocities increase with increasing age. Volume flow measurement obtained from B-mode and Doppler ultrasound which requires knowledge of velocity profile within the vessel and it limits the accuracy of method. Normal variations are found in the origin of carotid artery 1st variant which is found is named as bovine arch in which origin of brachiocephalic trunk and left common carotid artery have the same origin. Ratio of bovine arch is 7-27% in patients. In 2.5% of patients another variant found in which right common carotid artery arising directly from the aortic arch and right sub-clavian artery arise distally from the arch and right common carotid artery is considered to be the 1st branch of the arch. third variant found have the same origin of left common carotid artery and sub-clavian artery which can lead to the formation of bilateral symmetrical brachiocephalic trunk [11]. Internal

carotid artery remains in the carotid sheath and retains the same relationship with internal jugular vein and vagus nerve at the point which is located above the bifurcation of carotid artery into external and internal carotid arteries. Point of bifurcation of carotid arteries is superior border of the thyroid cartilage. Fusiform dilatation is seen at the point of carotid bifurcation due to presence of carotid bulb and carotid sinus which is encompassing the distal common carotid and proximal internal carotid and is present in almost 40% of cases [12]. Blood flow in the region of carotid artery bifurcation area reflects complex vessel anatomy in this segment. Blood flow adjacent to the opposite wall of the carotid sinus is characterized by recirculation documented by ultrasonography in young individuals. Beginning at early or peak systole and persisting for about 20% of the cardiac cycle flow reversal occupied about one third of the carotid sinus. Blood flow in the portion of bulb is stagnant in diastole [13]. Research work in recent ere in elastic models of cadaver bifurcations using Newtonian pattern of flow and physiologic pulsatile flow stagnant region in the posterior bulb seems to act as a buffer in systole high shear region and deflecting streamlines anteriorly into a high flow. Ultrasonography of carotid artery is a most popular tool for the evaluation of carotid artery diseases like atherosclerosis in the carotid artery to check the blood flow to brain in case of CVA and also in case of plaque characterization. Plaque ulceration could be a cause of future embolic event. Plaque morphology such as surface of plaque, echogenicity of plaque, presence of ulceration and stenosis is important for prediction of cardiovascular events.

METHODS

It was a prospective cross sectional study. The study was conducted at Imperial Diagnostic and Research Centre, Imperial College of Business Studies, Lahore, Pakistan. The research took place over the course of four months. Convenient sampling was done and all subjects fulfilling the inclusion criteria who volunteered and gave consent for the participation in the study were included. Healthy subjects without any history of stroke or transient ischemic attack, space occupying lesion in the brain, known atheromatous disease and uncontrolled hypertension were included in the study. A total of 50 patients were included in the study. The subject was made to lie comfortably in a supine or semi-supine position, with his or her neck somewhat hyperextended and rotated away from the side being checked. The architecture of the carotid artery, including intima media thickness and diameter, was documented using a high frequency linear transducer with a frequency of 7.5 MHz. By angulating the transducers caudally in the supraclavicular region and cephalically at the level of the

mandible, the carotid arteries were attempted to be viewed as clearly and completely as feasible. Grey-scale ultrasonography was used to obtain IMT at the near or far wall of the CCA, bulb, and ICA. The intima, which appears to be echogenic, and the media, which appears to be echo-poor, were also measured. A Doppler sample was put in the vessel's centre, with the Doppler angle kept below 60 degrees while keeping parallel to the blood flow. At the proximal section of the CCA and ICA, the flow velocity (peak systolic and end-diastolic flow velocities) was assessed using pulsed Doppler (at least 1.5 cm distal to the bulb). Same procedure on other side. Pre-designed questionnaire questionnaires and data collecting sheets were used to record the information. These were then uploaded to EXCEL, where relevant statistical tests were applied using MEDCALC. The Pearson's correlation coefficients between Doppler indices and subject ages were then determined, and a normogram of these values was created utilizing the available data.

RESULTS

Table 1 shows the demographic data. Total 50 participants are included in this study, 44 were males and 6 were females. The demographic data includes mean value of age, blood pressure (diastolic and systolic), height and weight. Table 2 includes Doppler indices for common carotid and internal carotid arteries. Table 3 shows the involved Pearson's correlation Indexes of different factors of Common carotid (R&L) & internal carotid (R&L) including diameter, Intima media thickness, End diastolic velocity, Pulsatility Index, Peak systolic velocity, Resistive Index and systolic and end diastolic ratio.

	Mean	CI	Mean	CI
Age	27	16.4-37.5	28.68	25.55-31.81
BP-(Dia)	75	66.87- 83.2	78.63	75.8- 81.4
BP-(Sys)	113	108- 118	118.2	115.4- 120.9
Height	5.2	5.03-5.36	5.64	5.5 -5.7
Weight	49	46.51- 51.5	64.9	60.8- 68.9

Table 1: Shows the demographic details of the subjects(n=50) M=Male, F=Female, BP=Blood pressure, Dia=Diastole, Sys (Systole)

Index Laterality	Internal Carotid	p-value
Dia.	Left	0.08
	Right	0.7
EDV	Left	0.004*
	Right	0.00012*
IMT	Left	0.28
	Right	0.08
PI	Left	0.2
	Right	0.36
PSV	Left	0.4
	Right	0.016*

RI	Left	0.5
	Right	0.46
SD Ratio	Left	0.04*
	Right	0.27

Table 2: Details of the Doppler indices in common carotid arteries and Internal carotid of normal subjects

Index	RCCA	LCCA	RICA	LICA
Diameter	0.7	0.75	0.71	0.05
IMT	0.05	0.0001	0.0003	0.0001
EDV	0.04	0.06	0.58	0.5
PI	0.03	0.5	0.55	0.14
PSV	0.11	0.01	0.02	0.001
RI	0.04	0.6	0.02	0.45
S/D ratio	0.34	0.001	0.9	0.9

Table 3: The Pearson's correlation Indices of Common carotid (R&L) & Internal carotid (R&L)

R CCA=Right Common carotid artery, L CCA=Left Common carotid artery, R ICA= Right Internal carotid artery, L ICA=Left Internal carotid artery, IMT= Intima media thickness, EDV= End diastolic velocity, PI= Pulsatility Index, PSV= Peak systolic velocity, RI= Resistive Index, S/D ratio= Systolic and end diastolic ratio

Index Laterality	Internal Carotid	p-value
Dia.	Left	0.63
	Right	0.76
EDV	Left	0.4
	Right	0.71
IMT	Left	0.17
	Right	0.26
PI	Left	0.25
	Right	0.06
PSV	Left	0.2
	Right	0.03*
RI	Left	0.68
	Right	0.7
SD Ratio	Left	0.005*
	Right	0.008*

Table 3:

DISCUSSION

Another study categorize the participants in three age groups: one is of adults, 2nd is of middle age, third is of old age group. This study showed a significant correlation between increased CA-IMT with age older healthy people have increased CA-IMT than middle age group and adults. CA-IMT have a significant correlation with gender distribution male in comparison female group have an increase thickness of carotid artery intima media layer [16]. The recognition of normal patterns of the Doppler indices in the arteries supplying the brain therefore remains important as only in this way we will be able to identify the changes produced as a result of abnormalities. The issue of lack of validation data that directly relate to duplex carotid

velocities should be addressed and reference standards for velocity criteria should be set up in order make the patients get benefitted from the diagnostic and therapeutic procedures such as CEA. The values of velocities such as PSV and EDV found in our study (19 cm/sec in left ICA and 24cm/sec in right ICA) were in complete agreement with the previously reported results i.e. normal ICAs PSV should be <125 cm/sec and EDV be <40cm/sec. Similarly the flow in the CCA should be greater than 45 cm/sec in normal healthy individuals [17]. As expected the values of IMT showed a significant degree of correlation with the advancement of age. These however did not differ in both the genders significantly. This finding is also in accordance with the previous studies [18-20]. This study of ours provides basic knowledge crucial to detect the abnormality found in vascular system. These data will serve as foundation or reference for the future studies. The limitation of our study however included the small sample size due to time restraints.

CONCLUSION

The study provides the information about normal Doppler indices, which might be useful in the evaluation of cases of carotid artery diseases. These values can form the basis for better knowledge about the pathogenesis of ischemic cerebrovascular events.

REFERENCES

- [1] Kaźmierski P, Pająk M, Bogusiak K. Concomitance of atherosclerotic lesions in arteries of the lower extremities and carotid arteries in patients with abdominal aorta aneurysm. *Artery Research*. 2016 Dec 1;16:11-7. doi:10.1016/j.artres.2016.08.003
- [2] Silitongo M, Mulipilwa MD, Mwaba C, Mutemwa S. Common Trunk Origin of the Brachiocephalic and Left Common Carotid Arteries from the Aortic Arch. *MOJ Anat&Physiol*. 2017;3(2):00086. doi:10.15406/mojap.2017.03.00086
- [3] Li W, Yang L, Lyu H. A Rare Case of Carotid Body Tumor Presenting with Internal Carotid Artery Blood Supply and Carotid Sinus Syndrome. *Chin Med J (Engl)*. 2016 Feb 20;129(4):496-7. doi: 10.4103/0366-6999.176085.
- [4] Hossein-Nejad H, Mohammadinejad P, Ahmadi F. Internal jugular vein/common carotid artery cross-sectional area ratio and central venous pressure. *J Clin Ultrasound*. 2016 Jun;44(5):312-8. doi: 10.1002/jcu.22339.
- [5] Todua F, Gachechiladze D. Common Carotid Artery Intima-Media Layer Changes. In *Noninvasive Radiologic Diagnosis of Extracranial Vascular Pathologies 2018* (pp. 137-142). Springer, Cham S
- [6] Egilmez OK, Uzun L, Kalcioglu MT, Tekin M. Multiple variations in carotid arteries: lower common carotid bifurcation, hypoplastic and tortuous internal carotid artery. *British Journal of Medicine and Medical Research*. 2017;21(11):14. doi:10.9734/BJMRR/2017/33449
- [7] Foreman PM, Harrigan MR, Griessenauer CJ, Loukas M, Tubbs RS. Access to the carotid artery bifurcation: Cadaveric study with application to nasotracheal intubation as a technique to improve access to a high carotid artery bifurcation. *Br J Neurosurg*. 2015;29(6):865-7. doi:10.3109/02688697.2015.1071331.
- [8] Nieddu M, Boatto G, Pirisi MA, Dessi G. Determination of four thiophenethylamine designer drugs (2C-T-4, 2C-T-8, 2C-T-13, 2C-T-17) in human urine by capillary electrophoresis/mass spectrometry. *Rapid Commun Mass Spectrom*. 2010 Aug 30;24(16):2357-62. doi: 10.1002/rcm.4656.
- [9] Girsowicz E, Georg Y, Lefebvre F, Lejay A, Thaveau F, Roy C, Ohana M, Chakfe N. Anatomical Study of Healthy Aortic Arches. *Ann Vasc Surg*. 2017 Oct;44:179-189. doi: 10.1016/j.avsg.2017.03.196.
- [10] Awad IA, Abbas HY. Ultrasound evaluation of carotid artery intima-media thickness in patients with risk factors for cardiovascular disease. *Int. J. Diagn. Imaging*. 2017;4:16. doi:10.5430/ijdi.v4n2p16
- [11] Chen SY, Hsu HY. Analysis of Doppler blood flow waveform of cerebral arteries and common abnormal findings. *J Med Ultrasound*. 2014 Mar 1;22:3-6. doi:10.1016/j.jmu.2013.12.004
- [12] Kamenskiy AV, Dzenis YA, Mactaggart JN, Desyatova AS, Pipinos II. In vivo three-dimensional blood velocity profile shapes in the human common, internal, and external carotid arteries. *J Vasc Surg*. 2011 Oct;54(4):1011-20. doi: 10.1016/j.jvs.2011.03.254.
- [13] Cheng Q, Huang CB, Wang JY, Jiang B, Zhang LB, Zeng M, Chen YB, Zhang HF, Chen FH. Application of 3-Dimensional Computerized Tomography Angiography for Defining Cavernous Sinus Aneurysms and Intradural Aneurysms Involving the Internal Carotid Artery Around the Anterior Clinoid Process. *World Neurosurg*. 2017 Oct;106:785-789. doi: 10.1016/j.wneu.2017.06.172.
- [14] Steinke W, Kloetzsch C, Hennerici M. Carotid artery disease assessed by color Doppler flow imaging: correlation with standard Doppler sonography and angiography. *AJNR Am J Neuroradiol*. 1990 Mar-Apr;11(2):259-66.
- [15] Rohren EM, Kliwer MA, Carroll BA, Hertzberg BS. A spectrum of Doppler waveforms in the carotid and vertebral arteries. *AJR Am J Roentgenol*. 2003

- Dec;181(6):1695-704. doi: 10.2214/ajr.181.6.1811695.
- [16] Ishigami D, Ota T. Spontaneous Bilateral Cervical Internal Carotid Artery Dissection Treated with Simultaneous Bilateral Carotid Artery Stenting: A Case Report. *NMC Case Rep J*. 2019 May 25;6(3):71-74. doi: 10.2176/nmccrj.cr.2018-0257.
- [17] Lee W. General principles of carotid Doppler ultrasonography. *Ultrasonography*. 2014 Jan;33(1):11-7. doi: 10.14366/usg.13018. Epub 2013 Dec 11. PMID: 24936490;doi:10.14366/usg.13018
- [18] Casella IB, Sotelo FJ, Yamazaki Y, Presti C, Vassoler A, Melo HA. Comparison of common carotid artery intima-media thickness between Brazilian Euro-descendants and Afro-descendants with atherosclerosis risk factors. *Clinics (Sao Paulo)*. 2009;64(7):65764. doi:10.1590/S18075932200900070009.
- [19] Kiechl SJ, Staudt A, Stock K, Gande N, Bernar B, Hochmayr C, Winder B, Geiger R, Griesmacher A, Anliker M, Kiechl S, Kiechl-Kohlendorfer U, Knoflach M, Pechlaner R; Early Vascular Ageing (EVA) Study Group *. Predictors of Carotid Intima-Media Thickness Progression in Adolescents-The EVA-Tyrol Study. *J Am Heart Assoc*. 2021 Sep 21;10(18):e020233. doi: 10.1161/JAHA.120.020233.
- [20] Bae JH, Kim WS, Lee MS, Kim KS, Park JB, Youn HJ, Park CG, Hong KS, Kim JY, Jeong JW, Park JC, Lim DS, Kim MH, Woo JT. The changes of individual carotid artery wall layer by aging and carotid intima-media thickness value for high risk. *Cardiovasc Ther*. 2016 Dec;34(6):397-403. doi: 10.1111/1755-5922.12209.



Original Article

Occupational Impact on The Respiratory Health & Function of Women, Working in The Glass Bangle Industry

Arshad Sattar Lakho¹, Akbar Gohar Abro², Abdul Hafeez Thebo², Khalil Kazi³, Saba Bashir⁴, Ghulam Shahar Bano⁵¹Department of Medicine, Liaquat University of Medical & Health Sciences, Jamshoro, Pakistan²Department of Pulmonology, Liaquat University of Medical & Health Sciences, Jamshoro, Pakistan³Department of Community Medicine, Indus Medical College, Pakistan⁴Indus Medical College, Pakistan⁵Liaquat University of Medical & Health Sciences, Jamshoro, Pakistan

ARTICLE INFO

Key Words:

Occupational Health, Occupational Disease, Women's Health, Respiratory Function and Respiratory Impairment

How to Cite:

Sattar Lakho, A. ., Gohar Abro, A. ., Hafeez Thebo, A. ., Kazi, K. ., Bashir, S. ., & Shahar Bano, G. . (2022). Occupational Impact on The Respiratory Health & Function of Women, Working in The Glass Bangle Industry: Occupational Impact on the Respiratory Health & Function of Women, Working in The Glass Bangle Industry. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.534>

*Corresponding Author:

Arshad Sattar Lakho
 Dept. of Medicine, Liaquat University of Medical & Health Sciences, Jamshoro
docarshadlakho@hotmail.com

Received Date: 8th June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

The International Labor Organization (ILO), "reiterate every year the concern of ever-increasing burden of occupational illnesses, especially among less empowered population in less developed countries such as Pakistan. One such industry is the bangle industry wherein women work in poor conditions and are exposed to various heavy metals, such as arsenic, lead, zinc, copper, manganese, cobalt, cadmium, and selenium (used as coloring agents), putting their health at risk. **Objective:** To determine the respiratory health and function of women, working in the bangle industry. **Methods:** This observational, cross-sectional study included a sample of 100 women, (selected using snowball sampling) working in the bangle industry in Southern Pakistan. The women were approached, and their respiratory function and oxygen saturation gauged using appropriate apparatus. The data was analyzed using SPSS. V. 21.0. **Results:** The mean values of various spirometric variables (FVC, FEV₁, IMBC, and PEFr) were within normal range. However, FEV₁/FVC% was reduced significantly ($p < 0.001$) among the study participants. Additionally, a high prevalence (26%) of respiratory impairment was noted. The respiratory impairment observed indicated primarily restrictive pattern of pulmonary abnormality (18%). The effect of the duration of exposure on the prevalence of respiratory impairment in the glass bangle industry was significant" ($p < 0.05$). **Conclusion:** Women employed in the glass bangle industry have poor respiratory health and continue to suffer from increasingly high levels of respiratory impairment.

INTRODUCTION

There has been rapid industrialization in south-east Asia during the last four decades and it is likely to accelerate further in the coming years. [1] Industrialization and "urbanization are creating new problems and new challenges in the field of industrial health. [2] Increased respiratory morbidity in industrial workers and inhabitants of industrial towns has been well recognised and many surveys conducted from time to time have clearly established it. [3] Amongst the respiratory diseases, chronic bronchitis

has been a matter of concern in Britain for a long time and was even called 'Englishman's disease'. [4] It is now well known that chronic bronchitis is prevalent in almost all countries particularly in industrialized ones. [5] The prevalence of chronic bronchitis varies not only from country to country but also from one set of people to another living in different geographical areas. [6, 7] It also varies in people of different ethnic origins and engaged in different occupations in a single country. [8] Chronic

bronchitis surveys have been carried in the neighboring country (India) in two types of population groups, firstly in general populations and secondly in different occupational groups as a part of health surveys. Surveys reported a prevalence of 1% to 12.5% of chronic bronchitis in different population groups. The study conducted by Industrial Toxicology Research Centre, Lucknow, India in the glass bangle Industry of Firozabad has revealed the prevalence of chronic bronchitis in 23.9% of glass bangle workers. [9, 10] Glass bangle workers are exposed to a wide variety of toxicants at their work places. The studies conducted revealed a very high prevalence of chronic bronchitis (22.6 and 23.9% respectively) and pulmonary tuberculosis (15.2%) in the glass bangle industry. [11 - 13] The reported risk factors associated with chronic bronchitis in different occupational groups in the glass bangle industry. [14] However, there is scant information on the types of pulmonary function impairment in glass bangle workers suffering from chronic bronchitis except that of few investigators which dealt with the respiratory status of healthy and pneumoconiotic bangle workers". [15] The present study was undertaken to evaluate the prevalence of different types of respiratory abnormalities in chronic bronchitis and the occupational factors responsible for the physiological dysfunction among the glass bangle workers.

METHODS

This observational, cross-sectional study included a sample of 100 women, (selected using snowball sampling) working in the bangle industry in Southern Pakistan. The women were approached, and their respiratory function and oxygen saturation gauged using appropriate apparatus. The data was analyzed using SPSS. V.21.0.

RESULTS

The mean values of various spirometry variables (FVC, FEV1, IMBC, and PEFR) were within normal range. However, FEV1/FVC% was reduced significantly ($p < 0.001$) among the study participants. Additionally, a high prevalence (26%) of respiratory impairment was noted. The respiratory impairment observed indicated primarily restrictive pattern of pulmonary abnormality (18%). The effect of the "duration of exposure on the prevalence of respiratory impairment in the glass bangle industry was significant ($p < 0.05$).

Characteristics	Group	Percentages
Age Group	15 -29	37%
	30 - 45	52%
	46 - 60	11 %
Education	Not Formally Educated	34%
	Primary	47%
	Secondary	12%
	Higher	07%

Marital Status	Married	64%
	Single	23%
	Widowed / Divorced	13%
Smoking Status	Never	73%
	Current Smoker	21%
	Former Smoker	06%
Respiratory System Status	Normal	74%
	Impaired	26%

Table 1: Sample Description

Characteristics	Group	Mean + SD	P - Value
Spirometric Values	FVC	87.4% + 5.7%	> 0.05
	IMBC	175 + 13.2 l/min	> 0.05
	PEFR	354.5 + 6.54l/min	> 0.05
	FEV ¹ /FVC	53.4% + 3.2%	< 0.001*
Duration of Exposure	Less than 6 Months	05%	> 0.05
	More than 6 Months	21%	< 0.05**

Table 2: Respiratory Functions

DISCUSSION

The tests of ventilation conducted on glass bangle workers suffering from chronic bronchitis showed an obstructive type of ventilatory dysfunction. The high prevalence (23.9%) of chronic bronchitis associated with obstruction could be attributed to a variety of pulmonary toxicants prevailing in the work environment of glass bangle industry. Other factors, like smoking habits, also play a role. Different studies reported that smoking is the most important risk factor for chronic respiratory diseases and accompanying air flow obstruction. They further observed that cigarette smoke affects both the airways and the lung paren- chyma. [16, 17] In addition to smoking, there are also a number of putative risk factors for the development of chronic obstructive pulmonary diseases which include occupational and environmental factors, such as exposure to dust and gases, air pollution, and environmental tobacco smoke. Industrial hygiene studies conducted to assess the pollution levels in the glass bangle industry indicated high levels of suspended par- ticulate matter in the work environment ranging from 12.65 mg/m³ to 162.63 mg/m³ of air. [18, 19] While the suspended particulates contained a number of heavy metals, the concentration of most of the metals like cadmium, copper, manganese, nickel, chrome, arsenic, and selenium was within the normal threshold limit values (TLVs) set by the American Conference of Governmental Industrial Hygienists. Bangle workers involved in the mixing process were particularly exposed to cadmium, copper, and manganese while the concentrations of lead and zinc were appreciably higher than the prescribed maximum allowable concentration (MAC values) recommended for ambient air. The glass bangle workers, particularly those who worked near the different furnaces and those engaged in the baking

process, were exposed to high concentrations of lead. This could be due to the fact that there is a high density of coal based furnaces in the work environment of the glass bangle industry. [18 - 20] It has been reported a very high prevalence of respiratory morbidity in the glass bangle workers (51.7%) and the control population (38.6%), which was attributed to high concentrations of suspended particulates, sulfur dioxide, and coal dust in the ambient air emanating from the glass bangle industries. The prevalence of pulmonary tuberculosis was also found to be quite high in the glass bangle workers (15.2%) and in the general population (7.8%). The low socio-economic profile and unhygienic living and working conditions may be the etiological factors in the development of the disease in the glass bangle workers and the general population of Firozabad. [21, 22] They reported that 7.2% of the glass bangle workers suffered from radiological abnormalities suggestive of mixed pneumoconiosis caused possibly by chronic exposure to dust and fumes containing different metals in the work environment. High levels of air pollution in Firozabad were also reported. [23] They found high concentrations of sulfur dioxide and suspended particulates in the ambient air. [24] Studies reported a sulfur dioxide level of 0.159 ± 0.243 mg/m³ of air inside the glass bangle industry. However, the allowable concentration of sulfur dioxide was below the MAC value published. It has been reported that a high prevalence of chronic bronchitis from different cities with high pollution levels which were attributed to high levels of air pollution to large amounts of coal burnt in various industrial units of Firozabad. Presence of zinc and lead in the air samples to industrial pollution was also reported to be in high concentrations of heavy metals such as chromium, copper, cadmium, and manganese in hair samples of the bangle workers, confirming the findings of the industrial hygiene studies. In such a situation of exposure to a wide variety of toxicants in the work environment in a number of occupations in the glass bangle industry, it is difficult to implicate any one particular agent as a causative factor responsible for chronic bronchitis" and associated ventilatory dysfunction. [25]

CONCLUSION

The high prevalence of "bronchial obstruction observed in the chronic bronchitic glass bangle workers is in all likelihood the result of chronic exposures to flue products emanating from various coal furnaces and to multimetals prevailing in the work environment. Women in particularly, employed in the glass bangle industry have poor respiratory health" and continue to suffer from increasingly high levels of respiratory impairment.

REFERENCES

- [1] Hill H. Rapid Industrialisation in ASEAN: Some Analytical and Policy Lessons. *Agenda: A Journal of Policy Analysis and Reform*. 1997 Jan 1:419-32. doi:10.22459/AG.04.04.1997.03
- [2] Kuddus MA, Tynan E, McBryde E. Urbanization: a problem for the rich and the poor? *Public Health Rev*. 2020 Jan 2;41:1. doi: 10.1186/s40985-019-0116-0.
- [3] Tchounwou PB, Yedjou CG, Patlolla AK, Sutton DJ. Heavy metal toxicity and the environment. *Exp Suppl*. 2012;101:133-64. doi: 10.1007/978-3-7643-8340-4_6
- [4] Burney P. Chronic respiratory disease - the acceptable epidemic? *Clin Med (Lond)*. 2017 Feb;17(1):29-32. doi: 10.7861/clinmedicine.17-1-29.
- [5] Dotan Y, So JY, Kim V. Chronic Bronchitis: Where Are We Now? *Chronic Obstr Pulm Dis*. 2019 Apr 9;6(2):178-192. doi: 10.15326/jcopdf.6.2.2018.0151.
- [6] Jarhyan P, Hutchinson A, Khaw D, Prabhakaran D, Mohan S. Prevalence of chronic obstructive pulmonary disease and chronic bronchitis in eight countries: a systematic review and meta-analysis. *Bull World Health Organ*. 2022 Mar 1;100(3):216-230. doi: 10.2471/BLT.21.286870.
- [7] Alam DS, Chowdhury MA, Siddiquee AT, Ahmed S, Clemens JD. Prevalence and determinants of chronic obstructive pulmonary disease (COPD) in Bangladesh. *COPD: Journal of Chronic Obstructive Pulmonary Disease*. 2015 Nov 2;12(6):658-67.
- [8] Munn Z, Moola S, Riitano D, Lisy K. The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. *Int J Health Policy Manag*. 2014 Aug 13;3(3):123-8. doi: 10.15171/ijhpm.2014.71.
- [9] Ciapponi A, Alison L, Agustina M, Demián G, Silvana C, Edgardo S. The epidemiology and burden of COPD in Latin America and the Caribbean: systematic review and meta-analysis. *COPD*. 2014 Jun;11(3):339-50. doi: 10.3109/15412555.2013.836479.
- [10] Finney LJ, Feary JR, Leonardi-Bee J, Gordon SB, Mortimer K. Chronic obstructive pulmonary disease in sub-Saharan Africa: a systematic review. *Int J Tuberc Lung Dis*. 2013 May;17(5):583-9. doi: 10.5588/ijtld.12.0619.
- [11] McKay AJ, Mahesh PA, Fordham JZ, Majeed A. Prevalence of COPD in India: a systematic review. *Prim Care Respir J*. 2012 Sep;21(3):313-21. doi: 10.4104/pcrj.2012.00055.
- [12] Chapman KR, Mannino DM, Soriano JB, Vermeire PA, Buist AS, Thun MJ, Connell C, Jemal A, Lee TA, Miravitlles M, Aldington S, Beasley R. Epidemiology and costs of chronic obstructive pulmonary disease. *Eur Respir J*. 2006 Jan;27(1):188-207. doi:

- 10.1183/09031936.06.00024505
- [13] Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009 Jul 21;339:b2535. doi: 10.1136/bmj.b2535.
- [14] Dutta S, Deshmukh PR. Prevalence and determinants of self-reported chronic bronchitis among women in rural Central India. *Med J Armed Forces India*. 2015 Jan;71(1):48-52. doi: 10.1016/j.mjafi.2014.10.002.
- [15] Jindal SK, Aggarwal AN, Gupta D, Agarwal R, Kumar R, Kaur T, Chaudhry K, Shah B. Indian study on epidemiology of asthma, respiratory symptoms and chronic bronchitis in adults (INSEARCH). *Int J Tuberc Lung Dis*. 2012 Sep;16(9):12707. doi: 10.5588/ijtld.12.0005
- [16] Mahesh PA, Jayaraj BS, Prabhakar AK, Chaya SK, Vijaysimha R. Identification of a threshold for biomass exposure index for chronic bronchitis in rural women of Mysore district, Karnataka, India. *Indian J Med Res*. 2013 Jan;137(1):87-94.
- [17] Mahesh PA, Jayaraj BS, Chaya SK, Lokesh KS, McKay AJ, Prabhakar AK, Pape UJ. Variation in the prevalence of chronic bronchitis among smokers: a cross-sectional study. *Int J Tuberc Lung Dis*. 2014 Jul;18(7):862-9. doi: 10.5588/ijtld.13.0048
- [18] Biswas RS, Paul S, Rahaman MR, Sayeed MA, Hoque MG, Hossain MA, Hassan MM, Faiz MA. Indoor biomass fuel smoke exposure as a risk factor for chronic obstructive pulmonary disease (COPD) for women of rural Bangladesh. *Chattagram Maa-O-Shishu Hospital Medical College Journal*. 2016 Jul 17;15(1):8-11. doi:10.3329/cmshmcj.v15i1.28753
- [19] Mukhmohit S, Bhardwaj A, Saini S, Mukherjee AK, Kannan R. COPD—prevalence and risk study among females of rural area, district Ambala, Haryana, India. *Journal of Evolution of Medical and Dental Sciences*. 2014 Apr 21;3(16):418392. doi:10.14260/jemds/2014/2416
- [20] Sinha B; Vibha, Singla R, Chowdhury R. An epidemiological profile of chronic obstructive pulmonary disease: A community-based study in Delhi. *J Postgrad Med*. 2017 Jan-Mar;63(1):29-35. doi: 10.4103/0022-3859.194200
- [21] Mahesh PA, Lokesh KS, Madhivanan P, Chaya SK, Jayaraj BS, Ganguly K, Krishna M. The Mysuru stUdies of Determinants of Health in Rural Adults (MUDHRA), India. *Epidemiol Health*. 2018 Jun 23;40:e2018027. doi: 10.4178/epih.e2018027.
- [22] Arora S, Rasania SK, Bachani D, Gandhi A, Chhabra SK. Air pollution and environmental risk factors for altered lung function among adult women of an urban slum area of Delhi: A prevalence study. *Lung India*. 2018 May-Jun;35(3):193-198. doi: 10.4103/lungindia.lungindia_263_17
- [23] Chaturvedi R, Muzammil K, Singh N, Davey S, Singh JV. Prevalence of COPD in rural population, Muzaffarnagar. *Indian Journal of Community Health*. 2015 Dec 31;27(4):467-71.
- [24] Mukherjee S, Roychoudhury S, Siddique S, Banerjee M, Bhattacharya P, Lahiri T, Ray MR. Respiratory symptoms, lung function decrement and chronic obstructive pulmonary disease in pre-menopausal Indian women exposed to biomass smoke. *Inhal Toxicol*. 2014 Dec;26(14):866-72. doi: 10.3109/08958378.2014.965560.
- [25] Panigrahi A, Padhi BK. Chronic bronchitis and airflow obstruction is associated with household cooking fuel use among never-smoking women: a community-based cross-sectional study in Odisha, India. *BMC Public Health*. 2018 Jul 27;18(1):924. doi: 10.1186/s12889-018-5846-2.



Original Article

Prevalence and Risk Factors of hepatitis B and C infections in general population of Tehsil Arifwala

 Mahtab Ahmad¹, Muhammad Kamran², Haroon Amin², Saba Zafar³, Samra Asghar⁴, Uswa Siddique⁵, Aimen Khalid⁵, Alia Sarfraz⁶, Mohsin Khurshid⁵, Irfan Ullah⁷
¹ Faculty of Allied Health sciences, Riphah International College, Dera Ghazi Khan, Pakistan² Department of Medical Laboratory Technology, Islamabad Medical & Dental College Islamabad, Pakistan³ Department of Biotechnology, The Women University Multan, Multan, Pakistan⁴ Faculty of Rehabilitation and Allied Health Sciences, Riphah International University Faisalabad Campus, Faisalabad, Pakistan⁵ Department of Microbiology, Government College University Faisalabad, Pakistan⁶ Department of Forensic Medicine, Islamabad Medical & Dental College Islamabad, Pakistan⁷ Department of Life Sciences, School of Science, University of Management and Technology (UMT), Lahore, Pakistan

ARTICLE INFO

Key Words:

Prevalence, Hepatitis B virus, Hepatitis C virus, Risk Factors

How to Cite:

 Ahmad, M., Kamran, M. . ., Amin, H. . ., Zafar, S. . ., Asghar, S. . ., Siddique, U. . ., Khalid, A., Sarfraz, A. . ., Khurshid, M. . . & Ullah, I. . (2022). Prevalence and Risk Factors of hepatitis B and C infections in general population of Tehsil Arifwala: Hepatitis B and C Infections in General Population. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.526>

*Corresponding Author:

 Mohsin Khurshid
 Department of Microbiology, Government College University Faisalabad, Pakistan
mohsinkhurshid@gcuf.edu.pk

Received Date: 8th June, 2022

Acceptance Date: 22nd June, 2022

Published Date: 30th June, 2022

ABSTRACT

According to the WHO, over 350 and 250 million individuals have been estimated as chronic carriers of HBV and HCV, worldwide. About 1.34 million deaths are attributed to HBV and HCV, globally. **Objective:** To estimate the seroprevalence of HBV and HCV-related hepatitis. **Methods:** For this purpose, a population of 300 individuals was screened for HBsAg and Anti-HCV antibodies. Data were collected from tested individuals included their age, gender, occupation. Prevalence of HBV and HCV was found at 10% and 14% respectively. Co-infection of both pathogens was observed in 1.33% of individuals. Male (18%) were more infected with these viruses as compared to females (6%). The highest percentage (75%) of HBV/HCV was in adult patients of age between 31-50 years. The various risk factor associated with the spread of viral hepatitis were also considered for a better understanding of the routes of spread of these viral infections. **Results:** Out of 300 screened individuals, 21% had a history of going through any dental procedure, followed by 17% with needle stick injuries. Only 7.6% of persons had a history of any blood transfusion. Conducting such type of seroprevalence studies can help the administration and health care authorities to take necessary control measures to minimize the chances of acquiring these infections by eliminating risk factors. **Conclusion:** Further, these surveillance studies can also play a significant role in the launch of vaccination programs in areas of high prevalence.

INTRODUCTION

Hepatitis due to HBV and HCV is extremely prevalent around the globe and a substantial burden is exerted by these problematic pathogens on the health care settings. According to the WHO, over 350 and 250 million individuals worldwide are estimated the chronic carrier of HBV and HCV, respectively [1]. Significantly high global morbidity and mortality are associated with them, and approximately one million deaths per annum are attributed to HBV and

HCV-related liver diseases and their sequelae of hepatocellular carcinoma [2]. By the rough estimation of WHO, approximately 4.3 million individuals are infected by HBV in the Eastern Mediterranean region, each year [3]. Pakistan was also considered one of the most prominent countries with a 7% prevalence of HBV in the late 1980s, it was classified as a country with an intermediate prevalence of HBV [4]. It has been estimated that the

economic burden due to chronic HCV infections exceeds \$10 billion/ year, in the USA alone [5]. Unsafe and contaminated blood products, unhealthy dental procedures, contaminated barber tools, catheters, tattooing, unsafe sexual intercourse without precautionary measures, and different fluids of the body are the main sources of the spread of the causative agents [6]. HCV and HBV are the major etiological factors involved with hepatocellular carcinoma (HCC). Globally, of all tumor types, the HCC is the 5th most prevalent tumor, and 3rd leading cause of cancer-related deaths [6,7]. When these infections are accompanied by inflammatory reactions, destruction of the hepatocytes triggers the regeneration and scar formation (fibrosis), which then ultimately can lead to liver HCC and cirrhosis [8]. Hepatitis B virus is responsible for transient as well as chronic infections of the liver. Transient infections have a short span of a few months, while chronic infections have a long course [9]. It is estimated that transient hepatitis B infections result in serious illness, of which only 0.5% end with incurable fulminant hepatitis [10]. Chronic infections pose more serious consequences with 25% of the cases terminating permanent liver cancer [11]. The death toll due to liver cancer related to Hepatitis B virus infections reaches up to one million per year, worldwide. HBV has a very high mortality rate. Globally, a population of about 257 million has been estimated to have long-life chronic HBV infections. By an estimation, chronic hepatitis leading to liver cirrhosis, along with hepatocellular carcinoma results in 887,000 deaths/year, worldwide. Transmission of these deadly pathogens may occur through unprotected sexual contact, sharing the needles, unsterile surgical and medical equipment including syringes, scissors and cutters, and from mother to the fetus during birth. In Pakistan the percentage of infection is 61.45% due to infected needles and 10.62% because of unhealthy dental and surgical procedures. The WHO's global hepatitis report 2015 estimated that 71 million individuals were positive for HCV, which makes up 1% of the world's population, 2.3 million Individuals also had co-existence of HIV along with HCV infection. Uneven distribution of HCV infection is observed in the world, but the highest prevalence of HCV infections is seen in Eastern Mediterranean and The European. The individual prevalence rates in different cities of Punjab and provinces are as in Gujranwala 0.4-31.9%, in Lahore 23.8%, in Faisalabad 16% and 16% in Islamabad While in Gilgit Baltistan is 25.7%, in KPK province 1.5% and Sindh is 1.1-9% [12]. Similarly, screening of blood donors showed 2.60% positive results for anti-HCV patients in CMH Peshawar, Pakistan [13]. In various areas of the world, and also in Pakistan, the sero epidemiological various studies and research have been conducted in past,

but there is a lapse in available epidemiological data on HBV and HCV in Tehsil Arifwala, which is still much required and questioned. The present study showed a true picture of the cumulative prevalence of infections caused by Hepatitis B and Hepatitis C virus and made the comparison possible with available data on HCV and HBV in other cities of Pakistan.

METHODS

For estimating the seroprevalence of HBV and HCV in district Arifwala, province Punjab, a descriptive cross-sectional study was conducted and 300 individuals were screened by ICT kit method followed by confirmation through ELISA. Immunochromatographic tests (ICT) were used to screen for HBV and HCV-positive samples. According to the manufacturer's directions, accurate Acon (Acon, USA) strips were utilized. ICT-positive samples were subsequently confirmed through ELISA. SPSS version 23.0 and Microsoft Excel 2016 were used for the data analysis.

RESULTS

Out of 300 screened individuals, 24% (n=72) were found positive for either HBV or HCV. Prevalence of HCV was 14% (n=42) followed by HBV with 10% (n=30). Of tested population, 71.7% (n=215) were male and 28.3% (n=85) were female. Prevalence of viral hepatitis was high in males (18%, n=54) followed by females (6%, n=18). The patient's age ranged from a minimum of 13 years to a maximum of 63 years. With the highest frequency, 79.7% (n=239) of individuals were adults of age between 25-64 years followed by 20% (n=60) of young ones who fell in the age group 15-24 years, and only 0.3% (n=1) children of age 13 years. Marital status of 66.67% (n=200) was 'married' while 33.33% (n=100) person were unmarried. By occupation, the highest proportion was of shopkeepers with 25.3% frequency, followed by the farmers, teachers, and health care personnel with frequencies of 17.7%, 16.7%, and 14.7%, respectively. It is interesting to note that the highest number of tested individuals were under matriculation in their studies with 34.7% frequency, followed by persons with the education of FA/F.Sc with 32% frequency. The person who was master's and M. Phil counted for only 5.3% and 0.7% of the total sample population (Table 1).

Demographic Characteristics		Number (N)	Percentage (%)
Gender	Female	85	28.3%
	Male	215	71.7%
Age	Children (0-14 Years)	1	0.3%
	Youth (15-24 Years)	60	20.0%
	Adults (25-64 Years)	239	79.7%
Marital Status	Married	200	66.67%
	Unmarried	100	33.33%
	Businessman	31	10.3%
	Farmer	53	17.7%

Occupation	Health Care	44	14.7%
	Shopkeeper	76	25.3%
	Student	46	15.3%
	Teacher	50	16.7%
Residence	Arifwala	300	100.00%
Education	FA	96	32.0%
	Graduate	82	27.3%
	M.Phil	2	0.7%
	Master	16	5.3%
	Under metric	104	34.7%
Transfusion	No	277	92.3%
	Yes	23	7.7%
Dental Procedures	No	237	79.0%
	Yes	63	21.0%
Needle Stick Injuries	No	249	83.0%
	Yes	51	17.0%
Sharing Shaving Razors	No	268	89.3%
	Yes	32	10.7%
Endoscopyc / Colonoscopy	No	252	84.0%
	Yes	48	16.0%
Total		300	100.0%

Table 1: Overview of collected data for estimating seroprevalence of HBV and HCV in Arifwala

Out of 42 HCV positive patients, 9.5% (n=4) were also detected positive for HBsAg, while 90.5% (n=38) were negative for HBsAg. With respect to the total population of samples, 1.3% (n=4) individuals were found infected with HBV as well as HCV (Table 2).

HBsAg	HCV Negative	HCV Positive
Negative	77.33% (n=258)	12.67% (n=38)
Positive	8.67% (n=26)	1.33% (n=4)

Table 2: Co-existence of HCV with reactive HBsAg

A direct relation was observed between occupation and the prevalence of viral hepatitis. Both HBV and HCV were prominent in health care workers with 3% (n=9) and 2.66% (n=8) prevalence, followed by shopkeepers with 2.66% (n=8) and 4.66% (n=14) prevalence of HBV and HCV respectively (Figure 1).

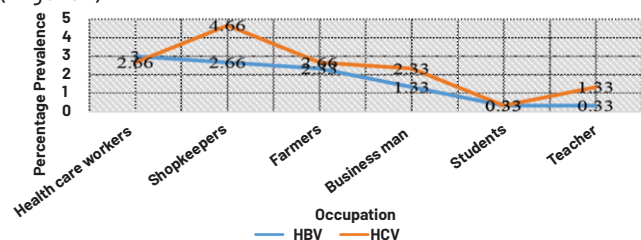


Figure 1: Association of Relative prevalence with occupation

Of the tested population, the highest frequency of HBV/HCV positive individuals was of those who have gone through any dental procedure (n=63) followed by individuals who experienced needle stick injuries (n=51). Only 23 individuals had a history of blood transfusion, of which 10 were HCV positive followed by 7 with reactive HBsAg (Table

3).

Viral infections	Blood transfusion	Dental procedures	Needle stick injuries	Endoscopy	Sharing shaving tools
HBV	23 (7)	63 (14)	51 (16)	48 (8)	32 (7)
HCV	23 (10)	63 (25)	51 (20)	48 (16)	32 (15)

Table 3: Risk factors associated with HBV & HCV

DISCUSSION

In the present study, a total of 24% test population was screened positive for either HBV or HCV. HBV was less prevalent as compared to HCV. Seroprevalence of HBV is estimated at 10% in Arifwala through this study. Similar results were observed during a study conducted in Shenzhen People's Hospital between August 2015 to September 2018, and 9.69% of individuals were detected positive for HBsAg [14]. Similarly, a Nationwide survey on the prevalence of HBV estimated the seroprevalence of HBV as high as 13.7%, in Taiwan [15]. Another study conducted in Cameroon reported an 11.2% seroprevalence of HBV [16]. While the prevalence of HCV was found at 14% in the present study. A study carried out in DHQ Mardan of province KPK reported a 9% prevalence of HCV [17]. A cross-sectional study at Paediatric Medicine Unit in Teaching Hospital Dera Ghazi Khan reported only 3.9% HCV carriers [18]. This unevenly disturbing of HCV in varying patterns around different geographical regions suggests that the prevalence of HCV is significantly co-related with the non-availability of vaccines and directly depends on the living conditions, literacy, public awareness, and also upon the healthcare facilities. While almost even distribution of HBV might be due to the easy availability of vaccines. In fact, after the availability of the HBV vaccine in the 1980s worldwide, the prevalence of HBV declined remarkably. Gender is another prominent factor that has a direct imprint on the prevalence of viral hepatitis in a specific region due to respective behavioral differences of genders, social trends and cultural follows of the community. The present study reported 75% (n=54) of the positive individuals as males while only 25% (n=18) as females. An almost similar trend was observed in a study conducted in Rawalpindi, Pakistan, with 7.15% male patients and 5.35% female patients [19]. In contrast, a study conducted in Vehari, Pakistan reported that 35.19% of males and 37.8% of females had viral hepatitis [20]. In the present study, HBV and HCV infections were more prevalent in patients of age between 31-50 years. 37.5% (n=27) of patients with viral hepatitis were falling in the age group 31-40 years and 41-50 years. Similar results were observed in a work carried out in Khyber College of Dentistry, Peshawar. This work reported the highest frequency of HBV and HCV in age groups 56-65 years and 34-45 years respectively [21]. Similarly, another study conducted in western Rajasthan, India also reported

the highest (54.3%) prevalence in patients of age 30-49 years [22]. Several miscellaneous risk factors are associated with the spread of HCV and HBV. Most prominent of these factors may include unhygienic living conditions, septic medical and surgical procedures including the dental procedures that are carried out without sterilization of tools, unprotected sexual intercourse, transfusion of body fluids especially the transfusion of blood, and unhygienic routine practices like sharing the shaving razors and injection syringes among the drug abusers. In the present study, the tested population had a significant number of individuals who had a history of experiencing one of these risk factors. 63 out of a total of 300 persons had gone through any dental procedure. Of these 63 individuals, 39.68% (n=25) were anti-HCV positive, while 22.22% (n=14) were positive for HBsAg. Another study conducted in Iraq reported that 77% and 75% of HBV and HCV-positive patients with a history of any dental procedure [23]. According to the Fact sheet on hepatitis 2017, by WHO, dental quackery is unrestrainedly practiced in that area of underdeveloped countries that have the highest burden of hepatitis [24]. In the meanwhile, of 300 individuals, only 23 had a history of blood transfusion. Of these 23 people, 43.48% (n=10) were anti-HCV positive followed by 30.43% (n=7) HBsAg positive individuals. A study carried out by the general public in Malaysia reported that 8% of HCV-positive individuals had a history of blood transfusion [25]. This low frequency of transfusion-related transmission of HCV/HBV is due to the practice of blood screening that is followed in every health care setting in routine.

CONCLUSIONS

In underdeveloped areas like Arifwala, a lack of adequate blood screening facilities and a lack of understanding about probable HBV and HCV transmission channels contribute significantly to the infection's spread among people. Proper sanitation and screening measures must be made essential in public health care facilities to avoid a much greater hazards of HCV infection. Policymakers should enact legislation and enforce its implementation prohibiting untrained dental quacks from practicing in specific sections of the province.

REFERENCES

- [1] Aljarbou AN. The Emergent Concern of Hepatitis B globally with special attention to Kingdom of Saudi Arabia. *International journal of health sciences*. 2013 Nov; 7(3):333-40. doi: 10.12816/0006062.
- [2] Wong MCS, Huang JLW, George J, Huang J, Leung C, Eslam M, et al. The changing epidemiology of liver diseases in the Asia-Pacific region. *Nature reviews Gastroenterology & hepatology*. 2019 Jan; 16(1):57-73. doi: 10.1038/s41575-018-0055-0.
- [3] Papastergiou V, Lombardi R, MacDonald D, Tsochatzis EA. Global epidemiology of hepatitis B virus (HBV) infection. *Current Hepatology Reports*. 2015 Sep; 14(3):171-8. doi: 10.1007/s11901-015-0269-3
- [4] Te HS, Jensen DM. Epidemiology of hepatitis B and C viruses: a global overview. *Clinics in Liver Disease*. 2010 Feb; 14(1):1-21, vii. doi: 10.1016/j.cld.2009.11.009.
- [5] El Khoury AC, Klimack WK, Wallace C, Razavi H. Economic burden of hepatitis C-associated diseases in the United States. *Journal of viral hepatitis*. 2012 Mar; 19(3):153-60. doi: 10.1111/j.1365-2893.2011.01563.x.
- [6] Nabih HK. The Significance of HCV Viral Load in the Incidence of HCC: a Correlation Between Mir-122 and CCL2. *Journal of Gastrointestinal Cancer*. 2020 Jun; 51(2):412-417. doi: 10.1007/s12029-019-00281-2.
- [7] Ozakyol A. Global Epidemiology of Hepatocellular Carcinoma (HCC Epidemiology). *Journal of Gastrointestinal Cancer*. 2017 Sep; 48(3):238-240. doi: 10.1007/s12029-017-9959-0.
- [8] Di Poto C, He S, Varghese RS, Zhao Y, Ferrarini A, Su S, et al. Identification of race-associated metabolite biomarkers for hepatocellular carcinoma in patients with liver cirrhosis and hepatitis C virus infection. *PLoS One*. 2018 Mar; 13(3): e0192748. doi: 10.1371/journal.pone.0192748.
- [9] Kadelka S, Dahari H, Ciupe SM. Understanding the antiviral effects of RNAi-based therapy in HBeAg-positive chronic hepatitis B infection. *Scientific Reports*. 2021 Jan; 11(1):200. doi: 10.1038/s41598-020-80594-6.
- [10] Torres HA, Shigle TL, Hammoudi N, Link JT, Samaniego F, Kaseb A, et al. The oncologic burden of hepatitis C virus infection: A clinical perspective. *CA: a cancer journal for clinicians*. 2017 Sep; 67(5):411-431. doi: 10.3322/caac.21403.
- [11] Tu T, Block JM, Wang S, Cohen C, Douglas MW. The Lived Experience of Chronic Hepatitis B: A Broader View of Its Impacts and Why We Need a Cure. *Viruses*. 2020 May; 12(5):515. doi: 10.3390/v12050515.
- [12] Ilyas M, Ahmad I. Chemiluminescent microparticle immunoassay based detection and prevalence of HCV infection in district Peshawar Pakistan. *Virology Journal*. 2014 Jul; 11:127. doi: 10.1186/1743-422X-11-127.
- [13] Zaidi A, Tariq WZ, Haider KA, Ali L, Sattar A, Faqeer F, et al. Seroprevalence of hepatitis B, C and HIV in healthy blood donors in Northwest of Pakistan. *Pakistan Journal of Pathology*. 2004; 15(1):11-6.
- [14] Tao J, Zhang W, Yue H, Zhu G, Wu W, Gong W, et al.

- Prevalence of Hepatitis B Virus Infection in Shenzhen, China, 2015-2018. *Scientific Reports*. 2019 Sep; 9(1):13948. doi: 10.1038/s41598-019-50173-5.
- [15] Chen CL, Yang JY, Lin SF, Sun CA, Bai CH, You SL, et al. Slow decline of hepatitis B burden in general population: Results from a population-based survey and longitudinal follow-up study in Taiwan. *Journal of Hepatology*. 2015 Aug; 63(2):354-63. doi: 10.1016/j.jhep.2015.03.013.
- [16] Bigna JJ, Amougou MA, Asangbeh SL, Kenne AM, Nansseu JR. Seroprevalence of hepatitis C virus infection in Cameroon: a systematic review and meta-analysis. *BMJ Open*. 2017 Aug; 7(8): e015748. doi:10.1136/bmjopen-2016-015748.
- [17] Khan MS, Khalid M, Ayub N, Javed M. Seroprevalence and risk factors of Hepatitis C virus (HCV) in Mardan, NWFP: A hospital based study. *Rawal Medical Journal*. 2004; 29(2):57-60.
- [18] Channer MS, Akram A, Saleem MA. Seroprevalence of Hepatitis-C Carriers Among Children Between 6 Months to 15 Years of Age in Dera Ghazi Khan. *Journal of University Medical & Dental College*. 2017 Jun; 8(2):53-6.
- [19] Khan MI, Kalsoom F, Batool F, Kazmi A, Zahra Qua BM, Ali R, et al. Undiagnosed Hepatitis B and C Virus Infection at a Teaching Hospital in Rawalpindi. *Journal of Pure and Applied Microbiology*. 2020 Jun; 14(2):1279-86. doi.org/10.22207/JPAM.14.2.23
- [20] Ahmed MZ, Shahzad H, Rao T, Ali A, Samad N. Seroprevalence of Hepatitis C Virus (HCV) and Hepatitis B Virus (HBV) In District Vehari, Pakistan. *Journal of the College of Physicians and Surgeons Pakistan*. 2020 May; 30(5):550-551. doi: 10.29271/jcsp.2020.05.550.
- [21] Haider J, Lufullah G, Nazli R, Akhtar T, Shah A. Screening of adult dental patients visiting Khyber College of Dentistry, Peshawar for HBV and HCV infections and identifying the associated risk factors. *Pakistan journal of medical sciences*. 2017 May-Jun; 33(3):615-620. doi: 10.12669/pjms.333.12260.
- [22] Rawat N, Mathur N, Rawat K, Mathur M, Chauhan N, Kakkar R, Tinna R. Prevalence of hepatitis B, hepatitis C and human immunodeficiency virus infection among haemodialysis patients in a tertiary health care centre of Western Rajasthan. *International Journal of Medical Science and Public Health*. 2017 Apr; 6(4):7247. DOI:10.5455/ijmsph.2017.105782412016
- [23] Hussein NR, Haj SM, Almizori LA, Taha AA. The prevalence of hepatitis B and C viruses among blood donors attending blood bank in Duhok, Kurdistan region, Iraq. *International Journal of Infections*. 2017 Jan; 4(1): e39008. DOI: 10.177915/iji-39008
- [24] WHO. (2017). Global hepatitis report 2017: World Health Organization. [Last accessed on: 18 June, 2022]. Retrieved from: <https://www.who.int/publications/i/item/9789241565455>
- [25] Muhamad NA, Ab Ghani RM, Abdul Mutalip MH, Muhammad EN, Mohamad Haris H, Mohd Zain R, et al. Seroprevalence of hepatitis B virus and hepatitis C virus infection among Malaysian population. *Scientific Reports*. 2020 Dec; 10(1):21009. doi: 10.1038/s41598-020-77813-5.



Original Article

Prevalence of Cervicogenic Vertigo Among Patients with Cervical Spondylosis; A Cross Sectional Survey

Hamza Dastgir¹, Ayma Hashmi², Maria Asghar³, Muhammad Hanan Zafar⁴, Muhammad Faizan Hamid^{5*} and Asma⁶¹The University of Lahore Pakistan²Physiotherapist University of Bradford (UK)³Mohi-ud-Din Institute of Rehabilitation Sciences Mirpur, AJ&K⁴Riphah International University, Lahore Pakistan⁵Department of Allied Health Sciences, University of South Asia, Cantt Campus Lahore, Pakistan⁶The University of Faisalabad Pakistan

ARTICLE INFO

Key Words:

Prevalence of Cervicogenic Vertigo Among Patients with Cervical Spondylosis

How to Cite:

Dastgir, H. ., Hashmi, A. ., Asghar, M. ., Hanan Zafar, M. ., Faizan Hamid , M. . & Asma , . (2022). Prevalence Of Cervicogenic Vertigo Among Patients with Cervical Spondylosis; A Cross Sectional Survey: Prevalence of Cervicogenic Vertigo Among Patients with Cervical Spondylosis. Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.546>

*Corresponding Author:

Muhammad Faizan Hamid
Department of Allied Health Sciences, University of South Asia, Cantt Campus Lahore, Pakistan
biostats1000@gmail.com

Received Date: 12th June, 2022

Acceptance Date: 27th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Cervical vertigo is a phrase used to describe to-and-fro vertigo and unsteadiness of gait caused by neck lesions. Cervicogenic dizziness is caused by cervical spine involvement. Cervical vertigo is caused by a variety of etiologies and processes. **Objective:** The study was to find Prevalence of Cervicogenic Vertigo Among Patients with Cervical Spondylosis. **Methods:** This study included 78 individuals who had a confirmed diagnosis of cervical spondylosis. Data was obtained from several hospitals in Lahore using a standardized vertigo questionnaire from all participants after clearance from the university ethics council and IRB UOL. Data was collected using a convenient sampling strategy. **Results:** Total of 78 people were selected in study. There were 45 men and 33 women among them. In this study, 65 people reported experiencing lightheadedness when dizzy, while 13 persons reported not experiencing lightheadedness when dizzy. In this study, 65 people reported experiencing blacking out when dizzy, whereas 13 persons reported not experiencing blacking out when dizzy. **Conclusion:** According to the findings of this investigation, cervicogenic vertigo is prevalent in senior individuals with cervical spondylosis.

INTRODUCTION

Cervical vertigo is a phrase used to describe to-and-fro vertigo and unsteadiness of gait caused by neck lesions. It has been identified as a possible cause of neurological disorders. The most prevalent cause of signs and symptoms has been identified as direct cervical compression of cervical nerve roots and spinal cord by osteophytes, degenerative discs, and misplaced vertebrae [1,2]. Patients complaining of dizziness often pose a diagnostic challenge because of the varied possible

etiologies responsible for this symptom [3,4]. Because many illnesses, both benign and dangerous, can induce dizziness, a thorough differential diagnosis for a patient complaining of dizziness is not only challenging but also necessary. Cervicogenic dizziness is dizziness caused by cervical spine involvement. Cervical vertigo is caused by a variety of etiologies and mechanisms [5,6]. Cervicogenic dizziness is caused by three processes, one of which is irritation of the cervical sympathetic nerve system. The

vertebral artery is mechanically compressed or stenosed. Involvement of upper cervical spine proprioceptors induced by functional abnormalities in segments C0-C3 [7,8]. Cervical vertigo associated with neck movement appears to be more common in individuals with cervical disorders than in the general population. Vertigo is known to be caused by cervical spine spondylitis alterations [9,10]. Walking is a common human movement, but sustaining postural balance requires a multisensory and sensorimotor capacity that includes biomechanics, sensory function, sensorimotor integration, and exercise-preprogrammed modifications. Even in elderly adults who show no signs of sickness, there is evidence of degeneration in several sensorimotor systems that enable postural regulation [11,12]. Without increasing mortality, dizzy older adults are more likely to become handicapped than those who are not. There is a severe lack of community-based research on the causes of dizziness, particularly in the elderly. Nonetheless, certain demographic studies indicate that patients over the age of 60 have a higher incidence of vertigo [13,14]. Dizzy patients are generally treated through primary care. Final diagnoses are classified into three categories: peripheral vestibular diseases, central neurological illnesses, and cardiovascular disorders. As a result, it appears that the primary care physician is having difficulty selecting the appropriate expert for referral and further examination of senior patients [15,16]. The goal of this study was to determine the prevalence of cervicogenic vertigo in geriatric individuals with cervical spondylosis. The importance of this study is that it will aid in understanding the balance and gait issues linked with vertigo in the elderly. This study will also aid in determining the potential injuries associated with vertigo in the elderly such as falls, bone fractures etc. The objective of this study was to find out the prevalence of cervicogenic vertigo in geriatric patients with cervical spondylosis.

METHOD

This study included 78 individuals of age ranging 45-70 years who had a confirmed diagnosis of cervical spondylosis. Data was obtained from different hospitals in Lahore and Faisalabad cities utilizing a standardized vertigo questionnaire from all participants after clearance from the university ethics council and IRB UOL [17]. Exclusion criteria was Past medical or surgical history related with cervical region, Presence of any metabolic or systemic diseases other than cervical spondylosis, Congenital cervical anomalies, Vertigo due to other cause than cervical spondylosis, Cervical disc prolapse and Recent cerebral stroke [17]. Before distributing the questionnaire to the participants, signed informed permission was obtained. Data were collected using a

convenient sampling strategy. Data were analyzed using SPSS version 21.0 after receiving informed written consent. All qualitative data, including gender, were provided as frequency, while quantitative data, such as age, were presented as mean \pm SD.

RESULTS

In this study, a total of 78 participants were included, out of which 45 were male and 33 were females. In this study, 7 participants reported that their dizziness first occurred during last 1 week, 6 participants reported it started in last 2 weeks, 13 participants reported it started in last 3 weeks, 13 participants reported it started in last 4 weeks, 4 participants reported it started in last 1 month, 4 participants reported it started in last 2 months, 2 participants reported it started in last 3 months, 3 participants reported it started in last 4 months, 8 participants reported it started in last 1 year, 5 participants reported it started in last 2 years and 13 participants reported it started more than 2 years ago, Table 1.

First occurrence of dizziness	Frequency	Percent
Last 1 Week	7	9.0%
Last 2 Weeks	6	7.7%
Last 3 Weeks	13	16.7%
Last 4 Weeks	13	16.7%
Last 1 Month	4	5.1%
Last 2 Months	4	5.1%
Last 3 Months	2	2.6%
Last 4 Months	3	3.8%
Last 1 Year	8	10.3%
Last 2 Years	5	6.4%
More Than 2 Years	13	16.7%
Total	78	100%

Table 1: First occurrence of dizziness Among participants

In this study, 65 participants reported when they are dizzy, they experience lightheadedness while 13 participants reported they don't experience lightheadedness when they are dizzy. 65 participants reported when they are dizzy, they experience loss of consciousness while 13 participants reported they don't experience loss of consciousness when they are dizzy. 65 participants reported when they are dizzy, they experience tendency to fall to the right, to the left, forward, backward and 13 participants reported they did not experience tendency to fall to the right, to the left, forward, backward. 65 participants reported when they are dizzy, they experience nausea or vomiting, and 13 participants reported they did not experience nausea or vomiting. 65 participants reported they are completely free of dizziness between attacks and 13 participants reported they are not completely free of dizziness between attacks. 65 participants reported changes of position made them dizzy and 13 participants reported changes in position did

not make them dizzy. 65 participants reported they know of anything that will stop their dizziness or make it better and 13 participants reported they did not know of anything that will stop their dizziness or make it better. 65 participants reported they know of anything that will make your dizziness worse and 13 participants did not know of anything that will make your dizziness worse. 17 participants reported they had a head injury and 61 participants reported they did not have any head injury. All 78 participants reported they take their medicines regularly, Table 2.

Conditions during Dizziness		Frequency	Percent
Lightheadedness	Yes	65	83.3%
	No	13	16.7%
	Total	78	100%
Loss of consciousness	Yes	65	83.3%
	No	13	16.7%
	Total	78	100%
Tendency to fall	Yes	65	83.3%
	No	13	16.7%
	Total	78	100%
Nausea or vomiting	Yes	65	83.3%
	No	13	16.7%
	Total	78	100%
No dizziness between attacks	Yes	65	83.3%
	No	13	16.7%
	Total	78	100%
Changing position make dizzy	Yes	65	83.3%
	No	13	16.7%
	Total	78	100%
Changing position make dizzy	Yes	65	83.3%
	No	13	16.7%
	Total	78	100%
Knowledge of anything that will Stop dizziness	Yes	65	83.3%
	No	13	16.7%
	Total	78	100%
Knowledge of anything that will Make Dizziness worse	Yes	65	83.3%
	No	13	16.7%
	Total	78	100%
Injured head	Yes	17	21.8%
	No	61	78.2%
	Total	78	100%
Regular medicines	Yes	78	100%

Table 2: Conditions of participants during dizziness

30 participants reported they did not experienced numbness of face or extremities, 24 participants reported they constantly experienced numbness of face or extremities and 24 participants reported they experienced numbness of face or extremities in episodes. 30 participants reported they did not experience blurred vision or blindness, 24 participants reported they constantly experienced blurred vision or blindness and 24

participants reported they experienced blurred vision or blindness in episodes.

Experiences during dizziness	Frequency	Percent	
Numbness of face or extremities	No	30	38.5%
	Constant	24	30.8%
	In Episodes	24	30.8%
	Total	78	100%
Blurred vision or blindness	No	30	38.5%
	Constant	24	30.8%
	In Episodes	24	30.8%
	Total	78	100%

Table 3: Experience of numbness or Blurred vision during dizziness.

We can say that cervicogenic vertigo is prevalent in males whose ages are above 54 and in females that are above 65 years, Table 4.

Gender	N	Age (Mean+SD)
Male	45	54.4+3.6
Female	33	65.1+3.1

Table 4: Group statistics

DISCUSSION

Previous research revealed that dizziness can be a sign of a variety of illnesses. Some of these disorders can only be managed with Physical Therapy. Musculoskeletal problems that cause disequilibrium-type dizziness are frequently treatable with merely Physical Therapy. Many illness processes that cause dizziness, however, necessitate a medical-surgical referral instead of or in addition to proper Physical Therapy treatments. This demonstrates the importance of both a comprehensive screening examination and, if the screening examination suggests that the patient is suitable for Physical Therapy, a Physical Therapy differential diagnosis to determine additional relevant tests and procedures. The findings of this investigation and the prior study were identical [18,19]. As in earlier research, women were shown to suffer equally or more than men in terms of reported dizziness and impairment. Females reported higher dizziness/unsteadiness symptoms than males. Females ligamentous structures of the neck may be more vulnerable to injury and/or biomechanical stressors due to less muscle support, resulting in discomfort and impairment --[20,21]. Numerous variables each showed a modest relationship with dizziness. This is unsurprising given that dizziness is a feeling of disequilibrium or instability caused by a mismatch or failure in one or more of the several domains that contribute to stability. Dizziness as a geriatric syndrome does not rule out the possibility that a particular illness is predominantly responsible for dizziness in a subgroup of people. [22,23]. This study emphasizes hypotensive cardiovascular diseases, a case

not previously addressed, as a prevalent contributing cause of dizziness. Cardiovascular illnesses were responsible for 28% of the symptoms, whereas peripheral vestibular disorders, such as vestibular neuronitis, benign positional vertigo, and Meniere's disease, were responsible for 18% of the symptoms. Radiographically verified cerebrovascular illness, severe cervical spondylosis, bilateral substantial carotid artery stenosis, drop attacks, and basilar migraine all contributed to symptoms in 14% of patients. This research did not agree with our findings since it focused on different causes of vertigo [24,25]. Although it is commonly missed, dizziness is a common migraine symptom. migraine patients' dizzy episodes were debilitating and severe enough to merit tertiary referral to a university medical Centre. Nausea and vomiting were common complaints, as were hypersensitivity to motion, sleep relief, and postural instability. Many of the patients noted vertigo, which is defined as a sensation of motion in one's surroundings or in relation to oneself that occurs in discrete, recognized episodes. The remaining patients described a motion-sickness-like sensation inside their minds as swimming or rocking, but with no sense of movement in relation to their surroundings. While the dizziness came in fits and starts, it frequently lasted days to weeks. Long bouts of motion sickness were regularly broken by bouts of vertigo. This study contradicted our findings since it focused on different causes of vertigo [26,27].

CONCLUSION

This study revealed that cervicogenic vertigo is common in individuals with cervical spondylosis, and it is more common in males over the age of 54 and females over the age of 65. Cervicogenic dizziness is a diagnosis defined by dizziness and disequilibrium in individuals with cervical disease and neck discomfort.

REFERENCES

- [1] Brandt T. Vestibular disorders in (frontal) roll plane. In *Vertigo 2003* (pp. 175-197). Springer, New York, NY. doi.10.1007/978-1-4757-3801-8_10
- [2] Brandt T. Approaching the patient. In *Vertigo 2003* (pp. 23-48). Springer, New York, NY. doi.10.1007/978-1-4757-3801-8_2
- [3] 3 R. Oku, K. Shigeno, H. Kumagami, and T. Kobayashi, "Ocular Torsion in an Upright Position in Normal Subjects," *Equilibrium Research*, vol. 61, no. 1, pp. 6-10, 2002. doi.10.3757/jser.61.6
- [4] Robertson DD, Garber LZ, Ireland DJ. Ocular torsion monitoring in chemical labyrinthectomy. *The Journal of Otolaryngology*. 1996 Jun 1;25(3):171-7.
- [5] Johnson EG. Vertebral artery testing in dizzy patients: a review of the literature and clinical considerations. *Dizziness: Vertigo, Disequilibrium and Lightheadedness*. 2009.
- [6] 6. Maffei G. Vertigo in the pathology of the cervical spine. *Acta bio-medica de L'Ateneo parmense: organo della Societa di medicina e scienze naturali di Parma*. 1983;54:21-6.
- [7] 7. Huijbregts P, Vidal P. Dizziness in orthopaedic physical therapy practice: Classification and pathophysiology. *Journal of Manual & Manipulative Therapy*. 2004 Oct 1; 12(4):199-214. doi.10.1179/106698104790825095
- [8] 8. Risman BJ. *Gender vertigo: American families in transition*. Yale University Press; 1998.
- [9] 9. Brandt T, Baloh RW. Rotational vertebral artery occlusion: a clinical entity or various syndromes?. *Neurology*. 2005 Oct 25; 65(8):1156-7. doi.10.1212/01.wnl.0000183154.93624.ac
- [10] 10. Nwaorgu OG, Onakaoya PA, Usman MA. Cervical vertigo and cervical spondylosis—a need for adequate evaluation. *Nigerian Journal of Medicine: Journal of the National Association of Resident Doctors of Nigeria*. 2003 Jul 1;12(3):140-4.
- [11] 11. Brandt T. Vertigo, dizziness, and falls in the elderly. In *Vertigo 2003* (pp. 385-392). Springer, New York, NY. doi.10.1007/978-1-4757-3801-8_27
- [12] 12. Bird JC, Beynon GJ, Prevost AT, Baguley DM. An analysis of referral patterns for dizziness in the primary care setting. *British journal of general practice*. 1998 Dec 1;48(437):1828-32
- [13] 13. Sloane PD. Dizziness in primary care. *J Fam Pract*. 1989;29(1):33-8.
- [14] 14. Brandt T. Cervical vertigo—reality or fiction?. *Audiology and Neurotology*. 1996;1(4):187-96. doi.10.1159/000259201
- [15] 15. Lawson J, Fitzgerald J, Birchall J, Aldren CP, Kenny RA. Diagnosis of geriatric patients with severe dizziness. *Journal of the American Geriatrics Society*. 1999 Jan; 47(1):12-7. doi.10.1111/j.1532-5415.1999.tb01895.x
- [16] 16. Kroenke K, Lucas CA, Rosenberg ML, Scherokman B, Herbers Jr JE, Wehrle PA et al. Causes of persistent dizziness: a prospective study of 100 patients in ambulatory care. *Annals of internal medicine*. 1992 Dec 1; 117(11):898-904. doi.10.7326/0003-4819-117-11-898
- [17] 17. Brandt T. *Vertigo: its multisensory syndromes*. Springer Science & Business Media; 2013 Jun 29. doi.10.1007/978-1-4471-0527-5_10
- [18] 18. Schenk RP, Coons LB, Bennett SE, Huijbregts PA. Cervicogenic dizziness: a case report illustrating orthopaedic manual and vestibular physical therapy comanagement. *Journal of Manual & Manipulative*

- Therapy. 2006 Jul 1; 14(3):56E-68E. doi.10.1179/jmt.2006.14.3.56E
- [19] Whitney SL, Rossi MM. Efficacy of vestibular rehabilitation. *Otolaryngologic Clinics of North America*. 2000 Jun 1; 33(3):659-72. doi.10.1016/S0030-6665(05)70232-2
- [20] Humphreys BK, Bolton J, Peterson C, Wood A. A cross-sectional study of the association between pain and disability in neck pain patients with dizziness of suspected cervical origin. *Journal of whiplash & related disorders*. 2002 Jan 1; 1(2):63-73. doi.10.3109/J180v01n02_05
- [21] Chole RA, Parker WS. Tinnitus and vertigo in patients with temporomandibular disorder. *Archives of Otolaryngology-Head & Neck Surgery*. 1992 Aug 1; 118(8):817-21. doi.10.1001/archotol.1992.01880080039010
- [22] Tinetti ME, Williams CS, Gill TM. Dizziness among older adults: a possible geriatric syndrome. *Annals of internal medicine*. 2000 Mar 7; 132(5):337-44. doi.10.7326/0003-4819-132-5-200003070-00002
- [23] FROEHLING DA, SILVERSTEIN MD, MOHR DN, BEATTY CW, OFFORD KP, BALLARD DJ. Benign positional vertigo: incidence and prognosis in a population-based study in Olmsted County, Minnesota. In *Mayo Clinic Proceedings* 1991 Jun 1 (Vol. 66, No. 6, pp. 596-601). Elsevier. doi.10.1016/S0025-6196(12)60518-7
- [24] Hain TC. Cervicogenic causes of vertigo. *Current opinion in neurology*. 2015 Feb 1; 28(1):69-73. doi/10.1097/WCO.0000000000000161
- [25] Jones IH. *Equilibrium and vertigo c. 2*. JB Lippincott Company; 1918.
- [26] Cutrer FM, Baloh RW. Migraine-associated dizziness. *Headache: The Journal of Head and Face Pain*. 1992 Jun; 32(6):300-4. doi./10.1111/j.15264610.1992.hed3206300.x
- [27] Cope S, Ryan GM. Cervical and otolith vertigo. *The Journal of Laryngology & Otology*. 1959 Feb; 73(2):113-20. doi.10.1017/S0022215100055018



Original Article

Prevalence of *E. coli* and Coliform bacteria in the Dental Unit Waterlines of Private Clinics of Islamabad and Rawalpindi
 Muhammad Muhammad¹, Arsalan Hamid Khan², Muhammad Musab Sheth¹, Shanzar Butt¹, Asadullah Shakeel¹, Syed Saboor Tariq¹
¹Department of Operative Dentistry, Riphah International University, Islamabad, Pakistan

²Gandhara University, Peshawar, Pakistan

ARTICLE INFO

Key Words:

Dental unit water line (DUWL), pathogenic bacteria, water samples

How to Cite:

 Muhammad, M. ., Hamid Khan, A. ., Musab Sheth, M. ., Butt, S. ., Shakeel, A. ., & Saboor Tariq, S. . . (2022). Prevalence of E. coli and Coliform bacteria in the Dental Unit Waterlines of Private Clinics of Islamabad and Rawalpindi: E. coli and Coliform bacteria in the Dental Unit Waterlines. Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.585>

*Corresponding Author:

 Muhammad Muhammad
 Department of Operative Dentistry, Riphah International University, Islamabad, Pakistan
dr.muhammad@riphah.edu.pk

Received Date: 22nd June, 2022

Acceptance Date: 27th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Bacteria colonizing surfaces and forming biofilm in dental unit waterlines is a well-documented phenomenon. Pathogenic bacteria from contaminated dental unit water lines are transmitted with aerosols and splatter generated during dental procedures. **Objective:** To identify the presence of coliform bacteria and *E. Coli* in dental unit waterlines of private dental clinics in Islamabad and Rawalpindi to see whether they meet the criteria for drinking water. **Methods:** This is a quantitative study carried out on 30 active dental units. Triple syringe and handpiece outlet water samples were taken. Samples were evaluated by National Institute of Health (NIH) through Polymerase Chain Reaction (PCR). The cultures were incubated twice at 24 and 48 hours. The presence of coliform bacteria and *E. coli* in the samples was evaluated. **Results:** Approximately 20% of the samples were found to have coliform bacteria and *E. coli*. Some private dental clinics in Islamabad and Rawalpindi use dental unit waterlines that do not meet the criteria for drinking water. **Conclusions:** Dental unit water lines (DUWLs) must meet the set criteria for drinking water to reduce the risk of infections. Contamination with coliform bacteria and *E. Coli* were evident in some of the dental clinics. This contamination can be reduced by following Center for Disease Control (CDC) guidelines and using chemical treatment protocols for cleaning dental unit waterlines.

INTRODUCTION

Water is an indispensable component in the provision of dental care. It serves a variety of crucial purposes ranging from irrigation of the operating field and oral rinsing to cooling of rotary instrument [1,2]. The water used in the dental unit waterline systems may be derived from different sources. Common sources include municipal water supply and bottles (tanks) connected to the dental unit [3-5]. Microorganisms can inadvertently enter the dental unit water supply lines via aerosols and droplets generated by the dental instruments [6]. They may also reach the DUWL through contaminated bottled water or mains water. These microorganisms include bacteria,

fungi, protozoa, and viruses, some of which may be pathogenic. If present in greater than acceptable numbers, the pathogenic bacteria, such as *Legionella*, *Pseudomonas*, and *Mycobacteria*, may harm the dental staff and patients alike [7-9]. DUWL systems consist of long, narrow-diameter pipes composed of nylon or polyvinyl chloride material. Water may remain stationary for long periods in these pipes. This can lead to a rise in the water temperature. The fluid dynamics within the DUWL systems, therefore, provide the ideal environment for pathogenic bacteria to grow and form microbial biofilms [10]. Not only do biofilms show greater resistance to

antimicrobials than planktonic bacteria, but the subsequent sloughing of these bacterial biofilms within the dental unit water lines also plays an important role in the spread of infection. Even though fatal incidents reported because of contaminated DUWL are rare, the risk of infection should not be underestimated [11]. According to the Centers for Disease Control and Prevention (CDC), dental unit water used in nonsurgical treatments should have a CFU/mL of less than 500 [12]. The Environmental Protection Agency has set this guideline for drinking water (EPA) [13]. However, according to the American Dental Association (ADA) guidelines, the bacterial contamination of DUWL should not exceed 200 CFUs/ml. The guidelines also recommend a separate water reservoir other than the urban water source, the use of disinfecting chemical solutions in the tubes, routine cleaning of water reservoirs, the use of filters, flushing of the tubes for a few minutes before and after dental procedures, sterilization of handpieces with autoclave, and use of ultraviolet light for disinfection [14]. Many dental offices in Pakistan are connected to municipal water. The water used in dentistry is not standardized, so the minimum criteria to meet is the drinking water. This means the absence of *Escherichia coli* and other coliform bacteria [15]. This study aimed to identify the water sources and evaluate the presence of *E. coli* and coliform bacteria in the water/air syringe and handpiece outlets in private dental clinics of twin cities, Islamabad and Rawalpindi.

METHODS

This descriptive cross-sectional study was approved by the Ethical review board of Riphah International University (IIRC/IRC/2020/01/010). Water samples were collected from 30 private dental clinics in Islamabad and Rawalpindi from September to December 2020. Units with working air/water syringes and handpiece outlets were included. A convenient sampling technique was used. Permission was taken from concerned authorities prior to the conduction of the study. 100 ml of water from the water/air syringe and handpiece outlets of each dental unit was taken in sterile sample bottles, provided by the National Institute of Health (NIH). Samples were labeled appropriately with the date and time of collection as well as details of the dental units they were obtained from. These samples were then forwarded to the NIH's Department of Microbiology for microbial testing of coliform and *E. coli* bacteria. The data were analyzed by SPSS version 24.0.

RESULTS

In the present study, an evaluation of 30 water samples taken from the DUWLs of private dental clinics of Islamabad and Rawalpindi indicates that 20% of these

clinics do not meet the minimum criteria for drinking water (Table 1). Water should be free of coliform bacteria and fecal *E. coli* to be considered safe for use in dental practice.

Water samples	Number	Coliform bacteria and <i>E. coli</i> present (Frequency)	Coliform bacteria and <i>E. coli</i> present (%)	Coliform bacteria and <i>E. coli</i> absent (Frequency)	Coliform bacteria and <i>E. coli</i> absent (%)
Islamabad	15	2	13.3	13	86.6
Rawalpindi	15	4	26.6	11	73.3
Total	30	6	20	24	80

Table 1: Frequency and percentage of coliform bacteria and *E. coli* found in water samples of private dental clinics of twin cities

DISCUSSION

The current study was conducted to examine the microbial quality of DUWLs of private dental clinics within the twin cities, Islamabad and Rawalpindi. Water samples taken from 30 private clinics, 15 from each of the two cities, were evaluated by microbial testing through NIH. The results showed that 6 out of 30 dental units used water that was contaminated with Coliform bacteria and *E. coli*, which makes up for 20% of the DUWLs examined. This means that 80% of all private dental clinics evaluated use water that meets the criteria for drinking water. Only 13.3% of the DUWLs of dental clinics of Islamabad were found to contain these bacteria as compared to 26.6% in the clinics in Rawalpindi. This difference may be attributed to better quality of life, higher literacy rate and better socioeconomic conditions that prevails in Islamabad [16]. Numerous studies have been conducted worldwide to determine the bacterial quality of DUWLs [17]. Different studies have yielded considerably distinct results regarding the type, number, and virulence of these organisms. The disparity in these results is not only because of the different testing conditions and water sources but also because of the variable geographical locations in which the studies were conducted. Research conducted in Quito and Caracas, in South America, yielded undesirably high number total viable counts of heterotrophic bacteria and/or coliform bacteria and *Pseudomonas* in 73% of the water samples. These samples also contained non-tuberculous mycobacteria in large numbers [18]. Another similar study was undertaken in Brazil, however, it included evaluation of DUWLs of public dental clinics instead of private dental practices. In this study, *E. coli* was not detected in any of the water samples analyzed. However, nine of the thirty samples (30%) exhibited total coliforms. A study, conducted in Iran, demonstrated that 25.5% water samples were positive for coliform bacteria [19]. An audit performed in England, for determining the quality of DUWLs, showed 72 DUWL water samples were tested, and none was contaminated with *E. coli*, but coliforms were recovered from five of them (7%)

[20]. This may be attributed to better economy and higher standard of care provided in first world countries compared to developing nations. This variety of results is due to many factors, including but not limited to, socioeconomic circumstances, literacy rates, types of dental practices, professional ethics of practicing dentists, sources of water, protocols used for disinfection of DUWLs, methods of sample collection and testing, and living conditions prevalent in the areas of study. The results of the current study show that many private dental clinics in Islamabad and Rawalpindi, still use water that does not meet the minimum criteria set by the CDC. This emphasizes the need for obtaining water from better sources, use of distilled water for treatment, routine disinfection of DUWLs and regular monitoring of biofilms in the DUWLs, to reduce the risk of infection.

CONCLUSION

DUWLs must meet the criteria for drinking water to reduce the risk of infections. Contamination with coliform bacteria and E. Coli were evident in some of the dental clinics. This contamination can be reduced by following CDC guidelines and using chemical treatment protocols for cleaning of dental unit waterlines.

REFERENCES

- [1] Von Fraunhofer JA, Siegel SC, Feldman S. Handpiece coolant flow rates and dental cutting. Operative dentistry. 2000 Nov; 25(6):544-8.
- [2] Siegel SC, von Fraunhofer JA. Irrigation rates and handpieces used in prosthodontic and operative dentistry: results of a survey of North American dental school teaching. Journal of Prosthodont. 2000 Jun; 9(2):82-6. doi: 10.1111/j.1532-849x.2000.00082.x.
- [3] Spagnolo AM, Sartini M, Cristina ML. Microbial contamination of dental unit waterlines and potential risk of infection: a narrative review. Pathogens. 2020 Aug; 9(8):651. doi.10.3390/pathogens9080651
- [4] Jolanta S, Jolanta S. Bacterial hazards in a dental office: An update review. African Journal of Microbiology Research. 2012 Feb; 6(8):1642-50. doi.10.5897/AJMR11.1002
- [5] Shearer BG. Biofilm and the dental office. The Journal of the American Dental Association. 1996 Feb; 127(2):181-9. doi.10.14219/jada.archive.1996.0166
- [6] Kumar S, Atray D, Paiwal D, Balasubramanyam G, Duraiswamy P, Kulkarni S. Retracted: Dental unit waterlines: source of contamination and cross-infection. Journal of Hospital Infection. 2010 Feb; 74(2):99-111. doi.10.1016/j.jhin.2009.03.027
- [7] Tuvo B, Totaro M, Cristina ML, Spagnolo AM, Di Cave D, Profeti S et al. Prevention and control of Legionella and Pseudomonas spp. colonization in dental units. Pathogens. 2020 Apr; 9(4):305. doi.10.3390/pathogens9040305
- [8] Zemouri C, Awad SF, Volgenant CM, Crielaard W, Laheij AM, De Soet JJ. Modeling of the transmission of coronaviruses, measles virus, influenza virus, Mycobacterium tuberculosis, and Legionella pneumophila in dental clinics. Journal of dental research. 2020 Sep; 99(10):1192-8. doi.10.1177/0022034520940288
- [9] Porteous NB, Redding SW, Jorgensen JH. Isolation of non-tuberculosis mycobacteria in treated dental unit waterlines. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology. 2004 Jul; 98(1):40-4. doi./10.1016/j.tripleo.2004.02.006
- [10] Fan C, Gu H, Liu L, Zhu H, Yan J, Huo Y. Distinct Microbial Community of Accumulated Biofilm in Dental Unit Waterlines of Different Specialties. Front Cell Infect Microbiol. 2021 Jun; 11:670211. doi: 10.3389/fcimb.2021.670211.
- [11] Vestby B. Biofilm and its Role in the Pathogenesis of Disease. Antibiotics (Basel).(9). doi.10.3390/antibiotics9020059
- [12] Lal B, Ravindra K, Biswal M. Appraisal of microbial contamination of dental unit water systems and practices of general dental practitioners for risk reduction. Environmental Science and Pollution Research. 2018 Nov; 25(33):33566-72. doi.10.1007/s11356-018-3298-y
- [13] Karpay RI, Plamondon TJ, Mills SE, Dove SB. Combining periodic and continuous sodium hypochlorite treatment to control biofilms in dental unit water systems. The Journal of the American Dental Association. 1999 Jul; 130(7):957-65. doi.10.14219/jada.archive.1999.0336
- [14] Percival RS, Devine DA, Nattress B, Kite P, Marsh PD. Control of microbial contamination in dental unit water systems using tetra-sodium EDTA. Journal of applied Microbiology. 2009 Oct; 107(4):1081-8. doi.10.1111/j.1365-2672.2009.04299.x
- [15] Lisboa GM, Lisboa YR, Pinheiro TM, Stegun RC, da Silva-Filho EA. Microbial diversity in dental unit waterlines. Acta Odontológica Latinoamericana. 2014 Dec; 27(3):110-4.
- [16] Federman M, Garner TI, Short K, Cutter IV WB. What does it mean to be poor in America. Monthly Lab. Rev.. 1996;119:3. doi.10.1146/annurev.publhealth.23.112001.112349
- [17] de Biofilm EM. Microbiological water evaluation from biofilm adhered to dental unit waterlines. International Journal of Odontostomat. 2019;

- 13(3):357-62. doi.10.4067/S0718-381X2019000300357
- [18] Castellano Realpe OJ, Gutiérrez JC, Sierra DA, Pazmino Martinez LA, Prado Palacios YY, Echeverría G, de Waard JH. Dental Unit Waterlines in Quito and Caracas contaminated with Nontuberculous Mycobacteria: A potential health risk in dental practice. *International Journal of Environmental Research and Public Health*. 2020 Apr; 17(7):2348. doi.10.3390/ijerph17072348
- [19] Dobaradaran S, Nabipour I, Ramavandi B, Zazouli MA, Tahmasebi R, Ghaedi H et al. Microbial contamination of dental unit waterlines in Bushehr, Iran. *Fresenius Environmental Bulletin*. 2014 Jan; 23(4):1000-5.
- [20] Chate RA. An audit improves the quality of water within the dental unit water lines of general dental practices across the East of England. *British dental journal*. 2010 Oct; 209(7):E11-./ . doi.10.1038/sj.bdj.2010.885



Original Article

Severe Coronary Problems in Kidney Illness: Medical and Therapeutic Features

Niaz Hussain Abassi¹, Khalid Hussain Soomro¹, Abdul Qadir Bhutto^{1*}, Shah Muhammad Babar², Ali Asad², Muhammad Aslam³¹Department of Cardiology, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences Gambat, Pakistan²Intervention Cardiology Fellow NICVD, Karachi, Pakistan³NICVD, Nawab Shah, Pakistan

ARTICLE INFO

Key Words:

angiography, natriuretic peptide, myocardial infarction, CAD

How to Cite:

Hussain Abassi, N. ., Hussain Soomro, K. ., Qadir Bhutto, A. ., Muhammad Babar, S. ., Asad, A., & Aslam, M. . (2022). Severe Coronary Problems in Kidney Illness: Medical and Therapeutic Features: Severe Coronary Problems in Kidney Illness. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.529>

*Corresponding Author:

Abdul Qadir Bhutto
Department of Cardiology, Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences Gambat, Pakistan
qadira41@gmail.com

Received Date: 8th June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

CAD (coronary artery disease) has a link with the long-lasting kidney issues. The people suffering from some kidney issue may develop coronary artery disorder and its risk factors are very similar to the risk factors in other cases. **Objective:** To assess the parameters of CKD (coronary kidney disease) and CAD (coronary artery disease). There was need for the establishment of some efficient predictive methods or biomarkers for the indication of the coronary disorder. **Methods:** To proceed with this study 301 patients were selected. All of these patients were admitted in the cardiology ward of the hospital. Among them 151 patients had ACS along with CDK while on the other hand, 150 patients had ACS but they do not have any coronary artery disease. Both categories of the patients had made, according to the presence or absence of coronary artery disease. The progression of Coronary disease was estimated by KDIGO (improving global outcome). **Results:** For the prediction of results, all the attributes related to kidney issues as well as coronary artery were analyzed. Different parameters like disease history of the patients, regulatory parameter of both ACS and CKD, cardio graphical results and angiography states, were carefully estimated for both categories. The characteristics related to increased level of myocardial infarction indicated by STEMI. All these inferred that the level of initiation of coronary disease is much higher in the group without chronic kidney disease. It was estimated about 42 %. However, in the case of CKD group having coronary issues, the raise of non-segmented myocardial infarction is lower (28 %). **Conclusion:** There is increased level of CAD in case of kidney disease and in CAD. The different indicators and markers for the coronary and kidney disease as well as different cardiological methods were assessed in this study.

INTRODUCTION

The prevalence of CAD (coronary artery disease), in case of some kidney disorder was compared with the normal coronary issues in case of other disease. The atherosclerosis process increased, when link develop between cardiological disease and uremia related disease. Different unusual risk factors like RBCs deficiency, changes in the metabolism of calcium and phosphate, uremic issues and inflammation do increase when kidney fails to perform its normal function [1-3]. For the initiation of the atherosclerosis, dyslipidaemia have prime role. For the study of homeostasis, after some kidney issues, AURORA is used. With the help of this test, different factors

related to the disturbance of homeostasis evaluated as well as the role of these factors in the initiation of other diseases can also be studied [4-5]. During some kidney issues, lipid metabolism of the body also gets disturbed and plaques formed [6]. In more severe cases of coronary issues, NSTEMI (non-ST-segment myocardial infarction), STEMI (ST segment increase myocardial infarction), different restriction in coronary arteries and heart occur. However, in the kidney patients having CDK, the most common symptoms were pain in thoracic region, and different other issues observed [7-8]. The different kidney issues also disturb the necrosis of cardiac tissues and their

markers such as troponins of cardiac regions make the diagnosis of acute coronary syndrome difficult. In case of myocardial infraction, the level of biomarker troponin raises more than 99 %, which is quite higher than the normal condition. The raise of troponin induces pain in chest, and ECG graph alterations and cause ischemia of heart. Different protocol provided by international cardiac organization for the measurement of level of troponin [9-11]. Different kidney impairments also interfere with the normal function of the heart. As a result of kidney surgery revascularization of myocardial infraction was observed. The results of CKD and ACS have negative effects on different therapies such as thrombolytic therapy [12]. When therapeutic analysis of treatment of CKD and ACS considered, it also has a number of issues; there is no effective therapy, when patient has both kidney and coronary issue. For the treatment of this disease, aggressive reperfusion method was used which is a fibrinolytic therapy. Different trials begun to reduce the mortality rate by this combine kidney and coronary artery syndrome. There was an increase in the probability of bleeding, if a patient has more acute kidney issue or some kind of hemorrhage due to thrombolysis in case of coronary issue. The more effective therapy till date, for this syndrome is PCI (percutaneous coronary intervention). Several other therapies like syntax and bypass grafting, were also used for treatment [13-14]. The purpose of this study was to analyze the different parameters of ACS and CDK and to establish the management for emergency cases for the diagnosis.

METHODS

It was an observational study conducted at Pir Abdul Qadir Shah Jeelani Institute of Medical Sciences Gambat. In this study, 301 patients were included. All of these patients declared for the disease ACS by the cardiology lab of the hospital. The patients selected from 2020 to 2021. For the inclusion of the patients, it was mandatory to do ECG of all the patients. After ECG, patients with the raise of troponin level were include. All of the patients have symptoms for the coronary artery disease as well as some kidney issues like disturbance of homeostasis. Those patients were excluded, who had constant changes in Electrocardiogram, and not diagnosed with acute disease level (not suffering from kidney function alteration). The patients were divided into two categories, one with only ACS (150 patients) and the second one with ACS as well as CKD (151 patients). The permission was granted to the study group by ethical committee, and consent from patients was also taken. For the measurement of kidney infection level, creatinine formula used for the prediction of kidney function; the function was estimated and compared with

the function of threshold levels defined by National kidney base. The lowering of GFR level observed in case of renal malfunction, the level of GFR observed for consecutive 4 months. For the measurement of cardiac function, abnormal ECG changes was observed along with other symptoms like pain in thoracic region, and elevation of the level of troponin, a necrotic enzyme of cardiac system. For myocardial infraction, angiography was done to diagnose about the cardiac function. For the assessment of the efficiency of left ventricle, Killip Kimball classification used. The level of urea and uric acid was also estimated by different methods. After obtaining results from all of the tests, for all patients, different parameters of each individual patient was calculated and compared by using biostatistics and number of other test like Mann-Whitney test, Chi square and Kolmogorov-simirnov test. The confidence level was kept 0.05.

RESULTS

The incidence of the disease is similar in male and female. The calculated p-value for the gender based incidence don't show the significant difference. It was observed to be 0.76 for the control and experimental group. However, the data obtained after comparing the similar groups showed that the male are more prone to develop ACS. The p-value for the mean age was <0.01. The mean age of the reference lot was calculated to be 68.62. The significant p-value of the urban origin was <0.01, Table 1.

Features	Acute Coronary syndrome CKD group (n=151)		Acute Coronary syndrome without CKD group (n=150)		P-value
	Number	Percentage	Number	Percentage	
Women	102	67.54%	99	66%	0.76
Men	49	32.45%	51	34%	
Age					
Mean age	69 ± 9.9		64 ± 10.7		<0.01
Confidence level (95%)	48.78; 9		42.93; 86.1		

Table 1: The distribution of gender according to the AC syndrome with or without CKD group

The 97 patients were observed at the stage 3 of the glomerular filtration rate (GFR) in the ACS with CKD group. While 35 were observed at stage 4 and 18 at stage 5. The incidence of the MINOCA and STEMI is higher in the ACS group without CKD. The CKD group has the higher incidence of stable angina and chronic coronary syndrome, Table 2.

Characteristics	The ACS without CKD	P-value
STEMI	65	0.19
N-STEMI	42	0.04
Unstable angina	48	0.27
MINCOA	9	0.31

Table 2: The distribution of different characteristics in the ACS group without CKD

The associated comorbidities were studied for the both groups with or without CKD. The incidence of the heart failure in the CKD group is as higher as 41%. The incidence of diabetes mellitus and sequelae of myocardial infraction is also higher in this group. The incidence of thoracic pain was also greater in non-CKD group. The cardiogenic shock percentage was also higher in the CKD group, Table 3.

Features	ACS group with CKD (n=151)		ACS group without CKD (n=150)		P-value
	Number	Percentage	Number	Percentage	
Stable angina	59	39.07	38	25.33	<0.01
Chronic coronary syndrome	68	45.03%	38	25.33	<0.01
Angina pectoris Grading					
Degree I	9	5.96	7	4.6	0.59
Degree II	33	21.85	25	16.66	0.37
Degree III	19	12.58	7	4.61	0.01
NYHA II	36	23.84	17	1.33	<0.01
NYHA III	28	18.54	13	8.66	0.02
Previous heart failure	63	41.72	29	19.33	<0.01
Sequelae of myocardial I nfraction	33	21.85	17	11.33	0.01
Inferior territory	16	10.59	3	2	<0.01
Anterior territory	16	10.59	12	8	0.42
Lateral territory	0	0.00	1	0.66	0.31
Anterior and inferior territories	1	0.66	0	0.00	0.31
Peripheral artery disease	2	17.88	17	11.33	0.17
Previous ischemic stroke	72	18.54	2	1.33	<0.01
Diabetes mellitus	88	56.95	53	35.33	<0.01
Thoracic pain at admission	68	56.95	130	86.66	<0.01
Dyspnoea at admission	66	41.72	20	13.33	<0.01
Syncope at admission	33	1.98	0	0.00	0.16
Cardiogenic shock	20	13.24	10	6.66	0.07

Table 3: Percentage comorbidities in the ACS group with or without CKD

The biomarker that attest the cardiac origin of dyspnoea was considered as its prognosis predictor. The patients with impaired renal functions has higher mean values of marker while lower mean values were observed in the patients with proper renal functioning. The 89% cases included in the ACS with CKD group underwent coronary angiography while 99% cases of the ACS with non-CKD group underwent angiography. In the non-CKD group, the single vessel CAD was observed with the higher percentage, Table 4.

Features	ACS (n=150)		ACS/CKD (n=151)		P-value
	Number	Percentage	Number	Percentage	
CAD (single -vessel)	44	29.33	16	10.59	<0.01

CAD (double -vessel)	49	32.66	42	27.81	0.33
CAD (three-vessel)	34	22.66	42	27.81	0.42
LMCA	13	8.66	22	14.56	0.13
MINOCA	9	6	13	8.60	0.36
Patient without coronary angioplasty	1	0.66	18	11.92	<0.01

Table 4: The percentage characteristics of coronary artery disease in the CKD and non-CKD group

DISCUSSION

The atypical symptoms are observed in ACS. The higher number of cardiovascular diseases are associated with chronic kidney disease. The mortality rates of the patients having ACS with CKD are still unknown. It is the most prevalent disease now a day [15]. The biomarkers and echocardiography play important role in determining the prognosis of the patients. The worst prognosis of ACS is observed in the patient with associated CKD. CKD is also a predictor of the outcomes of ACS. The worst cardiac events are seen in the patients with associated cardiovascular diseases. The poor long/short term outcomes are associated with the CKD. The ACS in the CKD patients complicate the management of the patients. There is a need to develop the treatment strategies for the patients having CKD with ACS is highly [16-17]. The renal functioning must be considered before developing the treatment strategies. The congestive heart failure and cardiogenic shocks are predictor of mortality in the CKD patients with ACS. With the increase in the impaired renal functioning the incidence of non-traditional risk factors also increases. The patients with ACS having normal kidney functioning have characteristics thoracic pain predominantly. While in the patient having CKD with ACS has higher incident of dyspnea. The patients with retarded renal functions have ischemia predominantly. A study was conducted in which 356 patients were included, it was concluded that the incidence of myocardial infraction in the patient with CKD group is higher than the patients without CKD. It is observed that the diabetic neuropathy is associated with the phenomena. It is most highly observed pathology in the patients with CKD [18]. A similar study was conducted by the Sosnov et al., depicted that the incidence of thoracic pain is much higher in the patients included in the non-CKD group. It is not dependent on the diabetic neuropathy. Study also revealed that the CKD group has higher incidence of shortness of breath. Few studies indicated that the cardiovascular risk factors are not dependent on the renal functions. The ischemic CAD and obliterative CAD are highly influenced by the impairment of the renal function. Because of the presence of left ventricular hypertrophy, the CKD patients are not

characterized by the ischemia. Our study also revealed that the QS waves are generally observed in the patients with CKD [19-20]. Other studies were also conducted on the different people that also depicted that incidence of left bundle branch block is higher in the CKD group. The chronic inflammatory process leads to the ventricular remodeling that are more common in the CKD group. The patients having CKD with proper renal functioning have poor prognosis after ACS. During the drug eluting stents, the Chan et al., study depicted that the cardiac and cerebrovascular events ratio was lower. The CABG versus PCI also decreases the rate of myocardial revascularization. The myocardial revascularization do not affect the death significantly [21-22]. The CKD patients also have the higher incidence of stroke and myocardial infraction. The PCI group has higher incidence of repeated revascularization as compared to the CABG group. The same treatment was given to the patients diagnosed with the STEMI and CKD. CKD group has the higher incidence of cardiogenic shocks and other complication like left ventricle impairment and papillary muscle ischemia. The prognosis rate improves in the CKD patients that has undergone myocardial revascularization. The hemodynamic instability risks are also lower in such patients. The survival rates of the patients with CKD and STEMI, are influenced by the myocardial reperfusion [23].

CONCLUSIONS

CAD and CKD shared the strong association. The pathological conditions such as heart failure and ischemic stroke were associated with the CKD patients with coronary events. For evaluation of prognosis of such patients the elements like echocardiography and NT-pro BNP must be considered. The patients with the impaired renal functions have the characteristics of proximal CAD. For evaluation of the clinical characteristics of the patient new trial must be conducted on the patients with the CKD and ACS group. There is need to develop the strategy for improvement of outcomes of the ACS patients with CKD.

REFERENCES

- [1] Yamamoto S, Kon V. Mechanisms for increased cardiovascular disease in chronic kidney dysfunction. *Current opinion in nephrology and hypertension*. 2009 May; 18(3):181-8. doi: 10.1097/mnh.0b013e328327b360.
- [2] Deo R, Fyr CL, Fried LF, Newman AB, Harris TB, Angleman S, Green C, et al. Health ABC study. Kidney dysfunction and fatal cardiovascular disease—an association independent of atherosclerotic events: results from the Health, Aging, and Body Composition (Health ABC) study. *American heart journal*. 2008 Jan; 155(1):62-8. doi: 10.1016/j.ahj.2007.08.012.
- [3] Vanholder R, Massy Z, Argiles A, Spasovski G, Verbeke F, Lameire N; European Uremic Toxin Work Group. Chronic kidney disease as cause of cardiovascular morbidity and mortality. *Nephrol Dial Transplant*. 2005 Jun; 20(6):1048-56. doi: 10.1093/ndt/gfh813.
- [4] Levin A. *Clinical epidemiology of cardiovascular disease in chronic kidney disease prior to dialysis*. Oxford, UK: Blackwell Science Inc. In: *Seminars in Dialysis*. 2003 Mar-Apr; 16(2):101-5. doi: 10.1046/j.1525-139x.2003.16025.x.
- [5] Lopes NH, da Silva Paulitsch F, Pereira A, Garzillo CL, Ferreira JF, Stolf N, et al. Mild chronic kidney dysfunction and treatment strategies for stable coronary artery disease. *The Journal of thoracic and cardiovascular surgery*. 2009 Jun; 137(6):1443-9. doi: 10.1016/j.jtcvs.2008.11.028.
- [6] Azarbal A, Malenka DJ, Huang YL, Ross CS, Solomon RJ, DeVries JT, et al. Recovery of Kidney Dysfunction After Transcatheter Aortic Valve Implantation (from the Northern New England Cardiovascular Disease Study Group). *The American Journal of Cardiology*. 2019 Feb; 123(3):426433. doi: 10.1016/j.amjcard.2018.10.042.
- [7] Levin A, Djurdjev O, Barrett B, Burgess E, Carlisle E, Ethier J, et al. Cardiovascular disease in patients with chronic kidney disease: getting to the heart of the matter. *American journal of kidney diseases*. 2001 Dec; 38(6):1398-407. doi: 10.1053/ajkd.2001.29275.
- [8] Cirillo M, Lanti MP, Menotti A, Laurenzi M, Mancini M, Zanchetti A, et al. Definition of kidney dysfunction as a cardiovascular risk factor: use of urinary albumin excretion and estimated glomerular filtration rate. *Archives of internal medicine*. 2008 Mar; 168(6):617-24. doi: 10.1001/archinte.168.6.617.
- [9] Chonchol M, Cigolini M, Targher G. Association between 25-hydroxyvitamin D deficiency and cardiovascular disease in type 2 diabetic patients with mild kidney dysfunction. *Nephrol Dial Transplant*. 2008 Jan ; 23(1):269-74. doi: 10.1093/ndt/gfm537.
- [10] Schefold JC, Filippatos G, Hasenfuss G, Anker SD, von Haehling S. Heart failure and kidney dysfunction: epidemiology, mechanisms and management. *Nature Reviews Nephrology*. 2016 Oct; 12(10):610-23. doi: 10.1038/nrneph.2016.113.
- [11] Wall BM, Hardison RM, Molitch ME, Marroquin OC, McGill JB, August PA; BARI 2D Study Group. High prevalence and diversity of kidney dysfunction in patients with type 2 diabetes mellitus and coronary artery disease: the BARI 2D baseline data. *The American journal of the medical sciences*. 2010 May; 339(5):401-10. doi: 10.1097/MAJ.0b013e3181d430ad.

- [12] Deferrari G, Cipriani A, La Porta E. Renal dysfunction in cardiovascular diseases and its consequences. *Journal of Nephrology*. 2021 Feb;34(1):137-153. doi: 10.1007/s40620-020-00842-w.
- [13] Knight EL, Rimm EB, Pai JK, Rexrode KM, Cannuscio CC, Manson JE, et al. Kidney dysfunction, inflammation, and coronary events: a prospective study. *Journal of the American Society of Nephrology*. 2004 Jul; 15(7):1897-903. doi: 10.1097/01.asn.0000128966.55133.69.
- [14] Nakayama M, Metoki H, Terawaki H, Ohkubo T, Kikuya M, Sato T, et al. Kidney dysfunction as a risk factor for first symptomatic stroke events in a general Japanese population—the Ohasama study. *Nephrology Dialysis Transplantation*. 2007 Jul; 22(7):1910-5. doi: 10.1093/ndt/gfm051.
- [15] Moisi MI, Rus M, Bungau S, Zaha DC, Uivarosan D, Fratila O, et al. Acute Coronary Syndromes in Chronic Kidney Disease: Clinical and Therapeutic Characteristics. *Medicina (Kaunas)*. 2020 Mar; 56(3):118. doi: 10.3390/medicina56030118.
- [16] Dohi T, Kasai T, Miyauchi K, Takasu K, Kajimoto K, Kubota N, et al. Prognostic impact of chronic kidney disease on 10-year clinical outcomes among patients with acute coronary syndrome. *Journal of Cardiology*. 2012 Dec; 60(6):43842. doi: 10.1016/j.jjcc.2012.08.007.
- [17] Zaliūnas R, Slapikas R, Luksiene D, Slapikiene B, Statkeviciene A, Milvidaite I, et al. Metabolinio sindromo komponentu dažnis tarp susirgusiųjų ūminiais iseminiais sindromais [Prevalence of metabolic syndrome components in patients with acute coronary syndromes]. *Medicina (Kaunas)*. 2008; 44(3):1828. doi.org/10.3390/medicina44030023
- [18] Hawranek M, Gierlotka M, Gašior M, Hudzik B, Desperak P, Ciślak A, et al. Renal function on admission affects both treatment strategy and long-term outcomes of patients with myocardial infarction (from the Polish Registry of Acute Coronary Syndromes). *Kardiologia Polska (Polish Heart Journal)*. 2017 Jan; 75(4):332-343. doi: 10.5603/KP.a2017.0013.
- [19] Homorodean C, Iancu AC, Dregoescu IM, Spînu M, Ober MC, Tătaru D, et al. Renal Failure Impact on the Outcomes of ST-Segment Elevation Myocardial Infarction Patients Due to a Left Main Coronary Culprit Lesion Treated Using a Primary Percutaneous Coronary Intervention. *Journal of Clinical Medicine*. 2019 Apr 25; 8(4):565. doi: 10.3390/jcm8040565.
- [20] Wańha W, Kawecki D, Roleder T, Pluta A, Marcinkiewicz K, Morawiec B, et al. Long-Term Percutaneous Coronary Intervention Outcomes of Patients with Chronic Kidney Disease in the Era of Second-Generation Drug-Eluting Stents. *Cardiorenal Medicine*. 2017 Feb; 7(2):8595. doi: 10.1159/000452745.
- [21] Petronijević Z, Selim G, Petkovska L, Georgievsk-Ismail L, Spasovski G, Tozija L. The Effect of Treatment on Short-Term Outcomes in Elderly Patients with Acute Kidney Injury. *Open access Macedonian journal of medical sciences*. 2017 Aug 9; 5(5):635-640. doi: 10.3889/oamjms.2017.148.
- [22] Matějka J, Varvařovský I, Rozsívál V, Herman A, Bláha K, Večeřa J, et al. Heart failure is the strongest predictor of acute kidney injury in patients undergoing primary percutaneous coronary intervention for ST-elevation myocardial infarction. *Kardiologia Polska (Polish Heart Journal)*. 2016; 74(1):18-24. doi: 10.5603/KP.a2015.0115.
- [23] Hamzić-Mehmedbasic A, Rebić D, Balavac M, Muslimović A, Dzemiđić J. Clinical analysis of etiology, risk factors and outcome in patients with acute kidney injury. *Materia socio-medica*. 2015 Apr; 27(2):70-4. doi: 10.5455/msm.2015.27.71-74.



Original Article

Comparison of Metoclopramide and Dexamethasone in Post-Operative Vomiting

Abdul Rab¹, Sughra Parveen¹, Asif Ali¹, Mazhar Iqbal¹, Tanveer Ahmad¹, Abdul Waheed¹¹Jinnah Postgraduate Medical Center, Karachi, Pakistan

ARTICLE INFO

Key Words:

Abdominal Surgery, Post-Operative Vomiting, Metoclopramide, Dexamethasone, and Therapeutic Efficacy.

How to Cite:

Rab, A., Parveen, S., Iqbal, M., Ahmad, T., Ali, A., & Waheed, A. (2022). Comparison Of Metoclopramide and Dexamethasone in Post-Operative Vomiting: Comparison of Metoclopramide and Dexamethasone in Post-Operative Vomiting. Pakistan BioMedical Journal, 5(6).

<https://doi.org/10.54393/pbmj.v5i6.589>

*Corresponding Author:

Abdul Rab
Jinnah Postgraduate Medical Center, Karachi,
Pakistan
harm.version02@gmail.com

Received Date: 15th June, 2022

Acceptance Date: 24th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Postoperative nausea and vomiting are one of the most common complaints following anesthesia and surgery. This study was designed to evaluate the efficacy of dexamethasone and metoclopramide to prevent postoperative vomiting (POV) in patients undergoing abdominal surgeries. **Objective:** To compare the efficacy of injection metoclopramide with injection dexamethasone for POV after abdominal surgeries. **Methods:** This Randomized Double-Blind Controlled Trial was conducted in ward 3, Jinnah Postgraduate Medical Centre, Karachi for one year, upon a sample of 98 patients, aged 12 to 60 years and undergoing abdominal surgery (elective and emergency) divided into two groups (Group A: Injection Metoclopramide 10 mg, and Group B: Injection Dexamethasone 8mg), of 49 patients each. The incidence of POV were recorded during the first 24 h postoperatively. **Results:** The mean age of the sample stood at 31 (SD ± 03) years, with most of the sample comprising of males (72.45%). Vomiting was noted in both groups, with group A reporting vomiting among 07 individuals and group B reporting vomiting among 09 individuals. There was no statistical difference between the incidences of vomiting in both groups. **Conclusion:** After careful consideration, it may be concluded that both agents, namely metoclopramide and dexamethasone are efficacious at minimizing the incidence of POV and hence both may be used interchangeably or in conjunction among patients undergoing abdominal surgeries.

INTRODUCTION

Post-operative vomiting (POV) is among the most common causes of patients' distress [1]. In the absence of pharmacologic intervention, the POV incidence after surgery ranges from 20-30% [2] however, it may hike up to as high as seventy percent after abdominal surgeries [3]. POV can lead to dehydration, anxiety, wound disruption, metabolic abnormality, prolonged recovery, and other issues with a significant health expenditure burden [4]. Thus finding a pertinent solution to the issue is of utmost importance. Various aspects pertaining to the patient, such as the fairer gender, smoking habit, past POV history, and travel sickness are known to be significant factors increasing the risk of POV. Additionally, numerous factors pertaining to anesthesia, for example nitrous oxide and opioid use and general anesthesia duration have been

proposed to carry significant risk of POV [5]. Owing to this multifaceted causation of POV, neither of the present classes of anti-emetics is entirely curative for patients and a single best option continues to elude us. Among the many choices available for prophylaxis, the two most used drugs are a metoclopramide and dexamethasone [6]. Though metoclopramide is an established anti-emetic, the use of dexamethasone for this purpose is relatively new. Individual clinical research has noted dexamethasone to be an effective antiemetic agent capable of lessening the incidence of early PONV following abdominal surgeries [7]. It is also reported that dexamethasone usage is free from any marked adverse effects. Moreover, it may decrease postoperative pain after laparoscopic cholecystectomy [8]. In this modern era of medicine, patients demand to be

given the best evidence-based medicine to treat their condition. However, owing to a lack of direct comparative studies between the top two drugs for POV (metoclopramide and dexamethasone), healthcare professionals are often at loss for ample evidence to choose between either of the two. In this scenario, POV prevention, following abdominal surgeries is a test for the healthcare provider [9, 10]. Owing to the discomfort it brings to the patients and the increasing frequency of such surgeries being performed on daycare basis, knowledge regarding the most effective prophylactic therapy is becoming highly desirable for alleviation of undesirable POV symptoms and an early home discharge. The high incidence and much distress associated with POV merits the utmost attention. An ideal prophylactic regimen, if identified, can significantly decrease the morbidity associated with this condition. The aim of study was to compare the efficacy of injection metoclopramide with injection dexamethasone for POV after abdominal surgeries.

METHODS

This randomized double-blind controlled trial was conducted in Ward 3, Jinnah Postgraduate Medical Centre, Karachi, from November 2020 to November 2021, upon a sample of 98 patients, aged 12 to 60 years and undergoing abdominal surgery (elective and emergency) divided into two groups (Group A: Injection Metoclopramide 10 mg, and Group B: Injection Dexamethasone 8mg), of 49 patients each. The incidence of POV were recorded during the first 24 h postoperatively. All consecutive patients presenting to the study setting and meeting the eligibility criteria were allocated to either of the groups (A or B) using computer generated simple randomized numbers. The study medicines were given by slow (thirty seconds) IV injection. Postoperatively, all patients were monitored for POV for 24 hours. POV was checked at thirty minutes and 2, 4, 8 and 24 hours after surgery by the researcher. The intensity of POV was gauged using a visual analog scale ranging from no symptom (0 cm) to maximum intensity symptoms (10 cm). The visual analog scale was categorized into four parts: zero cm for no symptoms; one to three cm for mild symptoms; three to seven cm for moderate symptoms, and seven to ten cm for severe symptoms. Data was analyzed using the IBM SPSS version 21.0 and M.S Excel 2013. Descriptive statistics such as mean \pm standard deviation (SD) was used for continuous variables such as age and VAS Score. Numbers and percentages were used to describe the proportion of categorical variables such as sex and the frequency and severity of POV.

RESULTS

The mean age of the sample stood at 31(SD \pm 03) years, with

most of the sample comprising of males (72.45%). The summary of descriptive statistics is tabulated below in Table 1.

Variable		Group A	Group B	Cumulative
Mean Age		31.5 (SD \pm 03)	30.5 (SD \pm 03)	31 (SD \pm 03)
Gender	Male	35 (71.43%)	36 (73.47%)	71 (72.45%)
	Female	14 (28.57%)	13 (26.53%)	27 (27.55%)
Type of Surgery	Elective	37 (75.55%)	41 (83.67%)	78 (79.59%)
	Emergency	12 (24.49%)	08 (16.33%)	20 (20.41%)

Table 1: Descriptive statistics

Vomiting was noted in both groups, with group A reporting vomiting among 07 individuals and group B reporting vomiting among 09 individuals. There was no statistical difference between the incidences of vomiting in both groups, Table 2.

POV	Group A	Group B	P-Value
Incidence	07 (14.29%)	09 (18.38%)	0.971

Table 2: Incidence of POV in both groups

The severity of POV is tabulated below in both groups, Table 3.

Severity of POV	Group A	Group B	P-Value
No Symptoms	42 (85.71%)	40 (81.63%)	0.971
Mild	1 (2.045%)	3 (6.12%)	0.634
Moderate	5 (10.2%)	4 (8.16%)	0.929
Severe	1 (2.045%)	2 (4.09%)	0.711

Table 3: Severity of POV in both groups

DISCUSSION

A common complication encountered by patients following abdominal surgery is POV. The condition, though seemingly non-life threatening, is much distressful and at times, a stronger source of patient dissatisfaction than even post-operative pain [10]. POV may hinder the early discharge of otherwise recovered patients and thus add to burden on the already limited healthcare resources [11]. Having a post-operative incidence as high as 63% following certain abdominal surgeries, (in the absence of pharmacologic prophylaxis [12] there is a dire need to address this condition. Metoclopramide and dexamethasone are two commonly employed drugs known to offer prophylaxis against POV [13]. In this research, the incidence did not exceed 18.38% due to the pharmacologic prophylaxis. Research suggests that dexamethasone may offer successful prophylaxis against POV at a dose of 5–8mg. Similarly, there is evidence of metoclopramide too exhibiting successful prophylactic ability against POV at a dose of 4mg [14]. Existing RCTs have fallen short of identifying which among the two pharmacologic agents exhibits a better prophylactic ability and provides more relief to the patients from POV following abdominal surgeries [15, 16]. Research with contradicting claims have begun to surface recently, with some claiming

dexamethasone to be a better prophylactic agent (especially owing to its safety, cost-effectiveness and being free from any reported side effects in addition to offering pain relief) the while the others supporting ondansetron (due to its greater efficacy) [17, 20].

CONCLUSION

After careful consideration, it may be concluded that both agents, namely metoclopramide and dexamethasone are efficacious at minimizing the incidence of POV and hence both may be used interchangeably or in conjunction among patients undergoing abdominal surgeries.

REFERENCES

- [1] Myles PS, Wengritzky R. Simplified postoperative nausea and vomiting impact scale for audit and post-discharge review. *British journal of anaesthesia*. 2012 Mar; 108(3):423-9. doi: 10.1093/bja/aer505
- [2] Iitomi T, Toriumi S, Kondo A, Akazawa T, Nakahara T. Incidence of nausea and vomiting after cholecystectomy performed via laparotomy or laparoscopy. *Masui. The Japanese journal of anesthesiology*. 1995 Dec; 44(12):1627-31.
- [3] Tseng LH, Liou SC, Chang TC, Tsai SC, Soong YK, Wong SY. A randomized blinded study of the incidence of postoperative nausea and vomiting in women after major gynecologic laparoscopic surgery. *Journal of minimally invasive gynecology*. 2006 Sep; 13(5):413-7. doi: 10.1016/j.jmig.2006.05.003
- [4] Regasa T, Aweke Z, Neme D, Hailu S, Jemal B, and Mekonen S. Comparison of prophylactic dexamethasone, metoclopramide, and combination of dexamethasone and metoclopramide for prevention of post-operative nausea and vomiting for major gynaecological surgery in Hawassa university compressive specialized hospital, Ethiopia, 2019. *International Journal of Surgery*; 27(2): 18-24. doi:10.1016/j.ijso.2020.10.004
- [5] Gan TJ. Risk factors for postoperative nausea and vomiting. *Anesthesia & Analgesia*. 2006 Jun; 102(6):1884-98. doi: 10.1213/01.ANE.0000219597.16143.4D
- [6] Kwak KH. PONV prevention: still not enough. *Korean journal of anesthesiology*. 2017 Oct; 70(5):489. doi: 10.4097/kjae.2017.70.5.489
- [7] Sekhavat L, Davar R, Behdad S. Efficacy of prophylactic dexamethasone in prevention of postoperative nausea and vomiting. *Journal of epidemiology and global health*. 2015 Jun; 5(2):175-9. doi: 10.1016/j.jegh.2014.07.004
- [8] Tan M, Law LS, Gan TJ. Optimizing pain management to facilitate enhanced recovery after surgery pathways. *Canadian Journal of Anesthesia/Journal canadien d'anesthésie*. 2015 Feb; 62(2):203-18. doi: 10.1007/s12630-014-0275-x
- [9] Hammad RA, Eldeek AM, Hussien RM, Shendy AA. Dexamethasone versus ondansetron in prevention of postoperative nausea and vomiting after laparoscopic surgery. *The Egyptian Journal of Hospital Medicine*. 2018 Jul; 72(10):5479-84. doi: 10.21608/EJHM.2018.11362
- [10] AlJabari A, Massad I, AlZaben K. Post-operative nausea, vomiting and pain score in post anesthesia care unit (PACU) at Jordan university hospital. *Journal of Anesthesia and Clinical Research*. 2016; 7(595):2. doi:10.4172/2155-6148.1000595
- [11] Cao J, Liu B, Li X. Analysis of delayed discharge after day-surgery laparoscopic cholecystectomy. *International Journal of Surgery*. 2017 Apr; 40:33-7. doi: 10.1016/j.ijso.2017.02.055
- [12] Smith CA, Ruth-Sahd L. Reducing the incidence of postoperative nausea and vomiting begins with risk screening: An evaluation of the evidence. *Journal of PeriAnesthesia Nursing*. 2016 Apr; 31(2):158-71. doi: 10.1016/j.jopan.2015.03.011
- [13] Atashkhoei S, Bilehjani E, Fakhari S, Hanieh FA. Postoperative Nausea and Vomiting Prophylaxis with Ondansetron in Diagnostic Gynecologic Laparoscopy: Preemptive versus Preventive Method. *Advances in Reproductive Sciences*. 2017 Jan; 5(1):1-9. doi:10.4236/arsci.2017.51001
- [14] Awad K, Ahmed H, Abushouk AI. Dexamethasone combined with other antiemetics versus single antiemetics for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy: An updated systematic review and meta-analysis. *International journal of surgery*. 2016 Dec; 36:152-63. doi: 10.1016/j.ijso.2016.10.034
- [15] Firdaus K, Dan A, Maaya M. Dexamethasone 8 mg Versus Dexamethasone 4 mg with Propofol 0.5 mg/kg for the Prevention of Postoperative Nausea and Vomiting after Laparoscopic Gynaecology Procedure. *International Medical Journal*. 2016 Feb; 23(1).
- [16] Munishankar B, Fettes P, Moore C, Mcleod GA. A double-blind randomized controlled trial of paracetamol, diclofenac or the combination for pain relief after cesarean section. *International Journal of Obstetric Anaesthesia*. 2008 Sep; 17:9-14. doi: 10.1016/j.ijoa.2007.06.006
- [17] Chan A, Dore CJ, Ramachandra V. Analgesia for day surgery. Evaluation of the effect of diclofenac given before or after surgery with or without bupivacaine infiltration. *Journal of Anaesthesia*. 1996; 51:592-5. doi: 10.1111/j.1365-2044.1996.tb12574.x

- [18] Krzyzanowski SA, Kim K, Smith DC, Young M, Buffington CK. The Effects of a Dexamethasone-based Prophylaxis Protocol on Postoperative Nausea and Vomiting (PONV) and the Duration and Associated Cost of the Hospital Stay. *Surgery for Obesity and Related Diseases*. 2018 Nov; 14(11):S7. doi:10.1016/j.soard.2018.09.474
- [19] Gao C, Li B, Xu L, Lv F. Efficacy and safety of ramosetron versus ondansetron for postoperative nausea and vomiting after general anesthesia: a meta-analysis of randomized clinical trials. *Drug Des Devel Ther*. 2015;9:2343./doi.10.2147/DDDT.S80407
- [20] Merrikhihaghi S, Farshchi A, Farshchi B, Farshchi S, Dorkoosh FA. Tramadol versus Diclofenac in pain management after cesarean section: a cost analysis study. *Journal of Pharmacoeconomics and Pharmaceutical Management*. 2015; 1(1):22-4.



Original Article

Comparison of The Effectiveness of Maitland Manipulation of Thoracic Spine Versus Grade I and II Maitland Mobilization of Cervical Spine on Pain Intensity and Functional Status In Patients of Cervical Radiculopathy

Aqsa Aroob¹, Idrees Ahmed Zahoor², Momna Ghaffar³, Noman Ghaffar⁴, Arif Ali Rana⁴, Sidrah Shabbir⁵

¹Shahida Islam Medical College, Lodhran, Pakistan

²Central Park Medical College, Lahore, Pakistan

³Department of Sensory Therapist, University of child health sciences and children's Hospital, Lahore, Pakistan

⁴Department of Physical Therapy, Central Park Medical College, Lahore, Pakistan

⁵Akhter Saeed Medical and dental college, Lahore, Pakistan

ARTICLE INFO

Key Words:

Cervical Radiculopathy (CR), Maitland, thoracic spine, manipulation, cervical spine mobilization

How to Cite:

Aroob, A., Ahmed Zahoor, I., Ghaffar, M., Ghaffar, N., Ali Rana, A., & Shabbir, S. (2022). Comparison Of the Effectiveness of Maitland Manipulation of Thoracic Spine Versus Grade I And II Maitland Mobilization of Cervical Spine on Pain Intensity and Functional Status in Patients of Cervical Radiculopathy: Cervical Spine on Pain Intensity and Functional Status in Patients of Cervical Radiculopathy. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.560>

***Corresponding Author:**

Arif Ali Rana

Department of Physical Therapy, Central Park Medical College, Lahore, Pakistan
arifalirana@gmail.com

Received Date: 19th May, 2022

Acceptance Date: 26th May, 2022

Published Date: 31st May, 2022

ABSTRACT

Cervical radiculopathy (CR) is a most reported pathological problem mainly due to herniated disc material causing nerve compression or the formation of osteophytes. This impingement specifically causes cervical pain radiating to arm, numbness, and sensory deficit. It also affects the motor function of the neck and upper extremities. **Objectives:** To evaluate the comparative effectiveness of Maitland manipulation of thoracic spine versus grade I and II Maitland mobilization of cervical spine on Pain, intensity, and functional status in patients of cervical radiculopathy. **Methods:** Total 32 patients suffering from cervical radiculopathy were randomly assigned to receive Maitland manipulation on thoracic spine along with Conventional Physiotherapy (intermittent cervical traction, strengthening exercises) in Group A (n=16) and Maitland mobilization on cervical spines along with Conventional Physiotherapy in Group B (n=16). Total treatment sessions given to each group was 9 (3 sessions per week). To measure outcome numeric pain rating scale (NPRS) and neck disability index (NDI) questionnaire was used. Data collection was done at the beginning and post-treatment. **Results:** The study revealed that the mean age of patients was 47.59 with a range minimum of 27 years to a maximum of 59 years. Comparison of post-treatment of both groups showed mean NPRS score in group A (Maitland thoracic spine manipulation) was 4.56 ± 1.031 and group B (Maitland cervical spine mobilization) was 6.12 ± 0.50 , while post-treatment NDI score group A was 22.44 ± 10.09 and group B was 36.88 ± 8.437 with $p=0.000$ that was $p<0.05$. **Conclusion:** The study concluded that both Maitland thoracic spine manipulation and Maitland cervical spine mobilization techniques have similar effects in reducing cervical radiculopathy and increasing active range of motion. However, Maitland thoracic spine manipulation showed better results in neck pain reduction and improved functional status on the comparison.

INTRODUCTION

Musculoskeletal pain is most common in our society that including neck, shoulder, and back pain [1]. Cervical pain is the second most common pathology in our society [2]. Cervical radiculopathy occurs with such pathologies that have a direct effect on the nerve root, that can be compression traction, irritation, foraminal narrowing, or degenerative spondylitis changes such as arthritic changes [3,5]. C7 is the most common level of root

compression (43.6-69%) followed by C6 (17.6-19%), C5 is (2-6.6%) while C8 is least common (6.2-10%) [6]. A study from Salemi reported the prevalence of cervical radiculopathy was 3.5 cases per 1000 population [7]. Cervical radiculopathy (CR) is a serious pathological process mainly due to nerve compression from disc herniation, arthritic bone spur formation, tumor, or trauma that cause nerve root rupture [8-10]. It leads toward neck pain, radiating

pain in the arm, and numbness in the specific nerve root irritation area. Mostly this radicular pain along with the motor or sensory disturbances [11,12]. Cervical radiculopathy occurs with such pathologies that have a direct effect on the nerve root, that can be compression traction, irritation, foraminal narrowing, or degenerative spondylitis changes such as osteoarthritic changes [13]. C7 is the most common level of root compression (43.6-69%) followed by C6(17.6-19%), C5 is (2-6.6%) while C8 is least common (6.2-10%) [6]. Cervical radiculopathy's typical symptoms are neck pain, dermatomes pattern irradiating arm pain [14]. Myotome pattern muscle weakness, numbness, impaired reflexes, headaches, scapular pain, upper extremities motor and sensory dysfunction [15]. The pattern of symptoms and location vary from person to person depending upon the level of nerve root affected [16]. A study by Hurwitz et.al, manipulation treatment and mobilization exercises play a great role in long term improvement of neck pain but manipulation has a better effect on reducing the pain [17]. RXodine and Vernon in 2012, conducted a study on the effects of cervical spine manipulation on radiculopathy of cervical spine and neck disability index was used as measuring tool. The study showed that for cervical radiculopathy treatment spinal manipulation can be used but need precautionary measurements [18]. Kaur Interdeep et.al., done study on the effect of Maitland mobilization compare with mulligan mobilization at upper thoracic spine in the patient with non-specific neck pain [19]. There are multidimensional risk factors for developing cervical radiculopathy as general medical health, occupation environment, physical attributes, socioeconomic, status, physiological status [20]. To confirm the diagnosis of CR, electrophysiological tests (nerve conduction velocity, electromyography), Diagnostic imaging (magnetic resonance imaging) most commonly used [21-22]. Manually diagnosing the CR includes specific tests as the Spurling test, the Upper-Limb Tension Test (ULLT), and the distraction test [23].

The study was done to discover the research-based selection of the most reliable treatment regimes that is MTSM and MCSM for the patients with cervical spine radiculopathy. So, this study will be beneficial equally for physical therapists as well as patients.

METHODS

Single Blinded Simple Random Sampling technique was used for this study. The study was done from August 2017 to January 2018 with total time of 6 months. The sample size was 32 with 95% confidence interval. Total 32 patients were divided into two groups. Treatment given to Group 1

with Maitland thoracic spine manipulation, strengthening exercises, cervical traction and group 2 with Maitland grade I and II mobilization of the cervical spine, intermittent, and strengthening exercise). Both male and female patients of 20 years having cervical radiculopathy (due to disc herniation at cervical spine, bone spur formation) and patients with Spurling test positive, cervical distraction test, upper limb tension test (ULTT), was included in the study. All other patients who had osteoporosis, any tumor, fracture history, TOS and cervical rib formation, patients with CNS involvement were excluded. Total 32 patients who have complaints of cervical radiculopathy were selected. The patient's examination including Assessment, History, Palpation and Observation was carried out to rule out any active pathology or other causes of included systemic illness. All the subjects were observed from the front, back and lateral view to see the change in the alignment of the cervical spine and upper limb and to see in contour changes. Palpation of soft tissue structures around the cervical spine, shoulder, upper back, and arm to see the tenderness and temperature difference around these areas. Demographics data such as age, gender, marital status, occupation history were recorded by the predesigned Performa. Patients were allocated to the two treatment groups using computer-generated randomization. Patients of Group A (n=16) were treated with Maitland thoracic spine manipulation besides conventional Physiotherapy. Patients of Group B (n=16) were treated with Maitland Grade I and II cervical mobilization along with conventional physiotherapy. The Conventional Physiotherapy Protocol that was given to every patient was a hot pack for 10 minutes, Intermittent cervical traction (CT), Cervical muscle strengthening exercises (2 sets of 5 repetitions each). Each patient was given 9 sessions in 3 weeks (3 sessions per week). Outcome measures used for data collection were Numerical pain rating scale (NPRS) Neck disability index (NDI) questioner. A use of goniometer to measure cervical spine Ranges of motion. Data were entered and analyzed through SPSS version 16.0. All the qualitative variables were presented as frequency tables and percentages. All the quantitative variables were presented as mean \pm SD along with its (max-min). To compare the mean differences of quantitative variables T-test was applied. p-value <0.05 was taken as significant values.

RESULTS

From 32 patients, group A having 7 males and 9 females and group B having 9 males and 7 females. In 32 patients total 50% of males and 50% of females contributed to the study.

It shows that the minimum age was 27 years and the maximum age was 56 years, while in group B minimum age was 35 and the maximum age was 60 years

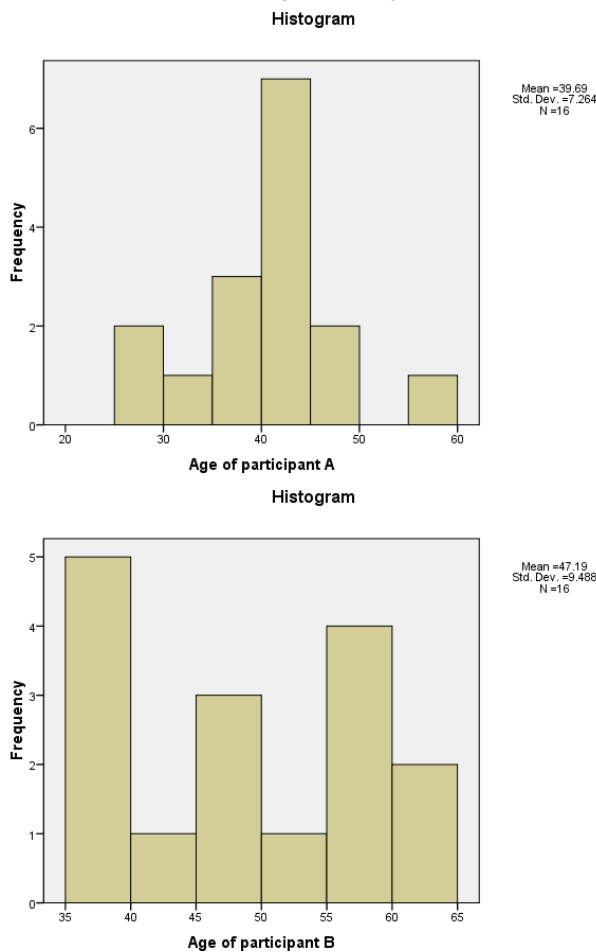


Figure 1: Age of participants

Group Statistics		N	Mean+SD	Std. Error Mean
Post numeric pain rating scale	A	16	4.56+1	.258
	B	16	6.12+0.5	.125
Post neck disability index	C	16	22.44+10.1	2.525
	D	16	36.88+8.4	2.109

	Levene's Test for Equality of Variances		t-test for Equality of Means						
	F	Sig.	t	Df	Sig.(2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
								Lower	Upper
NPS score (numeric pain rating scale)	7.607	.010	-5.455	30	.000	-1.562	.286	-2.147	-.978
			-5.455	21.689	.000	-1.562	.286	-2.157	-.968
NDI score (neck disability index)	.294	.591	-4.388	30	.000	-14.438	3.290	-21.156	-7.719
			-4.388	29.079	.000	-14.438	3.290	-21.165	-7.710

Independent Samples Test: Comparison of post-treatment of both groups has shown mean NPRS score in group A (Maitland thoracic spine manipulation) was 4.56± 1.031 and group B (Maitland cervical spine mobilization) was

6.12± 0.50, while post-treatment NDI score group A was 22.44± 10.09 and group B was 36.88± 8.437 with p=0.000 that was less than p=0.05. The results after statistical analysis showed that there is significant difference in mean value of Numeric Pain Rating Scale pretreatment score and Numeric Pain Rating Scale post treatment score (t = -5.455, p = .000). The both two groups showed significant levels of improvement in pain intensity (P < 0.000), at post treatment value (P < 0.000). As p = 0.000 is less than 0.05 so on the basis of these values null hypothesis will be rejected and research hypothesis will be accepted. Maitland manipulation of thoracic spine treatment protocol prove to be more effective than Maitland grade I and II cervical spine mobilization.

DISCUSSION

Treatment of cervical radiculopathy by several physiotherapy techniques. This study aimed to compare the effect of Maitland manipulation of thoracic spine and Maitland Grade I and II mobilization of cervical spine along with conventional physical therapy in decreasing pain and improved functionally, and cervical ranges of motion in patients of cervical radiculopathy. Within-group analysis showed that there was a marked reduction in patient-reported pain scores when pre intervention and post-intervention values were compared in both groups. Comparison of post-treatment of both groups showed mean NPRS score in group A (Maitland thoracic spine manipulation) was 4.56± 1.031 and group B (Maitland cervical spine mobilization) was 6.12± 0.50, while post-treatment NDI score group A was 22.44± 10.09 and group B was 36.88± 8.437 with p=0.000 that is less than p=0.05. So, post-treatment results showed that Maitland Manipulation of Thoracic spine is more beneficial than Maitland grade I and II mobilization of cervical spine in pain reduction and improving functional status in cervical radiculopathy. The limitations were that the Patients of this study were obtained from the Male and female department of Physiotherapy, Mayo Hospital, Lahore. So, the research may not give a larger perspective concerning the prevalence of the disease. There was a limitation of Sample size. Recommendations were that study can be improved by maximizing sample size and by using different hospital settings, follow-up should be more than 3 weeks to get better results.

CONCLUSION

This research concluded that both Maitland thoracic spine manipulation and Maitland cervical spine mobilization techniques are effective in reducing pain, functional status and better active range of motion outcome as p=0.000 that p<0.005 showed both techniques are statistically

significant but the mean value of Study group A was more than control group B, However, Maitland thoracic spine manipulation treatment showed better results in neck pain reduction and also improved functional status on comparison with group B.

REFERENCES

- [1] Auerbach JD, Weidner ZD, Milby AH, Diab M, Lonner BS. Musculoskeletal disorders among spine surgeons: results of a survey of the Scoliosis Research Society membership. *Spine*. 2011 Dec; 36(26):E1715-21. doi: 10.1097/BRS.0b013e31821cd140.
- [2] Waqas S, Ahmad A, Ahmad S, Shafi T, Shahid HA. Comparison of Maitland Thoracic Spine Manipulation Versus Maitland Cervical Spine Mobilization in Chronic Unilateral C6 to C7 Cervical Radiculopathy. *Annals of King Edward Medical University*. 2016 May; 22(2). doi.org/10.21649/akemu.v22i2.1285
- [3] Radhakrishnan K, Litchy WJ, O'Fallon WM, Kurland LT. Epidemiology of cervical radiculopathy. A population-based study from Rochester, Minnesota, 1976 through 1990. *Brain*. 1994 Apr; 117 (Pt 2):325-35. doi: 10.1093/brain/117.2.325.
- [4] Rajan Balakrishnan EY, Mahat MFB. Effectiveness of the core stabilisation exercise on floor and Swiss ball on individual with non-Specific low back pain. *International Journal of Physical Education Sports and Health*. 2016; 3(1):347-56.
- [5] Rao RD, Currier BL, Albert TJ, Bono CM, Marawar SV, Poelstra KA, et al. Degenerative cervical spondylosis: clinical syndromes, pathogenesis, and management. *Journal of Bone and Joint Surgery*. 2007 Jun; 89(6):1360-78. doi: 10.2106/00004623-200706000-00026.
- [6] Kuijper B, Tans JT, Schimsheimer RJ, van der Kallen BF, Beelen A, Nollet F, et al. Degenerative cervical radiculopathy: diagnosis and conservative treatment. A review. *European Journal of Neurology*. 2009 Jan; 16(1):15-20. doi: 10.1111/j.1468-1331.2008.02365.x.
- [7] Salemi G, Savettieri G, Meneghini F, Di Benedetto ME, Ragonese P, Morgante L, et al. Prevalence of cervical spondylotic radiculopathy: a door-to-door survey in a Sicilian municipality. *Acta Neurologica Scandinavica*. 1996 Feb-Mar; 93(2-3):184-8. doi: 10.1111/j.1600-0404.1996.tb00196.x.
- [8] Clarençon F, Law-Ye B, Bienvenot P, Cormier É, Chiras J. The Degenerative Spine. *Magnetic Resonance Imaging Clinics*. 2016 Aug; 24(3):495-513. doi: 10.1016/j.mric.2016.04.008.
- [9] Hari A, Krishna M, Rajagandhi S, Sharma A, Deshpande RV. Minimally invasive lateral foraminotomy with partial lateral facetectomy for lumbar radiculopathy-An evaluation of facet integrity and description of the procedure. *Neurology India*. 2017 Nov-Dec; 65(6):1358-1365. doi: 10.4103/0028-3886.217932.
- [10] Mashal YA, Samir MA, Morsy AA, Salama HH. Comparative Study between Implantation of an Empty Polyethylene Ketone Cage versus Cage with Bone Graft in Anterior Cervical Discectomy and Fusion. *The Egyptian Journal of Hospital Medicine*. 2022 Jul ; 88(1):2520-6. doi.org/10.21608/ejhm.2022.238381
- [11] Eubanks JD. Cervical radiculopathy: nonoperative management of neck pain and radicular symptoms. *American family physician*. 2010; 81(1):33-40.
- [12] Ellenberg MR, Honet JC, Treanor WJ. Cervical radiculopathy. *Archives of physical medicine and rehabilitation*. 1994 Mar; 75(3):342-52. doi: 10.1016/0003-9993(94)90040-x.
- [13] Olson KA. *Manual Physical Therapy of the Spine-E-Book: Elsevier Health Sciences*; 2015.
- [14] Thoomes EJ, van Geest S, van der Windt DA, Falla D, Verhagen AP, Koes BW, et al. Value of physical tests in diagnosing cervical radiculopathy: a systematic review. *The Spine Journal*. 2018 Jan; 18(1):179-189. doi: 10.1016/j.spinee.2017.08.241.
- [15] Kuijper B, Tans JT, Beelen A, Nollet F, de Visser M. Cervical collar or physiotherapy versus wait and see policy for recent onset cervical radiculopathy: randomised trial. *BMJ*. 2009 Oct; 339:b3883. doi: 10.1136/bmj.b3883.
- [16] Cleland JA, Whitman JM, Fritz JM, Palmer JA. Manual physical therapy, cervical traction, and strengthening exercises in patients with cervical radiculopathy: a case series. *Journal of Orthopaedic & Sports Physical Therapy*. 2005 Dec; 35(12):802-11. doi: 10.2519/jospt.2005.35.12.802.
- [17] Hurwitz EL, Aker PD, Adams AH, Meeker WC, Shekelle PG. Manipulation and mobilization of the cervical spine. A systematic review of the literature. *Spine (Phila Pa 1976)*. 1996 Aug; 21(15):1746-59; discussion 1759-60. doi: 10.1097/00007632-199608010-00007.
- [18] Rodine RJ, Vernon H. Cervical radiculopathy: a systematic review on treatment by spinal manipulation and measurement with the Neck Disability Index. *The Journal of the Canadian Chiropractic Association*. 2012 May; 56(1):18.
- [19] Inderpreet K, Arunmozhi R, Umer A. Effect of Maitland vs Mulligan Mobilisation Technique on Upper Thoracic Spine in Patients with Non-Specific Neck

- Pain-A Comparative Study. *International Journal of Physiotherapy and Research*. 2013;1(5):214-18.
- [20] Rubin DI. Epidemiology and risk factors for spine pain. *Neurologic Clinics*. 2007 May; 25(2):353-71. doi: 10.1016/j.ncl.2007.01.004.
- [21] Medicine AAoE. The electrodiagnostic evaluation of patients with suspected cervical radiculopathy: literature review on the usefulness of needle electromyography. *Muscle Nerve*. 1999;22(8):S213-S21.
- [22] Wilson DW, Pezzuti RT, Place JN. Magnetic resonance imaging in the preoperative evaluation of cervical radiculopathy. *Neurosurgery*. 1991 Feb; 28(2):175-9. doi: 10.1097/00006123-199102000-00001.
- [23] Association APT. Guide to Physical Therapist Practice. American Physical Therapy Association. *Physicaltherapy*. 2001;81(1):9



Original Article

Diagnostic Accuracy of Magnetic Resonance Imaging in Carcinoma of Cervix Taking Histopathology as Gold Standard

Sumayya¹, Heema², Zubair Janan Orakzai^{3*}, Mohsin Khan⁴, Nuzhat Malik Awan⁵, Khalid Shakeel Babar⁶

¹Department of Obstetrics and Gynecology, Qazi Hussain Ahmad Medical Complex Nowshera, Pakistan

²Department of Gynecology, Women and Children Hospital Kohat, KIMS/ KMU, Pakistan

³Department of Radiology, Bacha Khan Medical College (BKMC), Mardan, Pakistan

⁴Department of Radiology, Gajju Khan Medical College, Swabi, Pakistan

⁵Department of Gynecology and Obstetrics, Amna Inayat Medical College, Lahore, Pakistan ⁶Department of Radiology, Khyber Teaching Hospital, Khyber Medical College, Peshawar, Pakistan

ARTICLE INFO

Key Words:

Cervical carcinoma, pelvic lymph node metastasis, Histopathological examination(HPE).

How to Cite:

Sumayya, ., Heema, ., Janan Orakzai, Z. ., Khan, M. ., Malik Awan, N. ., & Shakeel Babar, K. . (2022). Diagnostic Accuracy of Magnetic Resonance Imaging in Carcinoma of Cervix Taking Histopathology as Gold Standard: Magnetic Resonance Imaging in Carcinoma of Cervix Taking Histopathology as Gold Standard. *Pakistan BioMedical Journal*, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.548>

***Corresponding Author:**

Zubair Janan Orakzai
 Department of Radiology, Bacha Khan Medical College(BKMC), Mardan, Pakistan
 Zjaurakzai@hotmail.com

Received Date: 19th May, 2022

Acceptance Date: 26th May, 2022

Published Date: 31st May, 2022

ABSTRACT

The crucial factor that plays important role in diagnosis and prompt treatment management of cervical cancer is staging. To stage cervical carcinoma Magnetic Resonance Imaging (MRI) is considered to be the most accurate and gold standard diagnostic tool. **Objective:** The aim of the present study was to elaborate the diagnostic accuracy of MRI in correlation with Histopathological Examination (HPE). **Methods:** The 53 patients diagnosed with cervical carcinoma attending the gynecology department of hospital from May 2021 to April 2022 were included in the study. Those patients who had undergone the abdomen and pelvis MRI fulfilled the inclusion criteria. The MRI and histopathological examination not only help in staging of cancer but also consider valuable in tracking tumor location, size and extension. The retroperitoneal lymphadenopathy, and involvement of the tumor to the adjacent areas was also evaluated by the study. Staging of all patient was done according to the International Federation of Gynecology and Obstetrics FIGO standards. Findings of MRI and HPE were assessed. For statistical evaluation of data, the SPSS version 22.0 was used. For quantitative variables the values were represented as mean with standard deviations. **Results:** The 54.46±9.29 years was the calculated mean age. Squamous cell carcinoma was diagnosed in almost 46 patients (87.5% cases). Stage IB carcinoma was diagnosed in almost 47.91% cases. Pelvic lymphadenopathy was observed in 8.34% cases, while metastasis of pelvic nodal lymph was observed in 4.16% cases on the HPE. **Conclusion:** Malignant diseases require early and accurate tool for their diagnosis. For identification of cancer stage and better planning of treatment of cervical carcinoma the highly non-invasive modality MRI can be used. With the advents in MR imaging, it is considered as gold standard diagnostic tool with better sensitivity, specificity and high accuracy for cervical carcinoma.

INTRODUCTION

The third most common gynecological malignancy among younger women is cervical carcinoma. In cervical carcinoma, the tissue of cervix and narrow end of uterus have malignant cells. The mean decisive age is 61 years [1-2]. Cervical cancer remains asymptomatic at the early stages, the later stages of cancer involve vaginal bleeding, lymphatic or ureteral compression and watery discharge. Many risk factors are associated with cervical carcinoma [2-3]. There is a strong association between cervical

cancer and Human Papilloma virus (HPV). HPV can be found in about 90-95% cases of cervical carcinoma. HPV-16 found in about 50% of cervical cancer patients HPV-18 in about 15% of cervical cancer patients and HPV-45 in about 8% of cases respectively. Smoking, Oral contraceptive pills, high parity, Intrauterine devices and weak immune system are other risk factor involved in causing cervical carcinoma [4-5]. For better planning of treatment, it is necessary to identify the significant factor play crucial role in prognosis

of cervical cancer. Squamous carcinoma and Adenocarcinoma are histological types of cervical carcinoma. Mucinous carcinoma, mesonephric carcinoma, and endometrioid carcinoma are included in Adenocarcinoma [6]. The squamous cell carcinoma shares almost 75% cases of cervical carcinoma. MR imaging most clearly depict many such factors. Adenocarcinoma, adenosquamous cell carcinoma are involved in other 10-15% cases [7-8]. Because of formal screening of cervical carcinoma in developed countries the total percentage of cases has reduced to half. But in the developing countries the cases are increasing. The most effective test for screening of cervical cancer is Papanicolaou (Pap) HPV test [9]. Surgery is recommended for the patients diagnosed with early stage cervical cancer (stages I and IIA), while radiation therapy in combination with chemotherapy is used to treat advanced stage cervical cancer (stage IIB or greater). It is difficult to distinguish the cervical cancer stages. According to former International Federation of Gynecology and Obstetrics (FIGO) the patients with the metastasis of lymph node are included in (stage IIIC) [10]. The common diagnostic tool for histopathological examination of cervical carcinoma is cervical biopsy. The efficient modality to track tumor location, its size, volume, extensions and depth of stromal invasion is MRI. It also plays crucial diagnostic role in evaluation of metastases of lymph node. The Non-invasive MRI has superseded the use of invasive techniques. MRI also play putative role in pre-treatment of uterine cervical carcinoma [11-12].

METHODS

It was a retrospective Study with statistical approach conducted in BKMC/ MMC, Mardan for the duration of six months from January 2020 to June 2020. This study was conducted on 53 patients presented with cervical carcinoma at gynecology department of hospital. The duration of the present study was 14 months from May 2021 to April 2022. The result obtained from Shweel MA et al., study depicted that the proportion of squamous cell carcinoma as 73.3%. The sample size of present study was calculated according to the Shweel MA et al., study squamous cell proportion [13]. The confidence level of the study was calculated as 95% with absolute precision of 13%. To reduce the standard error the infinite population correction was applied on the study. For calculation of sample size, the given formula; $n = \frac{Z^2 P(1-P)}{d^2}$

In the given formula the n is the sample size, z is the statistic for a level of confidence and p is the expected prevalence of proportion [14]. The P value for expected prevalence of proportion 73.3% is 0.733. The d is the precision. From the above formula the calculated n was 45. About 5% was the

non-participation rate. Hence 52 was calculated as sample size. The patients presented with diagnosed cervical carcinoma after MRI of abdomen and pelvis was included in the study. GE- Optima MR 360 1.5 T 16 channel was used for diagnostic purposes. Pelvis-3 Plane T2, T1 axial, STIR axial, diffusion was set as standard MRI protocols. Post-contrast-T1FS pre, dynamic contrast for uterus, 3 Plane T1 FS, Axial lava, Coronal lava. Screening of upper abdomen-T2FS Axial, Coronal T2 Haste, diffusion. Gadopentetate Dimeglunine Injection USP-10 mL was used as contrast agent. The patients with elevated renal parameters, and history of contrast allergy were excluded from contrast study. The stages of cervical carcinoma were allocated on the basis of 2018 FIGO revised staging system for cervical carcinoma. The data obtained from MRI and HPE were assessed. SPSS version 22.0 was used for the analysis.

RESULTS

The 53 patients attended the hospital was included in the study. The 54.46±9.29 years was the calculated mean age. The age of youngest patient was 32-years, while the oldest patient included in the study was 74-year-old. From HPE the 47% patients were diagnosed with mass lesion of cervix. Almost 16% has the extension of mass lesions to the upper 2/3rd of the vagina. The Two out of 53 was diagnosed with the micro-invasive carcinoma cervix and other two was diagnosed with pelvic lymph nodes. The results of HPE and MRI are highly correlated. About 47% cases of mass lesion of cervix was diagnosed by MRI. The mass lesion extension to the upper 2-3rd of vagina was observed in 16% cases, parametrical infiltration was observed in about 16% cases, and other 8% was diagnosed with Pelvic lymphadenopathy. About 6% cases was diagnosed with Retroperitoneal lymphadenopathy, 2% with the cervical extension to the lower 2-3rd of the vagina, 2% with cervical mass lesion Invasion of the urinary bladder, 4% with invasion of rectum. There was no patient with cervical mass lesion extension to the pelvic sidewall (showed in table 1). On HPE the majority of the (87%) patients were diagnosed with squamous cell carcinoma. Other 4% was diagnosed with squamous/adenocarcinoma and 4% with poorly differentiated carcinoma cervix, 2.1% with adenocarcinomas, and another 2.1% with carcinoma in situ. The majority of the patients 62% presented with cervical carcinoma complaint about white discharge. Other 60% were suffering from postmenopausal bleeding, 47.9% with lower abdominal pain and 16% with dysmenorrhea. The total diagnostic accuracy was 50%, as sensitivity of MRI was observed to be 47% with HPE specificity of 52%. MRI has 50% sensitivity in predicating HPE with 92% specificity. The diagnostic accuracy is 90%.

MRI has 100% diagnostic accuracy in predicting HPE, Table 1.

Extension	Percentage	Frequency
Mass lesion confined to the cervix	47%	25
Extension of lesion to the upper two-third of vagina	16%	9
Extension to the parametrial infiltrations	16%	9
Pelvic lymphadenopathy	8%	4
Retroperitoneal lymphadenopathy	6%	3
Extension of lesion to lower 2-3rd of vagina	2%	1
Invasion of the urinary bladder	2%	1
Rectum invasions	4%	2
Extension to the pelvis	0%	0
Histopathological Examinations (HPE) Findings		
Mass lesion of cervix	47%	25
Extension to upper two-third of the vagina	16%	9
Micro invasive carcinoma	4%	2
Pelvic lymph node	4%	2

Table 1: Clinical diagnosed cases distribution according to histopathological HPE and MRI findings

The staging of cervical carcinoma was done in accordance with FIGO standards. The 47% cases of stage I B, 16% cases of stage II A, 16% cases of stage II B was diagnosed. Stage I A, stage III C1, stage III C2 and stage IV A have equal share of 2%. The 1% cases of Stage III A were reported (shown in Table 2).

Staging of cervical carcinoma	Percentage	Number
Stage I B	47%	25
Stage II A	16%	9
Stage II B	16%	9
Stage I A	4%	2
Stage III C1	4%	2
Stage III C2	4%	2
Stage IV A	4%	2
Stage III A	2%	1

Table 2: Staging of cervical carcinoma and their respective percentage

DISCUSSION

Cervical carcinoma has highest mortality ratio in developing countries. This type of cancer shares second highest number among the women of age 15-44 years. The squamocolumnar junction are the most common origin sites of cervical carcinoma in younger women, while in older women the cancer mostly originates from endocervical canal [15]. The lesion of the cervix either protrudes to vagina or invades to myometrium. The standardized mortality rate of cervical carcinoma is also high. It is as most common gynecological malignancy with the highest morbidity rates [16]. For management and control of malignant diseases early and accurate diagnosis is required. In this regard, MRI and ultrasonography are widely used. The present study was conducted to evaluate the diagnostic accuracy of MRI in detection of cervical carcinoma [17]. The most commonly used screening test

for cervical carcinoma are HPV and Papanicolaou test. MRI and PET-CT are used for diagnostic purposes in the advanced disease cases. According to the results the 87.5% of patients was diagnosed with squamous cell carcinoma. The 4.2% patients have poorly differentiated carcinoma on HPE. 2.1% patients had in situ carcinoma [18]. The findings of our study were comparable to the study conducted by Colletini F. In their about 80-90% patients were diagnosed with squamous cell carcinoma. The stage IB carcinoma was diagnosed in about 47.91% patients, stage IIA carcinoma in about 16.67% patients. While other 16.6% were diagnosed with stage IIB carcinoma. According to the study conducted by Shweel MA et al. stage IB carcinoma was observed in 6.6%, Stage IIA in 40.3%, Stage IIB in 26.6% and another Stage IVA carcinoma in 26.6% [19]. The stage IB was observed in the most of the patients. In our study three patients was detected with stage IA with no abnormality seen under MRI. Both MRI and HPE are accurate in diagnosis of extension and involvement of carcinoma. The MRI and HPE both showed the similar results of cervix mass lesions in about 47.9%. Similarly, in about 16.66% the upper 2-3rd of the vagina was involved. The lymph node metastasis on HPE was observed in 4.16% patients, and other 8.33% has involvement of pelvic lymphadenopathy [20]. MRI not only help to clearly identify the paramaterial infiltration, urinary bladder. The results of HPE and MRI was comparable. The study conducted by Shweel MA et al., depicted that the results of magnetic resonance imaging are comparable to histopathological staging. Two patients were observed at Stage IIA. The one patient with Stage IIB disease was observed in our study [21-22]. The study conducted by Morimura et al., concluded that MRI has high specificity of about (99.2%) and high sensitivity of about (88.5%) for diagnosis of cervical carcinoma. The Shweel MA et al., showed that the sensitivity of MRI was 100% and specificity was 100%. With sufficient confidence level that are achievable through MRI the absence of rectal and bladder invasion can be diagnosed. MRI has low sensitivity in the cases where evaluation of metastasis in normal-sized lymph node is needed [23]. Parametrium invasions of cervical carcinoma has strong influenced on the staging and treatment of the cancer. Shweel MA et al., used MRI to detect parametrial infiltrations the sensitivity of MRI was about 100% with 85.7% specificity. In a study conducted by Nisha et al., the sensitivity and specificity was 60% and 100% respectively. The accuracy rate of MRI in diagnosis was calculated as 90%. In about 80% patients the cervical carcinoma was metastasized to pelvic lymph node. The sensitivity, accuracy and specificity was observed as 100%, 96% and 96.1% respectively in the study conducted by Kim

WY. The parametrial infiltration was detected in about 16.6% cases. MRI is a non-invasive modality. MRI not only help to diagnose the main prognostic factor involve in cervical carcinoma but also give insight for selection of best therapeutics approach. To depict primary tumor the imaging modality MRI is widely used. In our study the correlation between HPE and MRI was observed[24].

CONCLUSION

Staging is a crucial factor in order to determine the treatment strategy for the malignant diseases. Cervical carcinoma is common type of tumor among women globally. Its increasing prevalence and higher mortality and morbidity rates are raising it as a challenging type of cancer. Therefor the need of the hour is to determine best diagnostic tool for identification of stage of cancer, its location, size, lesions extensions and metastasis. MRI being a non-invasive imaging modality is proving to be more effective diagnostic method with higher accuracy and better specificity and sensitivity.

REFERENCES

- [1] Yogaraj K. Association between MRI Findings and Histopathological Examination in Carcinoma Cervix: A Retrospective Study. *International Journal of Anatomy, Radiology and Surgery*. 2021 Apr; 10(2): 61-4. DOI: 10.7860/IJARS/2021/46070:2642
- [2] Unni N, MN B, Thomas S, Puthussery PV. Diagnostic Accuracy in Staging of Carcinoma Cervix Using Magnetic Resonance Imaging versus Clinical Staging. *Journal of medical science and clinical research*. 2019 Jun; 7(6) :371-6. DOI: <https://dx.doi.org/10.18535/jmscr/v7i6.64>
- [3] Kalaivani C. Role of MR Imaging in Diagnosis, Staging and Follow Up of Patients with Carcinoma Cervix (Doctoral dissertation, Coimbatore Medical College, Coimbatore). 2019.
- [4] Vani CK, Murali N, Sundari N. Role of Magnetic resonance imaging in diagnosis, staging and follow up of patients with carcinoma cervix. *International Journal of Radiology and Diagnostic Imaging* 2020; 3(2): 101-6. DOI: <http://dx.doi.org/10.33545/26644436.2020.v3.i2b.105>
- [5] Sood M, Boricha A, Trivedi A, Dodiya C. Magnetic Resonance Imaging in Carcinoma of Cervix. *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*. 2018 Sep; 17(9): 23-9. DOI: 10.9790/0853-1709032329
- [6] Shahbaz S. Diagnostic Accuracy of Magnetic Resonance Imaging in Carcinoma of Cervix Taking Histopathology as Gold Standard. *Pakistan Journal of Radiology*. 2020 Feb; 29(4).
- [7] Kumari A, Pankaj S, Nazneen S, Kumari J, Kumari A, Choudhary V, et al. Diagnostic Accuracy of MRI with Clinical Staging in Cervical Cancer. *Journal of Indira Gandhi Institute of Medical Sciences*. 2019 Jan; 5(1):17.
- [8] Zubery MH, Rahman FB, Islam MN, Datta A, Rahman T, Mahdi R. A Comparative Study between Magnetic Resonance Imaging and Clinical FIGO Criteria in Different Stages of Carcinoma Cervix. *Mymensingh medical journal: MMJ*. 2021 Oct; 30(4):1131-8.
- [9] Anand AS, Abraham MM, Kuriakose VG. MRI versus clinical assessment in staging and response evaluation in locally advanced cervix cancer patients treated with concurrent chemo-radiation in a tertiary cancer center: a prospective study. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2017 Feb; 6(2):393. doi.org/10.18203/2320-1770.ijrcog20164826
- [10] Mahajan A, Sable NP, Popat PB, Bhargava P, Gangadhar K, Thakur MH, et al. Magnetic Resonance Imaging of Gynecological Malignancies: Role in Personalized Management. *Semin Ultrasound CT MR*. 2017 Jun; 38(3):231-268. doi: 10.1053/j.sult.2016.11.005.
- [11] Tsikouras P, Zervoudis S, Manav B, Tomara E, Iatrakis G, Romanidis C, et al. Cervical cancer: screening, diagnosis and staging. *J buon*. 2016 Mar 1; 21(2):320-5.
- [12] Jenkins D. Histopathology and cytopathology of cervical cancer. *Disease Markers*. 2007;23(4):199-212. doi: 10.1155/2007/874795.
- [13] Shweel MA, Abdel-Gawad EA, Abdel-Gawad EA, Abdelghany HS, Abdel-Rahman AM, Ibrahim EM. Uterine cervical malignancy: diagnostic accuracy of MRI with histopathologic correlation. *Journal of clinical imaging science*. 2012; 2:42. doi: 10.4103/2156-7514.99175.
- [14] Zand KR, Reinhold C, Abe H, Maheshwari S, Mohamed A, Upegui D. Magnetic resonance imaging of the cervix. *Cancer Imaging*. 2007 May; 7(1):69-76. doi: 10.1102/1470-7330.2007.0011
- [15] Devine C, Gardner C, Sagebiel T, Bhosale P. Magnetic resonance imaging in the diagnosis, staging, and surveillance of cervical carcinoma. In *Seminars in Ultrasound, CT and MRI*. WB Saunders. 2015 Aug; 36(4): 361-8.
- [16] Rockall AG, Ghosh S, Alexander-Sefre F, Babar S, Younis MT, Naz S, et al. Can MRI rule out bladder and rectal invasion in cervical cancer to help select patients for limited EUA? *Gynecologic Oncology*. 2006 May; 101(2):244-9. doi: 10.1016/j.ygyno.2005.10.012.

- [17] REHMAN WU, FAYAZ M. Magnetic Resonance Imaging: A Useful Tool for Diagnosing Malignancy- Diagnostic Accuracy of MRI in Detection of Malignancy of Cervix. *Diabetes*. 30:20-0.
- [18] Choi SH, Kim SH, Choi HJ, Park BK, Lee HJ. Preoperative magnetic resonance imaging staging of uterine cervical carcinoma: results of prospective study. *Journal of computer assisted tomography*. 2004 Sep-Oct; 28(5):620-7. doi: 10.1097/01.rct.0000138007.77725.0a.
- [19] Liu X, Wang J, Hu K, Zhang F, Meng Q, Wang W, et al. Validation of the 2018 FIGO Staging System of Cervical Cancer for Stage III Patients with a Cohort from China. *Cancer Management and Research*. 2020 Feb; 12:1405-1410. doi: 10.2147/CMAR.S239624.
- [20] Bhatla N, Aoki D, Sharma DN, Sankaranarayanan R. Cancer of the cervix uteri. *International Journal of Gynaecology and Obstetrics*. 2018 Oct; 143 Suppl 2:22-36. doi: 10.1002/ijgo.12611.
- [21] Cohen PA, Jhingran A, Oaknin A, Denny L. Cervical cancer. *Lancet*. 2019 Jan 12; 393(10167):169-82. doi: 10.1016/S0140-6736(18)32470-X.
- [22] Vizcaino AP, Moreno V, Bosch FX, Muñoz N, Barros-Dios XM, Borras J, et al. International trends in incidence of cervical cancer: II. Squamous-cell carcinoma. *International Journal of Cancer*. 2000 May; 86(3):429-35. doi: 10.1002/(sici)1097-0215(20000501)86:3<429:aid-ijc20>3.0.co;2-d.
- [23] Boss EA, Barentsz JO, Massuger LF, Boonstra H. The role of MR imaging in invasive cervical carcinoma. *European radiology*. 2000 Jan; 10(2):256-70. doi.org/10.1007/s003300050042
- [24] Patel-Lippmann K, Robbins JB, Barroilhet L, Anderson B, Sadowski EA, Boyum J. MR imaging of cervical cancer. *Magnetic Resonance Imaging Clinics*. 2017 Aug 1; 25(3):635-49. doi.org/10.1016/j.mric.2017.03.007



Original Article

Effects of Modified Eldoa Technique In Patients with Cervical Radiculopathy

Rimsha Arif¹, Hanan Azfar², Asna Waseem³, Shabana Nawaz³, Abdul Ghafoor Sajjad⁴¹ Department of Physiotherapy, Attock hospital (PVT) limited Pakistan² Department of Physiotherapy, Bhatti Hospital, Gujranwala, Pakistan³ Department of Allied Health Sciences, Central Park Medical college Lahore, Pakistan⁴ Shifa Tameer e Millat University Islamabad, Pakistan

ARTICLE INFO

Key Words:

Cervical radiculopathy, ELDOA, Modified ELDOA, Neurodynamic

How to Cite:

Arif, R., Azfar, H. ., Waseem, A. ., Nawaz, S. ., & Ghafoor Sajjad, A. . (2022). Effects Of Modified ELDOA Technique in Patients with Cervical Radiculopathy: Eldoa Technique in Patients with Cervical Radiculopathy. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.558>

*Corresponding Author:

Rimsha Arif
 Department of Physiotherapy, Attock hospital (PVT) limited Pakistan
 biostats1000@gmail.com

Received Date: 15th June, 2022

Acceptance Date: 27th June, 2022

Published Date: 30th June, 2022

ABSTRACT

ELDOA is a revolutionary technique for improvement of health and longevity of the spine which is introduced by French osteopath; Guy Voyer. The primary goal of ELDOA is to apply focused internal tension and load to decrease pressure on the discs of spine, increase blood flow and to reduce pain at cervical spine. There is little high-quality evidence on best no operative therapy for cervical radiculopathy. Objective: To determine the effects of Modified ELDOA technique in patients with cervical radiculopathy in terms of pain, nerve tension and disability. Methods: Thirty patients were randomly assigned either to a group that performed modified ELDOA along with conventional treatment aimed at decreasing the effects of pain, nerve tension and disability or to a group that performed ELDOA and received conventional treatment having the same goal as the former. Randomized controlled trial was selected as the design of study. Treatment protocol of control group included hot pack, TENS, PIR(MET) 4 reps with 6 sec hold, Maitland oscillations (20 reps in 3 sets), ELDOA at cervical spine, Neurodynamic stretching of involved nerve. Treatment protocol of experimental group included hot pack, TENS, PIR(MET) 4 reps with 6 seconds hold, Maitland oscillations (20 reps in 3 sets), modified ELDOA at cervical spine, Neurodynamic stretching of involved nerve. Each patient received 8 sessions on alternate days covered in a total span of 16 days. Assessments were done at 1st 8th session. The tools used were NDI, NPRS and ROM through goniometer. IBMSPSS-21 was used to analyze data. Results: The results demonstrated that treatment protocols of both the control and experimental groups have significant effects on reducing pain, tension and disability and improving mobility of cervical spine. Whereas, for difference in effectiveness of modified ELDOA and ELDOA, the overall p-values came out to be >0.05 while comparing the end values of both groups, showing that there is a non-significant difference in the effects of ELDOA and modified ELDOA. Conclusion: Modified ELDOA works effectively in posture correction hence improving the functional status of patient. Modified ELDOA and ELDOA postures help in treatment of cervical radiculopathy. The effectiveness of ELDOA and modified ELDOA has a non-significant difference.

INTRODUCTION

Cervical radiculopathy is defined as the marked nerve compression from arthritic bone spur or herniation of discs. Peak annual incidence of cervical radiculopathy is 2.1 cases per 1000 and occurs in fourth and fifth decades of life; 3.3 cases per 1000 cases of cervical radiculopathy are reported [1]. Common cause of symptoms in upper extremity is the spondylosis occurring at cervical spine and the herniation of disc leads to the cervical radiculopathy. Sometimes there is unknown cause for cervical

radiculopathy [2]. The cervical vertebrae are categorized into two categories, Atypical and Typical vertebra. Vertebral bodies of cervical spine mainly composed of trabecular or cancellous bone and small in comparison of other spinal vertebrae. Atypical vertebrae include Atlas C1, Axis C2 and Vertebra Prominens C 7 while C3 to C6 are included in the category of typical vertebra of cervical spine [3]. Skull is held by Atlas by the help of atlanto-occipital joint aiding in nodding movement of head. Axis

forms a pivot that aids in rotation of the Atlas.C7 vertebra is also atypical vertebrae of cervical spine due the prominent spinous process. The features of typical vertebrae are 2 transverse foramina, bifid spinous process and a vertebral foramen [4]. Fibro cartilaginous cushions are naturally occurring in between the adjacent vertebrae of the vertebral column, termed as intervertebral disc. This disc serves the spine as a shock absorbing component. The number of discs present in the cervical spine is 6. The intervertebral disc is divided into two portions [5]. One is the nucleus pulposus and the other is annulus fibrosus. The inner portion, nucleus pulposus, is resistant to axial forces and is gelatinous in nature along with higher water content [6]. The outer portion, annulus fibrosus, is comprised of an outer fibrous ring which is flexible as well as tough in nature and serves as keeping the vertebrae together and allowing movements in spine. In comparison to lumbar spine's intervertebral discs, the discs belonging to cervical spine are not having concentric laminate of collagen fibers in annular portion [7]. The collagen aligns in the form of crescent mass tapering the uncinat processes laterally and anteriorly more in thickness and in the posterolateral direction it is deficient forming thin layer paramedian [8]. Neck disorders have a major distinct of cervical radiculopathy. Cervical radiculopathy supervenes when nerve in neck is tamped down or peevd where it arms away from the spinal cord [9]. The wear away or malfunction of nerve that results if one of the nerve roots nears the cervical vertebrae is flattened (decreased circumference of intervertebral foramen), the condition is termed as cervical radiculopathy [10]. Depending on the site of vitiated nerve roots, afflict of nerve roots in the cervical region can initiate ache and decreased sensations on the nerve's tract into the arm and hand. Firing pain fanning out towards arm, neck, chest, upper back, and shoulders are distinct precursors of cervical radiculopathy [11]. One can undergo curtailment of sensory stimulations, fatigue in muscles of upper limb and prickling in hand and fingers [12]. ELDOA technique works tardily but expeditiously to build up the improvements in the postures adapted by our body because of the sedentary lifestyles. These postures were designed by Guy Voyer [13]. The purpose behind the development of these postures was to improve bad postures and dehydration of discs. ELDOA is basically a French acronym when translated to English is termed as LOADS (Longitudinal osteo-articular decertation stretches). It is an active traction exercise used for spacing the joints and works by creating tension in the Fascia of the body. Hence it would be explained as postural self-normalizing pedagogy organized for broadening the space within a selected articulation [14]. This is done by creating

facial tension to fix the vertebra above the marked disc. ELDOA poses are very specific examined to other techniques. Disc encryption existing at any level of spine can be addressed through specific ELDOA poses [15]. Position involving specific intervertebral level is conserved by ELDOA. Dissertation of the targeted intervertebral level occurs because of the myofascial tension induced between superior vertebra which is a wandering point and the inferior vertebrae which is a fixed point. Verbal cues are given to the subject for the encouragement goals and for maintaining proper position and not to drop a pose [13]. ELDOA tends at multilevel of spine and can target specific levels as well. Subject is asked to focus on the breathing pattern to achieve better results and aid mental relaxation. While performing ELDOA, marked articular level is felt by therapist and fine tuning of subject is attained. Maintain the position of ELDOA unless the decapitation movement is felt. Achievement of final position of ELDOA needs working of therapist on the patients. ELDOA involves different levels of spine. The effects of ELDOA are improvements in postures [15]. To determine the effects of Modified ELDOA technique in patients with cervical radiculopathy in terms of pain, Nerve Tension, and disability.

METHODS

Inclusion Criteria: Cervical Radiculopathy (Unilateral), Pain more than 3 on NPRS AT Neck, Both Gender, Age between 30 to 50years, three of the listed tests responds positively. ULTT for median, radial, or ulnar nerve, Limited ROM (anyone), Cervical Distraction test, Springing Test, Spurling's test. **Exclusion Criteria:** Malignancy, infection, trauma, bone deformities, Acute Disc Protrusion, Positive VBI, Positive Sharp purser test. **Measurement Tools:** Numeric pain rating scale. ROM (Goniometer), NDI, Neurodynamics [16]. **Intervention:** Intervention will be given for four weeks with 2 sessions per week. **Group A (Control):** HOT PACK, TENS, PIR (MET) 4 reps with 6 sec holds, Maitland Oscillations (20 reps in 3 sets), ELDOA of involved spinal segment, NE urodynamic stretching of involved nerve (median, ulnar or radial). **Group B (Intervention):** HOT PACK, TENS, PIR (MET) 4 reps with 6 sec holds, Maitland Oscillations (20 reps in 3 sets), Modified ELDOA of involved spinal segment, Neurodynamics stretching of involved nerve (median, or radial). A randomized control trial was conducted from February 2019 to July 2019(6 months) at Attock Hospital Limited, Rawalpindi. In this study total 38 subjects were assessed with neck pain moving towards arm but only 30 patients met the inclusion criteria. The subjects were divided into two groups randomly, one named as Control group 'A group' and one as Experimental/Intervention group or 'B group', by

lottery method using convenient sampling technique. Among them 15 patients were randomly assigned to each group. Hence, 30 patients were analyzed for further study. Group A included 15 patients that were treated by the protocol involving positions of ELDOA at cervical spine while Group B included 15 patients receiving treatment protocol following the positions of modified ELDOA at cervical spine. First and final assessments were done by structural questionnaire. Outcome measures included ROM (Goniometre), NPRS and NDI at baseline and last treatment sessions. For data analysis at baseline and end of treatment sessions IBM SPSS-21 was used. Firstly, Shapiro-Wilk test readings were noted for the consideration of the point that data distribution is normal or not. Parametric tests were applied on significant variables while for those whose significance was greater than 0.05 non-parametric tests were applied.

RESULTS

ULNTT1 was found positive in 60% of total subjects while negative in 40% subjects. In group The values came out to be 26.7% positive for ULNTT1 and 73.3% negative for ULNTT1. 73.3% of the total subjects showed positive ULNTT2 while 26.7% showed negative ULNTT2. In group A ULNTT2 was found positive in 26.7% subjects while negative in 73.3% subjects and for group B it was 13.3% positive and 86.7% negative. ULNTT3 was positive among 40% of subjects and negative for 60% of the subjects. In group A ULNTT3 was found positive in 73.3% and negative in 26.7% of subjects while in group B ULNTT3 was positive in 13.3% of subjects and negative in 86.7% of subjects. Man, Whitney U-test was applied on baseline to compare median values between control and experimental group. The median value of flexion for control group was 16.80 and for experimental group it was 14.20 with the IQR of 50(20.25) and p value of 0.416, which means values are not statistically significant. The median value for left side bending of control group was 15.60 and experiment group was 15.40 having IQR equals to 51.50(18) with the p value of 0.950 which is a non-significant value. NPRS value for control group was 17.67 and for experiment group was 13.33 with IQR of 08(01) and a p value of 0.129. NDI median value for control group was 10.97 and for experiment group was 20.03 with IQR of 42(11.89) and a p value equal to 0.05, Table 1.

S. No	Variable	Pre-Value	Post Value	Difference	P value
1.	Extension at cervical spine	57.80±9.97	67.53±3.94	-13.83±5.629	<0.05
2.	Right side bending at cervical spine	47.26±13.33	67.60±3.97	-128.11± 12.55	<0.05
3.	Left side bending at cervical spine	46.93±12.29	69.80±3.42	-29.70±16.03	<0.05
4.	Right rotation at cervical spine	58.73±8.56	70.53±4.22	-15.59±8.008	<0.05
5.	Left rotation at cervical spine	58.26±9.01	70.73±4.13	-17.20±7.73	<0.05

Table 1: Base Line Comparison Between Control Group and Experiment Group

To compare the pre and post mean values within the control group paired t-test was applied. The pre and post values of extension at cervical spine were 57.80 ±9.97 and 67.53 ±3.94 and a difference of -13.83 ±5.629 with a p-value being <0.05 which means the difference was statistically significant. The pre and post values of right side bending at cervical spine were 47.26 ±13.33 and 67.60 ±3.97 and a difference of -128.11±12.55 with a p-value<0.05. The pre and post values of left side bending came out to be 46.93±12.29 and 69.80 ±3.42 and a difference of -29.70 ±16.03 with a significant statistical value i.e.,<0.05. The pre and post values of right rotation at cervical spine were 58.73 ±8.56 and 70.53±4.22 with the difference of -15.59±8.008 and a p-value<0.05 which is significant in nature according to statistics. The pre and post values for left rotation at cervical spine were 58.26 ±9.01 and 70.73 ±4.13 and a difference of 17.20 ±7.73 having a p-value<0.05 which is significant value statistically. (Table no. 05). Wilcoxon signed rank test was also used to compare pre and post values in control group. The pre and post values of median and IQR in control group for flexion at cervical spine were 50(16) and 68(09) with z-value of -3.449 and statistically significant value of <0.05. The pre and post values of NPRS were 08(01) and 02(01) with a z-value of -3.449 and p-value<0.05. The pre and post values of NDI in control group were 37.70(17.11) and 12(10) and z-value -3.411 and p-value <0.05. (Table no.06).

Test Variable	Pre Median IQR	Post Median IQR	Z value	P value
Flexion (ROM)	50(16)	68(09)	-3.449	<0.05
NPRS	08(01)	02(01)	-3.449	<0.05
NDI	37.70(17.11)	12(10)	-3.411	<0.05

Table 2: Pre & Post Values

To compare pre and post mean values within the experimental group paired t-test was applied. The pre and post values for flexion at cervical spine were 48.93 ±11.76 and 63.66 ±4.48 and difference of -19.09 ±10.37 with a p-value <0.05 which is a significant value according to statistics. The pre and post values for extension at cervical

spine 54.13 ±11.34 and 65.60 ±5.35 and difference of -15.78 ±7.15 having p-value<0.05 which is significant statistically. The pre and post values right side bending at cervical spine were 44.20 ±14.68 and 64.86 ±4.79 with a difference of -27.88 ±13.44 having significance of<0.05. The pre and post values of left rotation at cervical spine 54.46 ±6.62 and 66.33 ±3.86 with difference -15.51 ±8.21 and p-value <0.05, Table 3.

S. No	Variable	Pre-Value	Post Value	Difference	P value
1.	Flexion at cervical spine	48.93±11.76	63.66±4.48	-19.09±10.37	<0.05
2.	Extension at cervical spine	54.13±11.34	65.60±5.35	-15.78±7.15	<0.05
3.	Right side bending at cervical spine	44.20±14.68	64.86±4.79	-27.88±13.44	<0.05
4.	Right rotation at cervical spine	55.53±7.04	66.06±4.63	-13.90±7.16	<0.05
5.	Left rotation at cervical spine	54.46±6.62	66.33±3.86	-15.51±8.21	<0.05

Table 3: Pre and Post Comparison in Control Group

Wilcoxon signed rank test was also used to compare pre and post values in experimental group. The pre and post values of left side bending at cervical spine were 53(26) and 65(04) and a z-value of -3.415 and p-value<0.05 which is statistically significant. The pre and post values of NPRS in experimental group were 07(01) and 02(01) having z-value of -3.415 with p-value<0.05. The pre and post value of NDI were 46(24) and 10(12) having z-value of -3.40 with p-value<0.05 which is a significant value according to statistics, Table 4.

Test Variable	Pre Median IQR	Post Median IQR	Z value	P value
Lt Side Bending(ROM)	53(26)	65(04)	-3.415	<0.05
NPRS	07(01)	02(01)	-3.412	<0.05
NDI	46(24)	10(12)	-3.40	<0.05

Table 4: Pre & Post Values Comparison in Experiment Group

To compare the means of end values between the control and experiment groups independent t-test was applied. The mean value of extension in control group was 67.53±1.01 and in experiment group was 65.50±1.38 having p-value .101 which is not significant statistically. The mean values of right side bending in control group came out to be 67.60±1.02 and in experimental group it was 64.86±1.23 with a non-significant p-value of .371. The mean values of left side bending in control group came out to be 69.80±0.88 and in experimental group it was 65.46±1.12 with a non-significant p-value of .537. The mean values of right rotation in control group came out to be 70.53±1.09 and in experimental group it was 66.06±1.19 with a significant p-value of .040. The mean values of left rotation in control group came out to be 70.73±1.06 and in experimental group it was 66.33±0.99 with a non-significant p-value of .860, Table 5.

S. No	Variable	Groups	Difference	P value
1.	ROM Extension at cervical spine	Control	67.53±1.01	.101
		Experiment	65.50±1.38	
2.	ROM Right side bending at cervical spine	Control	67.60±1.02	.371
		Experiment	64.86±1.23	
3.	ROM Left side bending at cervical spine	Control	69.80±0.88	.537
		Experiment	65.46±1.12	
4.	ROM Right rotation at cervical spine	Control	70.53±1.09	.040
		Experiment	66.06±1.19	
5.	ROM Left rotation at cervical spine	Control	70.73±1.06	.860
		Experiment	66.33±0.99	

Table 5: Pre and Post Comparison in Experiment Group

Variable	Groups	Median	IQR	P value
Flexion(ROM)	Control	16.50	64 (9)	.524
	Experiment	14.50		
NPRS	Control	15.60	2 (01)	.944
	Experiment	15.40		
NDI	Control	17.20	12(11.34)	.287
	Experiment	13.80		

Table 6: End Value Comparison Between the Groups

DISCUSSION

We conducted on 30 patients randomly distributed in two groups. Each group was having 15 patients. One group performed ELDOA along with soft tissue and joint mobilizations with Neurodynamics stretching while the other group also received the same protocol but performed modified ELDOA postures. Outcomes were measured in NPRS and NDI and ROM using goniometer. First objective of the study was to find the effectiveness of modified ELDOA in patients with cervical radiculopathy on pain, disability, and nerve tension. In experiment or intervention group its overall effectiveness on NPRS and NDI was found using Wilcoxon test. Both had p-value <0.05 which is significant. Second objective of the study was to find out the difference in effectiveness of modified ELDOA and ELDOA. The overall p-values came out to be >0.05 while comparing the end values of both groups, showing that there is a non-significant difference in the effects of ELDOA and modified ELDOA. ELDOA is postural self-normalizing techniques which aim to leverage fascia in body to produce a type of active traction for spinal joints. It has tremendous neurological benefits. Body is linked from crown/apex to bottom anatomically and biomechanically. The links are different myofascial links. All connective tissue, tendons, muscles, ligaments, deep nerves, and aponeurosis, they are all in link from top of head to bottom of foot. When you elicit a movement there is a direct link or effect all through a myofascial chain. There is a theory which explains that information can be transmitted instantaneously through a communication that is extra neural and explanation of that would be through fascia. External forces or muscle activity generates mechanical tension in fascia which plays passive role in regulation of movement and postures [17]. My study

supports the point that modified ELDOA and ELDOA postures have an effective way to restore good posture control and reduce effects of sedentary lifestyle. It also reduces the pain, nerve tensions and disability in the subjects having cervical radiculopathy. The joints of our spine are continuously under the effect of gravitational force which is compressing it. Gravity inverted postures unload the spine and help in increasing physical makeup of spine [18]. Performing ELDOA increases muscle performance and tone, decreases pain and works on posture improvement by increasing space between spinal joints and lengthens spine. My study also shows that pain is decreased in both groups up to a significant limit along with a significant improvement in range of motions. Long term effects of cervical laminectomy were studied. The outcome of the study showed that the recovery rate after 1 year and 5 years was less than 45% and was 32.8% at last follow-up review [19]. Physiotherapy treatment protocol including the traction, exercises and NSAID showed good outcome when applied on patients having cervical radiculopathy (24 of 26 patients treated successfully conservatively)[20]. Our study is also supporting the idea of successful physiotherapy management of cervical radiculopathy by utilizing manual physiotherapy techniques. We find out that Modified ELDOA is significantly effective in the treatment of cervical radiculopathy. It reduces the pain and disability of the patient. Application of ELDOA also reduces pain and disability in the patients of cervical radiculopathy. The outcomes of study conducted on fascia stretching in disc protrusion patients by Abdul Ghafoor Sajjad also support my findings [13]. Cervical range of motion is improved by the application of muscle energy technique with the effects lasting to almost seven days [15]. Our study also included the application of MET for soft tissue mobilization and increasing the length of shortened muscles that might be affecting range of motion at cervical spine. Findings of our study are that the application of MET along with joint mobilization, modified ELDOA and ELDOA postures result in increased range of motion at cervical spine and decreased pain and disability. ELDOA is effective in improving range of motion and decreasing physical tension and also works on the management of pain [14]. My findings also show that ELDOA manages pain effectively and increases range of motion significantly. Modified ELDOA also showed significant effects on pain and range of motions.

CONCLUSIONS

This study concluded that ELDOA and modified ELDOA has significant effects on enhancing ranges of motion and

functional status of the patients along with reduction of pain in patients with cervical radiculopathy. However, there is a non-significant difference between the effectiveness of ELDOA and modified ELDOA.

REFERENCES

- [1] Marcon RM, Cristante AF, Teixeira WJ, Narasaki DK, Oliveira RP, de Barros Filho TE. Fractures of the cervical spine. *Clinics (Sao Paulo)*. 2013 Nov; 68(11):1455-61. doi:10.6061/clinics/2013(11)12.
- [2] Abbed KM, Coumans JV. Cervical radiculopathy: pathophysiology, presentation, and clinical evaluation. *Neurosurgery*. 2007 Jan;60(1 Suppl 1):S28-34. doi:10.1227/01.NEU.0000249223.51871.C2.
- [3] Kang KC, Lee HS, Lee JH. Cervical Radiculopathy Focus on Characteristics and Differential Diagnosis. *Asian Spine Journal*. 2020 Dec; 14(6):921-930. doi: 10.31616/asj.2020.0647.
- [4] Panjabi MM, Oxland TR, Parks EH. Quantitative anatomy of cervical spine ligaments. Part II. Middle and lower cervical spine. *J Spinal Disord*. 1991 Sep; 4(3):277-85. doi: 10.1097/00002517-199109000-00004.
- [5] Bulge HA. Back Pain Chiropractic Chiropractic Examination Chronic Pain Functional Medicine Health Herniated Disc Neck Pain Sciatica Pain Spinal Decompression Spine Care Treatments Wellness June 20, 2020 1394 Views 0 Reactions.
- [6] Steilen D, Hauser R, Woldin B, Sawyer S. Chronic neck pain: making the connection between capsular ligament laxity and cervical instability. *Open Orthop J*. 2014 Oct;8:32645. doi:10.2174/1874325001408010326.
- [7] Bray JP, Burbidge HM. The canine intervertebral disk: part one: structure and function. *J Am Anim Hosp Assoc*. 1998 Jan/Feb;34(1):5563. doi:10.5326/15473317-34-1-55.
- [8] Mercer S, Bogduk N. The ligaments and annulus fibrosus of human adult cervical intervertebral discs. *Spine (Phila Pa 1976)*. 1999 Apr; 24(7):619-26; discussion 627-8. doi: 10.1097/00007632-199904010-00002.
- [9] Kuijper B, Tans JT, Schimsheimer RJ, van der Kallen BF, Beelen A, Nollet F, et al. Degenerative cervical radiculopathy: diagnosis and conservative treatment. A review. *Eur J Neurol*. 2009 Jan; 16(1):15-20. doi: 10.1111/j.1468-1331.2008.02365.x.
- [10] Edmeads J. Headaches and head pains associated with diseases of the cervical spine. *Med Clin North Am*. 1978 May; 62(3):533-44. doi: 10.1016/s0025-7125(16)31791-6.

- [11] 11. Ahmed GM, Ramzy GM, Rezk MY, Abdelaziz NG. The effect of mckenzie assessment and treatment method on patients with chronic low back pain with Radiculopathy, Single Blinded Randomized Controlled Trial. *International Journal of Health Sciences*. 2019 Mar; 7(1):7-17.
- [12] 12. Langevin P, Desmeules F, Lamothe M, Robitaille S, Roy JS. Comparison of 2 manual therapy and exercise protocols for cervical radiculopathy: a randomized clinical trial evaluating short-term effects. *J Orthop Sports Phys Ther*. 2015 Jan; 45(1):4-17. doi: 10.2519/jospt.2015.5211.
- [13] 13. Sajjad AG, Javed MS, Rasul A, Hussain SA, Naqvi SA. Comparison Of The Effects Of Decompression And Eldoa On Pain And Disability In Lumbar Disc Protrusion. *Rehman Journal Of Health Sciences*. 2021 Dec; 3(2):92-6.
- [14] 14. Clement AA. The prevalence of playing-related injuries in collegiate violinists and the physical, emotional, and mental effects of ELDOA, 2016.
- [15] 15. Hammer WI, editor. *Functional soft-tissue examination and treatment by manual methods*. Jones & Bartlett Learning; 2007.
- [16] 16. Nee RJ, Jull GA, Vicenzino B, Coppieters MW. The validity of upper-limb neurodynamic tests for detecting peripheral neuropathic pain. *J Orthop Sports Phys Ther*. 2012 May; 42(5):413-24. doi: 10.2519/jospt.2012.3988.
- [17] 17. Schleip R, Klingler W, Lehmann-Horn F. Active fascial contractility: Fascia may be able to contract in a smooth muscle-like manner and thereby influence musculoskeletal dynamics. *Med Hypotheses*. 2005; 65(2):273-7. doi: 10.1016/j.mehy.2005.03.005.
- [18] 18. Boocock MG, Garbutt G, Reilly T, Linge K, Troup JD. The effects of gravity inversion on exercise-induced spinal loading. *Ergonomics*. 1988 Nov; 31(11):1631-7. doi: 10.1080/00140138808966812.
- [19] 19. Kato Y, Iwasaki M, Fuji T, Yonenobu K, Ochi T. Long-term follow-up results of laminectomy for cervical myelopathy caused by ossification of the posterior longitudinal ligament. *J Neurosurg*. 1998 Aug; 89(2):217-23. doi: 10.3171/jns.1998.89.2.0217.
- [20] Saal JS, Saal JA, Yurth EF. Nonoperative management of herniated cervical intervertebral disc with radiculopathy. *Spine (Phila Pa 1976)*. 1996 Aug; 21(16):1877-83. doi: 10.1097/00007632-199608150-00008.



Original Article

Frequency of Ovarian Artery Doppler Indices in Patients of Polycystic Ovarian Syndrome

Zubair Janan Orakzai¹, Tabassum Begum^{1*}, Bakht Rokhan², Fahmida Sattar³, Fauzia Rashid⁴, Ayesha Kamran⁵¹Department of Radiology, Bacha Khan Medical College Mardan, Pakistan²Department of Radiology, Saidu Medical College / Saidu Teaching Hospital Saidu Sharif Swat, Pakistan³Department of Gynae/Obs, Seikh Khalifa bin Zayed Hospital Quetta, Pakistan⁴Department of Radiology, Hazrat Bari Imam Sarkar (HBS) General Hospital Islamabad⁵Department of Radiology, Sargodha Medical College Dhq Hospital Sargodha, Pakistan

ARTICLE INFO

Key Words:

Doppler Ultrasound, Polycystic Ovarian Syndrome, Deranged ovarian artery, Doppler indices

How to Cite:

Janan Orakzai, Z. ., Begum, T., Rokhan, B. ., Sattar, F. ., Rashid, F. ., & Kamran, A. . (2022). Frequency Of Ovarian Artery Doppler Indices in Patients of Polycystic Ovarian Syndrome: Ovarian Artery Doppler Indices in Patients of Polycystic Ovarian Syndrome. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.549>

*Corresponding Author:

Tabassum Begum
 Department of Radiology, Bacha Khan Medical College Mardan, Pakistan
 Dr.Tabkhan@gmail.com

Received Date: 13th June, 2022

Acceptance Date: 20th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Polycystic ovarian syndrome (PCOS) is a common endocrine disorder. It is characterized by changes in Doppler indices of ovarian arteries. These changes are more prominent than the morphological changes of ovary and uterus. **Objective:** The aim of the analysis was to calculate the percentage of deranged ovarian artery in patients with polycystic ovarian syndrome ovarian patients. **Methods:** This observational study was conducted on total 225 women of reproductive age ranging between 18-40 years presented with the PCOS at the hospital. The gold standard for diagnosis of deranged ovarian artery in PCOS is transvaginal ultrasound. The Doppler ultrasound helps to calculate the resistive and pulsatility indices of ovarian artery. The pulsatility Index and Resistive Index was calculated and percentage frequency was estimated from the calculated results. Ovarian blood flow is deranged if its indices are above or below the normal range. The resistive index (RI) measured by Doppler imaging was between 0.80 to 0.95 and pulsatility index (PI) range was between 2.01 to 4.30. The data were arranged according to BMI of patients. The age and duration of PCOS were also considered for data stratification. **Results:** The study showed that about 191 (85%) patients out of 225 with PCOS have deranged ovarian artery Doppler. The range of pulsatility index was between 2.01 to 4.30 while the range of resistive index was between 0.80 to 0.95. The mean duration of PCOS and means age of patient was calculated. It was found that the deranged ovarian blood flow was more common in the women of age 27-5.9 years. 18.4-7.1 months was the mean duration of PCOS. The mean BMI of the patient was 27.2-4.9kg/m². **Conclusion:** A significant number of women suffering from PCOS have deranged ovarian artery Doppler indices. This study evaluated the putative role of Doppler indices in diagnosis of suspicious PCOS patients.

INTRODUCTION

The most common and complex endocrine disorder of reproductive age women is Polycystic ovarian syndrome PCOS [1-2]. This is characterized by the various symptoms of oligomenorrhea, acne, obesity, menstrual irregularities and infertility². PCOS was diagnosed by Stein and Leventhal for the first time in 1935. It was named as Stein leventhal syndrome after the name of scientist. It is most common hormonal irregularity. The studies have showed that the capsule and sub capsular follicle enlarged in PCOS. The profound and rapid changes of vasculature of the

cycling ovary play a significant role in early maturation of follicle. To develop better understanding of pathogenesis of disease there is need to deeply analyze the vascular changes of the ovary and uterus. With the advent of color Doppler ultrasound, the ovarian artery can be identified at the lateral border of the ovary. PCOS not only affect the quality of life but also have negative physiological implications [2-3]. One frequent hypothesis regarding main cause of PCOS is that excessive production of androgen by ovaries that disturb the endocrine system

ultimately leads to PCOS [3-4]. Higher level of gonadotropic hormones and insulin resistance are also has significant role in PCOS process. The prevalence of PCOS in south Asian women is as high as 52% while its prevalence in developed countries is comparatively low as 15-20% [4-5]. The PI index of uterine artery is higher in the women diagnosed with the PCOS. This higher PI index ultimately leads to lower conception rates. In PCO syndrome the body mass Index BMI is considered to be predictor of fertility. The ovarian volume and BMI has direct relationship with each other. The women with PCOS have higher ovarian volume as compared to the normal women. BMI not only affect the ovarian volume but also have strong effect on endometrium thickness and uterine size. Hence, BMI and endometrium has positive correlation with each other. There is no single criterion to correctly diagnose the PCOS. Ultrasonography, hormonal assays and clinical features are currently used in diagnosis of PCOS [5-6]. Diagnosis through hormonal assays is an expensive process. The unreliability of these methods lies in the fact that they produce large number of false positive and false negative diagnostic results [7-8]. The most accurate tool to study the female reproductive system is transvaginal color Doppler ultrasonography. To assess the blood flow in obstetric, the combination of B-mode imaging and transvaginal color doppler ultrasound can be used [9-10].

METHODS

This cross-sectional study was conducted at the Radiology Department of BKMC / MMC, Mardan for the duration of six months from June 2020 to November 2020. The ethical review board of hospital approved the study and informed consent was taken. According to the Rotterdam consensus the polycystic ovarian syndrome can be characterized by presence of anovulation, hyperandrogenism, and 12 follicles in each ovary with enhanced ovarian volume. The 225 patients presented with PCOS was included in this descriptive study. The calculated confidence level was set as 95%. There was 5% margin of error. The deranged ovarian artery Doppler indices expected percentage was 83%. The Non-probability consecutive sampling approach was used to select patients. Those patients having PCOS who fulfil the Rotterdam criteria was involved in the study. Exclusion criteria was applied to the patients having evidence of hyperprolactinaemia and receiving contraceptive pills. On the basis of results obtained from laboratory screening methods, the patients having biochemical evidences of adrenal hyperplasia was also excluded from the study. For localization of ovarian arteries, the accurate tool, transvaginal ultrasonography was used. On average three to four waveforms was

obtained by setting the pulsed Doppler range gate across vessel. Ovarian Doppler indices were computed by computing Pulsatility index and Resistive index.

RESULTS

The data were divided into three equal groups on the basis of BMI. The age and duration of PCOS was also labelled as significant for data stratification. The p-value of each group was calculated. The ratio of the women with deranged ovarian artery indices was 84.8%. The percentage of women without deranged ovarian artery indices was 15.1%, Table 1.

Characteristics	Values
Total participants	225
Mean age (range)	17-45 years
Mean age	5.8-27years
Mean duration of PCOS	7-18.3 months
Mean Body index	21kg/m ² to 33 kg/m ²
Mean pulsatility index	0.70-3.32
Mean resistive index	0.03-0.87

Table 1: The calculated mean values

Deranged Ovarian artery Doppler indices	Percentage	Frequency
Patients with deranged Ovarian artery Doppler indices	191	84.8%
Patients without deranged Ovarian artery Doppler indicesTotal	34	15.1%
Total	225	100%

Table 2: Percentage and Frequency of deranged ovarian artery Doppler indices in reproductive age women

The reproductive aged women n= 225 ranging from 17-45 years presented with PCOS at the hospital was included in the study. The resistive and pulsatility index below or above the cut-off value was marked as deranged. The calculated mean age was 5.8 -27years. The means duration of PCOS calculated as 7-18.3 months. The mean body mass index of the women was between 21kg/m² to 33 kg/m². The means of pulsatility index was ranged between 0.70-3.32, while mean RI was between 0.03-0.87. On the basis of the subgroups created while considering age, body mass index and duration of the PCOS, the deranged ovarian artery indices frequency fluctuates significantly. Above table showed that out of 225 patients with PCOS, 191 have the deranged ovarian artery Doppler indices. The p-value of BMI group was 0.944, the group classified on basis of duration of PCOS was 0.931 and 0.995 of the data stratified on the basis of age. The prevalence of the deranged ovarian artery doppler indices is higher in the female of BMI group 30-34(kg/m²). While its prevalence is 85.7% in the women of BMI group 20-25(kg/m²). The women of the 25-30

(kg/m²) has 82.6% prevalence. The average duration of PCOS was observed to be 19–30 months in the 85.9% patients while it was 6–18 months in 85.5% patients. The prevalence of deranged ovarian artery doppler indices was higher in the women of age group 18–29 years, while it was 85.2% in the women of age group 30–40 years. The p-value less than 0.5 is normally considered significant. The calculated p-value of the different subgroups i.e BMI, duration of PCOS and age was not statistically significant as shown in the table 3. The frequency of the deranged ovarian artery doppler indices in the different subgroups was not statistically significant. There was no statistically significant difference was observed in deranged ovarian artery doppler indices frequency across the different subgroups.

Subgroups	Number	Ovarian artery deranged Doppler indices	P-value
BMI (kg/m²)			
20-25(kg/m ²)	63	54 (85.7%)	0.944
25-30(kg/m ²)	75	62 (82.6%)	
30-34(kg/m ²)	86	76 (88.3%)	
Duration of PCOS			
6-18 months	111	95 (85.5%)	0.931
19-30 months	114	98 (85.9%)	
Age (years)			
18-29 years	191	163 (85.3%)	0.995
30-40 years	34	24 (85.2%)	

Table 3: Prevalence of ovarian artery deranged Doppler indices

DISCUSSION

PCOS is complex endocrine disorder of the reproductive age women. It is characterized by ovarian dysfunctions [11–12]. The gold standard diagnostic tool for PCOS is transvaginal Doppler ultrasound. It not only helps to assess uterine and ovarian blood flow changes in normal state but also in menstrual state. In United States the PCOS has affected 4–5 million women of the reproductive age. Its prevalence is 6.6%. In the present study the frequency of the women having PCOS with deranged ovarian artery Doppler indices is 85%. The other 15% women diagnosed with PCOS don't have the deranged ovarian artery doppler indices. Artani et al reported the study similar to ours. The mean calculated age was 27–5 years. Wahab et al also conducted the quasi-experimental study on 35 patients having history of PCOS and showed that the mean age was 27.2–4.8 years [13–14]. The study conducted by Akram et al is comparable to our study with mean age of 27 – 4.9 years. The 85% of women having BMI between 20–25 kg/m² have deranged ovarian artery indices. The 82% of women having BMI ranging between 25–30 kg/m² have deranged ovarian artery Doppler indices. While 76% women has deranged ovarian artery indices with the BMI ranging between 30–34

kg/m². The duration of PCOS was between 6–18 months in 95% of women. While 98% having the PCOS ranging between 19–30 months. The mean age calculated by Usmani et al was 28–4.2 years. Chaudhari et al and Kumar et al also observed the mean duration of PCOS to be 28 – 7.6 years and 29 – 6.4 years respectively [15–16]. The mean of body mass index of 225 women with PCOS was 27 – 4 Kg/m². The means BMI of our patients is comparable to the mean BMI calculated by Akram et al and Qazi et al that is (27.6 – 5.7 Kg/m²) and (26.5 – 5.1 Kg/m²) respectively. The mean pulsatility index of present study is 3.32 – 0.70. The mean RI is 0.90 – 0.05. Out of the 225 patients followed for the study, the of deranged ovarian artery indices was observed in 84.8%. Bano et al conducted the similar study and the results of PI and RI are comparable to present study PI and RI, that is 3.89 – 0.76 and 0.93 – 0.10 respectively [17–18]. Noumana et al. designs the clinical study in which they included 140 patients out of which 70 was diagnosed with PCOS history, the mean RI value was 0.733 and mean PI value was 1. 6303. there were 43.5% patient of PCOS in the age group ranging from 15–25 while 61.8% patients of PCOS in the agr group 26–35. The age group 36–45 has lowest number of PCOS patients with the 42.9%. In a study conducted by battaglia et al. it was indicated that the women diagnosed with PCOS has decreased RI and increased PI. The result of present study is also in line with the results of the study conducted by Maciolek-Blewniewska et al. The mean PI (3.21 – 0.54) and mean resistive index (0.90 – 0.06) they reported are comparable to our study [19]. Our results are in line with the study conducted by Aleem et al. who conducted study on 40 patients with confirmed PCOS and 50 control patients reported similar PI and RI (3.34 – 0.18), (0.86 – 0.02) respectively in the 88% of women with PCOS [20–21]. The deranged ovarian artery Doppler indices play a putative role in diagnosis of PCOS in suspected patients. Our study not only establish the strong connection between deranged ovarian artery Doppler indices and PCOS, but also provide with the percentage frequency of ovarian artery deranged in PCOS women different subgroups created while considering the BMI, age and duration of PCOS.

CONCLUSION

This cross-sectional study provided the frequency of the deranged ovarian artery Doppler indices in women with PCOS. The frequency of patients with PCOs and deranged ovarian blood flow is 84%. Ovarian Doppler study has a putative role in diagnosis of PCOS suspected patients. RI and PI values provided an insight into pathophysiological state of affected ovary. For further elaboration of diagnostic role of deranged ovarian artery indices in

suspected PCOS patients, a cross-sectional study with the control group is highly suggested. Ovarian artery Doppler can help differentiate patients with PCOS from those who don't have PCOS and therefore the association between the Doppler induces and PCOS can be established by such analysis

REFERENCES

- [1] Sirmans SM, Pate KA. Epidemiology, diagnosis, and management of polycystic ovary syndrome. *Clinical epidemiology*. 2014; 6:1.doi.org/10.2147/CLEP.S37559
- [2] Solomon CG. The epidemiology of polycystic ovary syndrome: prevalence and associated disease risks. *Endocrinology and metabolism clinics of North America*. 1999 Jun; 28(2):247-63. [doi.org/10.1016/S0889-8529\(05\)70069-4](https://doi.org/10.1016/S0889-8529(05)70069-4)
- [3] Goodarzi MO, Dumesic DA, Chazenbalk G, Azziz R. Polycystic ovary syndrome: etiology, pathogenesis and diagnosis. *Nature reviews endocrinology*. 2011 Apr; 7(4):219-31. doi.org/10.1038/nrendo.2010.217
- [4] Dhingra D, Prateek S, Sinha R, Agarwal Y. Doppler flow velocities of uterine and ovarian arteries & hormonal patterns in patients with Polycystic Ovary Syndrome (PCOS). *International Journal of Healthcare and Biomedical Research*. 2017 Jul; 5(04):48-57.
- [5] Goodman NF, Cobin RH, Futterweit W, Glueck JS, Legro RS, Carmina E. American Association of Clinical Endocrinologists, American College of Endocrinology, and Androgen Excess and PCOS Society disease state clinical review: guide to the best practices in the evaluation and treatment of polycystic ovary syndrome-part 2. *Endocrine Practice*. 2015 Dec; 21(12):1415-26. doi.org/10.4158/EPI15748.DSCPT2
- [6] Hart R, Hickey M, Franks S. Definitions, prevalence and symptoms of polycystic ovaries and polycystic ovary syndrome. *Best Practice & Research Clinical Obstetrics & Gynaecology*. 2004 Oct; 18(5):671-83. doi.org/10.1016/j.bpobgyn.2004.05.001
- [7] Bano A. Diagnosis of Polycystic Ovarian Syndrome on Doppler Based Resistive Index and Pulsatility Index. *Journal of Rawalpindi Medical College*. 2016 Dec; 20(4):305-8.
- [8] Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, et al. Diagnosis and treatment of polycystic ovary syndrome: An Endocrine Society clinical practice guideline. *The Journal of Clinical Endocrinology & Metabolism*. 2013 Dec; 98(12):4565-92. doi.org/10.1210/jc.2013-2350
- [9] Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). *Human reproduction*. 2004 Jan; 19(1):41-7. doi.org/10.1093/humrep/deh098
- [10] Dokras A. Heart health in polycystic ovary syndrome: time to act on the data. *Fertility and Sterility*. 2022 May 1;117(5):885-6. doi.org/10.1016/j.fertnstert.2022.03.014
- [11] Giri A, Joshi A, Shrestha S, Chaudhary A. Metabolic Syndrome among Patients with Polycystic Ovarian Syndrome Presenting to a Tertiary Care Hospital: A Descriptive Cross-Sectional Study. *Journal of the Nepal Medical Association*. 2022 Feb; 60(246). doi.org/10.31729/jnma.7221
- [12] Kovacs GT, Fauser B, Legro RS, editors. *Polycystic ovary syndrome*. Cambridge University Press; 2022 May 31. doi.org/10.1017/9781108989831
- [13] Vrtacnik-Bokal E, Meden-Vrtovec H. Utero-ovarian arterial blood flow and hormonal profile in patients with polycystic ovary syndrome. *Human reproduction (Oxford, England)*. 1998 Apr; 13(4):815-21. doi.org/10.1093/humrep/13.4.815
- [14] Artini PG, Di Berardino OM, Simi G, Papini F, Ruggiero M, Monteleone P, et al. Best methods for identification and treatment of PCOS. *Minerva ginecologica*. 2010 Feb; 62(1):33.
- [15] Akram M, Roohi N. Endocrine correlates of polycystic ovary syndrome in Pakistani women. *Journal of the College of Physicians and Surgeons Pakistan*. 2015 Jan 1;25(1):22-6.
- [16] Bano A. Diagnosis of Polycystic Ovarian Syndrome on Doppler Based Resistive Index and Pulsatility Index. *Journal of Rawalpindi Medical College*. 2016 Dec; 20(4):305-8.
- [17] Wahab S, Karim R. Role of Metformin in Polycystic Ovarian Syndrome. *JPMI: Journal of Postgraduate Medical Institute*. 2013 Apr; 27(2).
- [18] Usmani A, Rehman R, Akhtar Z. Association of Body Mass Index and Dietary Habits with Ovarian and Uterine Morphology with Subfertile Polycystic Ovarian Syndrome. *JPMI: Journal of Postgraduate Medical Institute*. 2014 Apr; 28(2).
- [19] Maciołek-Blewniewska G, Kozarzewski M, Szpakowski M, Pertyński T, Nowak M. The evaluation of blood flow in uterine arteries in girls with polycystic ovary syndrome by transvaginal color Doppler ultrasonography. *Ginekologia polska*. 1999 May; 70(5):412-7.
- [20] Aleem FA, Predanic M. Transvaginal color Doppler determination of the ovarian and uterine blood flow

characteristics in polycystic ovary disease. Fertility and sterility. 1996 Mar; 65(3):510-6. [doi.org/10.1016/S0015-0282\(16\)58145-X](https://doi.org/10.1016/S0015-0282(16)58145-X)

- [21] Qazi II, Qazi AT, Ijaz F, Jawed S, Aftab RK, Qazi SR. Relationship of obesity with insulin resistance in polycystic ovarian syndrome. Pakistan Journal of Physiology. 2018 Aug; 14(3):46-9



Original Article

Incidental Dural Tears in Lumbar Decompressive Surgery: Incidence, Causes, Treatment, Results

Naeem Ul Haq¹, Inayat Shah¹, Musawer Khan¹¹Department of Neurosurgery, MTI Mardan Medical Complex, Bacha Khan Medical Collage, Mardan, KPK, Pakistan

ARTICLE INFO

Key Words:

Spinal Surgery, Dural Tear, Cerebrospinal Fluid Seepage, Durotomy, Herniation

How to Cite:

Haq, N. U. . . . , Shah, I., & Khan, M. (2022). Incidental Dural Tears in Lumbar Decompressive Surgery: Incidence, Causes, Treatment, Results: Incidental Dural Tears in Lumbar Decompressive Surgery. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.510>

*Corresponding Author:

Inayat Shah
 Department of Neurosurgery, MTI Mardan Medical Complex, Bacha Khan Medical Collage, Mardan, KPK, Pakistan
dr.inayatshahgmail.com

Received Date: 27th May, 2022
 Published Date: 20th June, 2022
 Acceptance Date: 30th June, 2022

ABSTRACT

Durotomy (Incidental dural tears or ID) is a very rarely occurring disorder when decompressive surgery (spinal surgery) of the patients takes place. This disorder has severe effects on patients. During different surgeries of the spinal cord, the chances of this durotomy vary greatly. **Objective:** The main objective of this research work is to evaluate the main reasons for the incidence of this durotomy disease. During different surgeries of the spinal cord surgeries (decompressive and compressive) within the different regions, many factors play their role in the initiation of this durotomy disease. It is the target of this work to find the initiation factors of the disease so that effective methods of treatment can also find out. **Methods:** It was a retrospective study with a statistical approach. This study was conducted in Neurosurgery unit, Mardan medical complex / Bacha Khan medical college, Mardan for the Duration of one year August 2020 to July 2021. To proceed with this study, 30 patients were selected with posterolateral and posterior compressive and decompressive surgeries within the different regions of the spinal cord. The patients were randomly selected from December 2020 to December 2021. **Results:** The incidence of this durotomy disease was investigated within all groups and the probability of this disease was only 12.65%. The occurrence of this disease also depends upon the type of surgery. Patients suffering from spinal trauma, stenosis of the spinal, different tumors, and vertebral disc herniation had exaggerating role in the incidence of durotomy in patients having some spinal surgery. **Conclusion:** The durotomy disease should be considered a serious issue with a number of other complications. For the treatment of this disease, prevention is the best method and to know about the complications is important because all of the factors involved in the incidence of durotomy should be considered while performing any kind of surgery.

INTRODUCTION

An unexpected tear of the dura mater during surgery or other invasive extradural operations such as epidural injections is known as an incidental durotomy. There may be some dura flaws that do not repair the following myelography. Durotomies are unfavorable yet reasonably common in spine surgery, whether they are pre-existing or arise after surgery [1]. The prevalence of inadvertent durotomy varies depending on the series examined and the type of surgical treatment performed. Different factors during spinal surgery play their role in the incidence of this durotomy disease. In this durotomy, multiple complications arise that may prove seriously problematic

[2]. The occurrence of an inadvertent durotomy during spinal decompression surgery is a rather uncommon complication that can have serious consequences. The rate of incidental durotomies varies greatly between writers (1-16 %) and is dependent on the nature and critical of the vertebral column surgeries in general. The majority of writers link a higher rate of dural tears to an increased rate of retreatments respectively with fibrosis of epidural and progressive spinal degrading alterations with a pale ligament in older patients having surgery. In recent decades, the frequency and complexity of spinal surgeries have increased, resulting in a higher occurrence of dural

tears. Overburdened nerve root tension during the elimination of large disc extrusions and replacement of spinal insertions is one of the primary intraoperative mechanisms [3,4]. Whenever dural injury develops, it is usually discovered intraoperatively, and initial treatment with recognized surgical protocols/procedures is required. Unfortunately, not all dural rips can be properly identified and healed. Inadvertent pin-hole-type durotomies may go unnoticed during surgery, even by skilled surgeons [5,6]. If a defect is not recognized or closed adequately, the patient may develop a headache that includes vomiting, fever, nausea, sleeping disorder, laziness and diplopia due to VI cranial nerve paresis, photophobia, tinnitus, and other symptoms. Cerebrospinal liquid/fluid (CSF) leaking as a result of dural rips can result in Cerebrospinal fluid formation of fistula, pseudomeningocele, arachnoiditis, and meningitis, and abscess epidural, among other complications [7,8]. The goal of this study was to assess the initiation of pre durotomies during various types of spinal decompressive, compressive, and reconstructive surgical protocols/procedures, as well as to identify the most common causes of incidental dural tears (durotomies), treatment facilities, and their impact on early and late outcomes. Different research groups are trying to find the most appropriate method for the identification of the factors involved in the initiation of this disease [9,10].

METHODS

This study was conducted in Neurosurgery unit, Mardan medical complex / Bacha khan medical college, Mardan for the Duration of one year August 2020 to July 2021. In this statistical study, 30 patients were selected with different spinal surgeries of posterolateral and posterior surgeries (with compressive, decompressive, and reconstructive surgeries). All the patients had a single time or multiple time surgeries. Patients were selected from December 2020 to December 2021. Some patients were kept in the control group while another one was those who have vertebral column surgeries to observe the changes in the physiology of these patients and to identify the effects of surgeries at different durations. Patients were kept in different groups on the basis of different spinal cord surgeries done in their life. Some of the patients undergo surgeries again in a spinal reconstruction manner. In the cases diagnosed with the initiation of durotomy, efforts were made to identify the possible reason for their disease initiation. Cerebrospinal fluid seepage occurs within these organisms. Patients were diagnosed with different symptoms such as headache, irritation of meningeal, neurological defects, fluid secretion from the sub cuticle, and a number of many other complicated problems were

also noted. When magnetic resonance imaging (MRI) of these patients was done after the symptom appearance, pseudo meningocele was identified. MRI was considered a method for the identification of this pseudo meningocele. In one patient CT myelography was diagnosed. In about 0.2 % of people having a spinal cord or vertebral column surgery, no observable scenes were identified. Among these some patients were retreated with surgery to prevent the seepage of CSF through wounded sites. To obtain the final results statistical methods were employed to calculate the probability value and to compare different patients, Student fisher test and t-test was used with average p-value less than 0.05 was considered significant.

RESULTS

The percentage incidence of IDs in the studied group is 13%. The incidences vary by varying surgical procedure. The higher incidence was seen in the group with cases of re-operation. It was observed to be 28%. The incidence of IDs in the cases of spinal traumatic injury was 20%. The incidence was seemed to be 11% in the patients with the degenerative spinal stenosis (Table 1). The patients with reconstructive spinal procedure has the 9% incidence of IDs. The postoperative functional status was observed to be worst in the patients experiencing re-operation.

Degenerative spine surgery indication	Total	Male	Female	Mean Age	Incidence
Patients with disc herniation	13	7	7	43.28	8%
Patients with degenerative spinal stenosis	8	3	4	51.3	11%
Spine trauma	4	3	1	41.3	20%
Reoperative surgery	3	1	2	48.7	28%
Tumor	2	1	1	67.6	10%
Total number	30	15	15	47	13%

Table 1: Percentage Incidence of IDs and Mean Age of the Patients
The higher VAS rates were observed in the patients with the IDs, the mean of those three patients who follow for one month was 4 while, the mean of the VAS-rates in the patients without the IDs was seemed to be 2. The results remain similar, even if the follow up increased to six or 24 months. The mean ODI of the patients was calculated for evaluation of the functional status. The 2 patients with ID were followed up for one year and the mean ODI calculated was 32%. The calculated ODI of the patients without ID was 25% (Table 2).

Procedures (surgical)	N	Percentage ID incidence
Decompression	19	11%
Decompression and fusion w/o instrumentation	2	9%
Decompression and fusion with instrumentation	6	9%
Reoperative spinal surgery	3	28%
Total number	30	13%

Table 2: Incidence of ID in the respective Surgical Procedures

DISCUSSION

The one of the most common complication of spinal surgery is incidental durotomy (ID). It has high percentage incidence in the patients who underwent spine surgery. Many postoperative complication have seen in the patients with spinal surgery and these includes arachnoiditis and fistulas. The range of reported ID incidence vary from one to sixteen percent. The health care costs are raising because of the IDs. It is also associated with poor patient's outcome [11]. The spinal procedure and its type opt for the surgery generally control the incidence of dural tears in the patients. In a study conducted by Hisatoshi et al., the revision surgery and corrective verbal osteotomy were observed to be the independent risk factors for IDs. The revision surgery has the major contribution and strong association with the IDs. The study conducted by Hannallah showed that the highest risk of IDs are associated with the cases of ossification of posterior longitudinal ligament (OPLL)[12,13]. For repairing the suture are used for primary closure. For the healing purposes the ventriculo-peritoneal shunt procedure is used. The surgeon recommend the longer bed rest period for the patients with the ID. Postoperative complications are higher in the patients with the longer bed rest period [14]. In a study conducted by Khan et al., the ID was reported in the 10% who underwent spine surgery. Different risk factors are associated with the postoperative ID. The percentage contribution of such factors in causing ID can be accessed through multivariate analysis before the spine surgery. The invasive surgical methods and instruments have raised the number of IDs in the patients [15]. Wange et al., study depicted that 14% patients who underwent lumbar spine surgery have the IDs complication. The research conducted by Godkin and Laska8 also showed that almost 16% patients have the complaint of post-operative IDs. Hence ID are proved to be highly associated with the spinal surgery [16]. These are highly observed in the old age patients as compared to the younger patients. The incidence of ID in the patient undergoing the microdiscectomy and cervical surgery procedures is low as compared to pateints with re-interventions. The results of the study conducted by Morghan-Hough represented that the percentage of IDs in the patients with the primary intervention was found to be 5% while it was 14% in the patients with the re-interventions. Out of the 30 patients included in the present study the incidence of IDs is 12% in the patients undergoing spinal surgery. The one patient was also observed with pseudo meningocele. The incidence of IDs is higher about 28% in the patients undergoing re-

interventions. The patients undergoing microdiscectomy have the lowest incidence of IDs about 8% while, other with the spinal trauma has the incidence of 20% [17,18]. The cerebrospinal fluid CSF leakage symptoms are representative of the IDs in the patients. These can diagnosed while surgery or in the postoperative period (after surgery). The risk of ID development is higher in the cases where surgeons manipulate the dural sacs or nerve roots. These manipulations are proved to be highly dangerous in the patients with the spinal stenosis and re-interventions. The tear can be repaired when the dural defects region is exposed to the surgeon. Small dural tears can also produce after the defective surgery in which the sharp bone particles left behind by negligence of surgeon. While recovering from the anesthesia the intradural pressure can cause CSF leakage or opening of arachnoid membrane that eventually convert the small dural tears into open ones [19,20]. CSF leakage is most common in the patients with IDs. Different procedure such as fascial graft and suture are used to immediately seal the CSF leakage. In most of the cases of surgery the IDs remain hidden or unattended. These leakages if remained undetected can lead to headache, dizziness and nausea. The CSF fistula formation and meningitis are commonly observed in the patients with the dural tears. CSF leakage are seemed to be fatal in rare cases [21]. Different studies were conducted on the postoperative patients with IDs. The Saxler et al., conducted the study based on 10-years post-operative follow up and concluded that the worse clinical results were seemed in the patients with the IDs. IDs also increased the risk for re-operations. Our results are comparable with the above studies, though the follow-up time of our study is one year [22].

CONCLUSION

The most serious and prevalent condition in the patients undergoing spinal surgery is dural tears. These raised the multiple unwanted consequences in the post-operative patients. The best way to treat this complication is prevention. For the better management and proper planning of the spinal surgical procedures the in-depth understanding of the underlying mechanism that caused inadvertent dural tears is necessary. The percentage IDs in the present study was observed to be 13% in the patients undergoing spinal surgery.

REFERENCES

- [1] Strömquist F, Sigmundsson FG, Strömquist B, Jönsson B, Karlsson MK. Incidental durotomy in degenerative lumbar spine surgery - a register study of 64,431 operations. *Spine J.* 2019 Apr;19(4):624-

630. doi: 10.1016/j.spinee.2018.08.012.
- [2] Ishikura H, Ogihara S, Oka H, Maruyama T, Inanami H, Miyoshi K et al. Risk factors for incidental durotomy during posterior open spine surgery for degenerative diseases in adults: A multicenter observational study. *PLoS One*. 2017 Nov 30;12(11):e0188038. doi: 10.1371/journal.pone.0188038.
- [3] Longo UG, Loppini M, Romeo G, Maffulli N, Denaro V. Errors of level in spinal surgery: an evidence-based systematic review. *J Bone Joint Surg Br*. 2012 Nov;94(11):1546-50. doi: 10.1302/0301-620X.94B11.29553.
- [4] Choi G, Pophale CS, Patel B, Uniyal P. Endoscopic Spine Surgery. *J Korean Neurosurg Soc*. 2017 Sep;60(5):485-497. doi: 10.3340/jkns.2017.0203.004.
- [5] Haddad S, Millhouse PW, Maltenfort M, Restrepo C, Kepler CK, Vaccaro AR. Diagnosis and neurologic status as predictors of surgical site infection in primary cervical spinal surgery. *Spine J*. 2016 May;16(5):632-42. doi: 10.1016/j.spinee.2016.01.019.
- [6] Kamenova M, Leu S, Mariani L, Schaeren S, Soleman J. Management of Incidental Dural Tear During Lumbar Spine Surgery. To Suture or Not to Suture? *World Neurosurg*. 2016 Mar;87:455-62. doi: 10.1016/j.wneu.2015.11.045.
- [7] Guler UO, Yuksel S, Yakici S, Domingo-Sabat M, Pellise F, Pérez-Grueso FJ et al. Analysis of the reliability of surgeons' ability to differentiate between idiopathic and degenerative spinal deformity in adults radiologically. What descriptive parameters help them decide? *Eur Spine J*. 2016 Aug;25(8):2401-7. doi: 10.1007/s00586-015-4366-3.
- [8] Carl B, Bopp M, SaB B, Nimsy C. Microscope-Based Augmented Reality in Degenerative Spine Surgery: Initial Experience. *World Neurosurg*. 2019 Aug;128:e541-e551. doi: 10.1016/j.wneu.2019.04.192.
- [9] Strömqvist F, Sigmundsson FG, Strömqvist B, Jönsson B, Karlsson MK. Incidental durotomy in degenerative lumbar spine surgery - a register study of 64,431 operations. *Spine J*. 2019 Apr;19(4):624-630. doi: 10.1016/j.spinee.2018.08.012.
- [10] Adogwa O, Huang MI, Thompson PM, Darlington T, Cheng JS, Gokaslan ZL et al. No difference in postoperative complications, pain, and functional outcomes up to 2 years after incidental durotomy in lumbar spinal fusion: a prospective, multi-institutional, propensity-matched analysis of 1,741 patients. *The Spine Journal*. 2014 Sep 1;14(9):1828-34. doi.org/10.1016/j.spinee.2013.10.023.
- [11] Ulrich NH, Burgstaller JM, Brunner F, Porchet F, Farshad M, Pichierri G et al. The impact of incidental durotomy on the outcome of decompression surgery in degenerative lumbar spinal canal stenosis: analysis of the Lumbar Spinal Outcome Study (LSOS) data—a Swiss prospective multi-center cohort study. *BMC Musculoskelet Disord*. 2016 Apr 18;17:170. doi: 10.1186/s12891-016-1022-y.
- [12] Du JY, Aichmair A, Kueper J, Lam C, Nguyen JT, Cammisa FP et al. Incidental durotomy during spinal surgery: a multivariate analysis for risk factors. *Spine (Phila Pa 1976)*. 2014 Oct 15;39(22):E1339-45. doi: 10.1097/BRS.0000000000000559.
- [13] Desai A, Ball PA, Bekelis K, Lurie JD, Mirza SK, Tosteson TD et al. Outcomes after incidental durotomy during first-time lumbar discectomy. *J Neurosurg Spine*. 2011 May;14(5):647-53. doi: 10.3171/2011.1.SPINE10426.
- [14] Gautschi OP, Stienen MN, Smoll NR, Corniola MV, Tessitore E, Schaller K. Incidental durotomy in lumbar spine surgery—a three-nation survey to evaluate its management. *Acta Neurochir (Wien)*. 2014 Sep;156(9):1813-20. doi: 10.1007/s00701-014-2177-7.
- [15] Herren C, Sobottke R, Mannion AF, Zweig T, Munting E, Otten P et al. Incidental durotomy in decompression for lumbar spinal stenosis: incidence, risk factors and effect on outcomes in the Spine Tango registry. *Eur Spine J*. 2017 Oct;26(10):2483-2495. doi: 10.1007/s00586-017-5197-1.
- [16] Hershman S, Cuellar VG, Bendo JA. Delayed presentation of incidental durotomy. *Bull Hosp Jt Dis (2013)*. 2013 Jul;71(3):231-4.
- [17] Bosacco SJ, Gardner MJ, Guille JT. Evaluation and treatment of dural tears in lumbar spine surgery: a review. *Clin Orthop Relat Res*. 2001 Aug;(389):238-47. doi: 10.1097/00003086-200108000-00033.
- [18] Cain JE Jr, Lauerman WC, Rosenthal HG, Broom MJ, Jacobs RR. The histomorphologic sequence of dural repair. Observations in the canine model. *Spine (Phila Pa 1976)*. 1991 Aug;16(8 Suppl):S319-23.
- [19] Cammisa FP Jr, Girardi FP, Sangani PK, Parvataneni HK, Cadag S, Sandhu HS. Incidental durotomy in spine surgery. *Spine (Phila Pa 1976)*. 2000 Oct 15;25(20):2663-7. doi: 10.1097/00007632-200010150-00019.
- [20] Eismont FJ, Wiesel SW, Rothman RH. Treatment of dural tears associated with spinal surgery. *J Bone Joint Surg Am*. 1981 Sep;63(7):1132-6.
- [21] Goodkin R, Laska LL. Unintended "incidental" durotomy during surgery of the lumbar spine: medicolegal implications. *Surgical neurology*. 1995 Jan 1;43(1):4-14. doi.org/10.1016/0090-3019(95)80031-B.

- [22] Wang JC, Bohlman HH, Riew KD. Dural tears secondary to operations on the lumbar spine. Management and results after a two-year-minimum follow-up of eighty-eight patients. *J Bone Joint Surg Am.* 1998 Dec;80(12):1728-32. doi: 10.2106/00004623-199812000-00002



Original Article

Leukocytosis and thrombocytopenia in pre-partum, post-partum cases and non-pregnant women

Afia Akhter¹, Fatima Saleem¹, Bushra Mubarak¹, Kainat Waheed¹, Iqra Munir¹, Marya Saadullah¹, Mian Muhammad Jehanzeb²¹University Institute of Medical Laboratory Sciences, The University of Lahore, Pakistan²Bahria Town International Hospital

ARTICLE INFO

Key Words:

Leukocytosis, Thrombocytopenia, Anemia, Pre-partum, Post-partum

How to Cite:

Akhter, A., Saleem, F., Jehanzeb, M. M., Mubarak, B., Waheed, K., Munir, I., Saadullah, M., & Anwar, M. (2022). Leukocytosis and thrombocytopenia in pre-partum, post-partum cases and non-pregnant women: Leukocytosis and thrombocytopenia in pre-partum, post-partum cases and non-pregnant women. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.551>

*Corresponding Author:

Bushra Mubarak
University Institute of Medical Laboratory Sciences,
The University of Lahore, Pakistan
Bushra.mubarak@yahoo.com

Received Date: 13th June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Thrombocytopenia is a serious condition that may cause fatal outcomes for both mother and infant, whereas leukocytosis is an essential mediator of the inflammatory process and a marker for infection during pregnancy. **Objective:** The aim of the study was to compare the frequency of thrombocytopenia and leukocytosis among pre-partum, post-partum cases and non-pregnant healthy controls. **Methods:** Total 600 samples were collected and categorized into three groups, pre-partum, post-partum and non-pregnant 200 in each. From selected groups 3-5 ml blood was collected in EDTA tube and Sodium Citrate vial. Platelets, WBCs, RBCs and Hemoglobin levels were analyzed on Sysmex KX-21. PT and APTT of all samples was performed manually. **Results:** Leukocytosis was detected in 60% pre-partum and 64% post-partum, there was not statistically significant difference ($p=0.596$). In pregnant and non-pregnant, there was significant difference statistically ($p<0.05$). Thrombocytopenia was detected in 11% pre-partum, 13% post-partum cases and there was no statistical difference ($p>0.05$). There was statistical difference in frequency of thrombocytopenia between pregnant and non-pregnant women ($p=0.03$). There was no statistically significant difference in PT and APTT between pre-partum and post-partum ($p>0.05$). APTT were significantly different between pregnant and non-pregnant cases ($p<0.05$). **Conclusion:** The study concluded that leukocytosis and thrombocytopenia was found in higher frequency among pregnant women than non-pregnant women but there was no significant difference in frequency of leukocytosis and thrombocytopenia between pre-partum and post-partum women.

INTRODUCTION

Thrombocytopenia is the deficiency of thrombocytes in circulatory blood and when it goes down from the certain level [1]. The amount of platelet (PLT) which are low than $<150,000/L$ during gestation period is known as gestational thrombocytopenia [2]. In previous 20 years, thrombocytopenia is most commonly diagnosed in pregnancy after anemia in hematological disorder [3]. During pregnancy thrombocytopenia is normally happened but there are less chances of connection with neonatal [4]. But there are chances of complications due to negligence of antenatal care [5]. During pregnancy, the platelets count is usually decrease due to the physiological change and

many other factors such as hem dilution, plasma volume, clearance of thrombocytes, demolition of thrombocytes in placenta, fluctuation in the activity of factor VIII, production of antibodies (Ab) against platelets, fluctuation in placental blood flow as well increase the gravidity of uterus. The other reasons in which platelet count is low because low production of platelet and the demolition of platelets and splenomegaly [6,7]. In second or third pregnancy thrombocytopenia is commonly occurred [8]. It can be inherited or associated with other diseases in which coagulation factors are disrupted. Low platelets delay the activation and inhibition of clotting factors which are

involve in formation of clot. Spontaneous bleeding occurs when there is severe thrombocytopenia. It may be reversible after pregnancy [9]. The possible etiology of thrombocytopenia in pregnancy is Thrombotic microangiopathy (TMA) [6,10]. Thrombocytopenia is mostly reported in mid half of second trimester and the platelet count could be greater than $100 \times 10^9/L$ and there is no fluctuation in active partial thromboplastin time (APTT) and prothrombin time (PT) which affects the hemostasis [11]. In Sudan, there are 15.5% women affected with gestational thrombocytopenia [12]. In Lahore, there are 16.5% of women are affected with thrombocytopenia [13]. Leukocytosis is an increase in white blood cells above their normal range. Leukocytosis is an essential mediator in the inflammatory process and simple marker for infection during pregnancy [14]. Leukocytosis during early days of pregnancy can be the sign of disease that will occur later in pregnancy. Leukocytosis occurs, if the female is suffering from pre-eclampsia that is the state of hypertension during pregnancy and goes away after delivery [15]. Leukocytosis may be a result of fertility treatments [16]. During 3rd trimester, immunity of females often reduces that causes immunological suppression that results in leukocytosis [17]. Antenatal Corticosteroids are given during pregnancy to females who are at risk of giving a preterm delivery. Corticosteroids administration during pregnancy causes leukocytosis [18]. Leukocytosis during pregnancy may occur because of the physiological stress that encourage by the gestation phase [19]. Neutrophils can be the reason that causes leukocytosis during gestation phase. Neutrophil count is almost double during gestation [20]. In Peshawar, there are 68% cases of leukocytosis [17]. In Israel, there are 0.94% cases of leukocytosis [14]. Gestational thrombocytopenia is mainly asymptomatic except bleeding which occurs in second half of pregnancy [21]. Fever, nausea, vomiting, and pain anorexia are some of the common symptoms of leukocytosis [22]. In case of gastrointestinal thrombocytopenia, before the birth prednisone's used in a daily dose for 10 days to raise the platelet count and avoid from obstetrical and anesthetic danger [21]. While using antibiotics the physiological leukocytosis should always be kept in mind to minimize its unnecessary use during postpartum period. In 2006, Dapper DV et al concluded that the female in the 1st trimester had the highest leukocyte count [23]. In 2010, Akmal M et al concluded that the severity of thrombocytopenia is proportional to severity of hypertensive disorders [24]. In 2013, Tazur T et al performed a study that 0.94% cases had leukocytosis in Israel [25]. In 2015, Enawgaw AF et al concluded that the females lived in rural area had higher rate of

thrombocytopenia [5]. The main objectives of the study were to compare the frequency of leukocytosis and thrombocytopenia among pre-partum and post-partum and control group.

METHODS

It was a cross-sectional study conducted from November, 2020 to March, 2020. The data were processed in Sir Ganga Ram Hospital, Lahore. The total numbers of samples taken were 600. They were divided into three categories, Group 1 200 pre-partum samples, Group 2 included 200 samples of postpartum & 200 sample (group 3) of non-Pregnant women as a control. From each pregnant and non-pregnant woman, 3-5 ml blood was collected from median cubital vein through venipuncture technique and dispense into Ethylene-diamine tetra-acetic acid/EDTA tube and Sodium Citrate vial. Pregnant women of age 18 to 45 years were enrolled and non-pregnant women with the same age group were considered as control in the study. Pregnant and Non-Pregnant women with confirmed infection or other autoimmune diseases were excluded from the study. The test were performed on automated hematology analyzer (Sysmex KX-21). Data were analyzed using Statistical Package for Social Sciences (SPSS) version 25. Mean and standard deviation was calculated for quantitative variable like age, WBC count, Hb level etc. Frequency and percentage were given for qualitative variables such as level of leukocytosis, anemia etc. Chi-square test was applied for association of qualitative variable between groups. Paired t-test was used for difference of qualitative variables between pre-partum and post-partum cases. p-value less than 0.05 was considered statistically significant.

RESULTS

Table 1 shows no significant difference ($p=0.650$) when the mean value of Hb compared between pregnant ($10.26 \pm 1.8g/L$) and non-pregnant ($10.88 \pm 2.2g/L$) women. No significant difference ($p=0.571$) was found in the mean level of WBCs compared between pregnant ($11.95 \pm 5.8 \times 10^9/L$) and non-pregnant ($10.08 \pm 4.4 \times 10^9/L$) women. There was statistically significant difference ($p=0.001$) in mean level of neutrophil and lymphocyte between pregnant and non-pregnant women ($65.94 \pm 21.0/59.65 \pm 19.4\%$) and ($26.18 \pm 19.2/31.45 \pm 19.1\%$) respectively. There was not statistically significant difference ($p=0.103$) in mean level of monocyte between pregnant and non-pregnant ($5.13 \pm 6.2/5.74 \pm 2.4\%$). The mean level of eosinophil between pregnant ($2.83 \pm 2.3\%$) and non-pregnant ($2.99 \pm 1.6\%$) was statistically significant different ($p<0.05$). The mean level of Hb showed statistically different ($p=0.003$) between pre-partum ($10.26 \pm 2.2g/L$) and post-partum ($10.34 \pm 1.7g/L$).

The mean level of WBC between pre-partum ($11.95 \pm 5.8 \times 10^9/L$) and post-partum ($12.25 \pm 4.8 \times 10^9/L$) was statistically different ($p=0.001$). There was statistically significant difference ($p=0.002$) in neutrophil count between pre-partum and post-partum ($65.94 \pm 21.0/73.85 \pm 13.2\%$). The mean level of lymphocyte between pre-partum ($26.18 \pm 19.2\%$) and post-partum ($19.44 \pm 11.1\%$) was statistically different ($p<0.05$). Monocytes and eosinophil count showed no significant difference ($p>0.05$) when compared between pre-partum and post-partum groups.

Parameters	Pre-partum group n=200	Post-partum group n=200	Control group n=200	P ₁ - Value	P ₂ - Value
Hb (g/L)	10.26± 1.8	10.34± 1.7	10.88± 2.2	0.003	0.650
WBC ($\times 10^9/L$)	11.95± 5.8	12.25± 4.8	10.08± 4.4	<0.001	0.571
Neutrophils (%)	65.94± 21.0	73.85± 13.2	59.65± 19.4	0.002	<0.001
Lymphocytes (%)	26.18± 19.2	19.47± 11.2	31.45± 19.1	0.006	<0.000
Monocytes (%)	5.13± 6.2	4.32± 3.10	5.74± 2.4	0.197	0.103
Eosinophil (%)	2.83± 2.3	2.25± 1.6	2.99± 1.6	0.436	0.005

Table 1: Comparison of Hematological parameters between pre-partum, post-partum and non-pregnant women.

P₁- Group 1 and Group 2

P₂-Group 1 and Group 3

Table 2 shows no statistically significant difference in mean level of Platelets and PT between pregnant and non-pregnant women. The mean level of APTT between pregnant (33.00 ± 2.8 Sec) and non-pregnant (33.70 ± 2.3 Sec) was statistically significant difference ($p=0.008$). There was no statistically significant difference ($p>0.05$) in mean level of Platelet and APTT between pre-partum and post-partum groups. The mean level of PT between pre-partum (15.19 ± 2.0 Sec) and post-partum (14.96 ± 1.8 Sec) was statistically significant different ($p=0.039$).

Factors	Pre-partum group n=200	Post-partum group n=200	Control group n=200	P ₁ - Value	P ₂ - Value
Platelet (109/L)	285.99± 223.7	254.75± 107.6	273.25± 154.3	0.508	0.076
PT (Sec)	15.19± 2.0	14.96± 1.8	14.76± 2.0	0.039	0.250
APTT (Sec)	33.00± 2.8	33.70± 2.3	33.36± 2.3	0.163	0.008

Table 2: Coagulation Profile compared between, pre-partum, post-partum and non-pregnant Women

P₁- Group 1 and Group 2

P₂-Group 1 and Group

DISCUSSION

The current study was designed to find the frequency of thrombocytopenia and leukocytosis in pre-partum and post-partum cases in Ganga Ram Hospital. Thrombocytopenia is the common hematological disorder after anemia in pregnancy often mismanaged and under diagnosed. Gestational thrombocytopenia is directly associated with a higher occurrence of intrauterine growth

problems and delivery before estimated time and it may also be an important risk factor for mother and baby at the time of delivery. Thrombocytopenia can occur at any point of pregnancy. In this study, (11%) pre-partum women had thrombocytopenia, and 7% pre-partum females had high platelet count. Thirteen percent (13%) females had low platelet count in post-partum. This study is in agreement with a study conducted in India on 856 pregnant women and found 11.68% pregnant women with thrombocytopenic condition [1]. In Ethiopia, a total of 217 women were enrolled in a study and 8.8% thrombocytopenia was observed [5]. Bai P and his coworkers, reported thrombocytopenia in 6% pregnant women in Pakistan [26]. During third trimester of pregnancy, the prothrombin time remains same mostly but active partial thromboplastin time usually shortened mainly due to increase in factor VIII. It plays an important role in hemostasis. In this study, there was no statistically significant difference found in values of PT between pregnant women and controls and there was statistically significant difference between PT values of pre-partum and post-partum cases. While between the values of APTT in the cases and controls there was a significant difference and no statistically significant difference found in the values of APTT between pre-partum and post-partum women. Obeagu El et al performed study on hematological profile of pregnant and non-pregnant women of Abia State, Nigeria. The study showed significant changes ($p<0.05$) in mean value of WBCs, lymphocytes, monocytes and eosinophil of the pregnant women relative to non-pregnant women [27]. The current study, was not in agreement with Obeagu et al in term of WBCs and monocytes which showed non-significant difference between pregnant and non-pregnant women. But neutrophil lymphocytes and eosinophil showed a significant level of difference which was in agreement with Obeagu et al findings [27].

CONCLUSION

There was high frequency of leukocytosis and thrombocytopenia among pregnant women than non-pregnant women but there was no significant difference in frequency of leukocytosis and thrombocytopenia between pre-partum and post-partum. Among leukocytosis, neutrophilia was more common during pregnancy as compare to other types of white blood cells. Further follow-up studies on larger sample size should be performed to find out the exact cause and types of anemia, leukocytosis and thrombocytopenia.

REFERENCES

- [1] Pandey A, Singh R. Thrombocytopenia during pregnancy: an institutional based prospective study

- of one year. *International Journal of Research in Medical Sciences*. 2017 Aug; 5(8):3502. doi.org/10.18203/2320-6012.ijrms20173550
- [2] Aloizos S, Seretis C, Liakos N, Aravosita P, Mystakelli C, Kanna E, et al. HELLP syndrome: understanding and management of a pregnancy-specific disease. *J Obstet Gynaecol*. 2013 May; 33(4):331-7. doi: 10.3109/01443615.2013.775231.
- [3] Nisha S, Amita D, Uma S, Tripathi AK, Pushplata S. Prevalence and characterization of thrombocytopenia in pregnancy in Indian women. *Indian Journal of Hematology and Blood Transfusion*. 2012 Jun; 28(2):77-81. doi: 10.1007/s12288-011-0107-x.
- [4] Sinha AA, Moerdler S, Frait E, Tal A, Rahmani NE, Morrone K. Hematology/Oncology. In *Pediatric Board Study Guide 2020* (pp. 345-390). Springer, Cham. doi.org/10.1007/978-3-030-21267-4_10
- [5] Asrie F, Enawgaw B, Getaneh Z. Prevalence of thrombocytopenia among pregnant women attending antenatal care service at Gondar University Teaching Hospital in 2014, northwest Ethiopia. *Journal of Blood Medicine*. 2017 Jun; 8:61-66. doi: 10.2147/JBM.S136152.
- [6] Mangla A, Hamad H. Thrombocytopenia Pregnancy. *The Journal of Obstetrics and Gynecology*. 2019;13(2):217-229.
- [7] Arora M, Goyal L, Khutan H. Prevalence of thrombocytopenia during pregnancy and its effect on pregnancy and neonatal outcome. *Annals of International Medical and Dental Research*. 2019; 3(2):4. doi.org/10.4103/ijh.ijh_17_18
- [8] Cines DB, Levine LD. Thrombocytopenia in pregnancy. *Hematology 2014, the American Society of Hematology Education Program Book*. 2017 Dec; 2017(1):144-51. doi: 10.1182/blood-2017-05-781971.
- [9] Thanoon AM, Jalal SD. Thrombocytopenia in Iraqi Pregnant Women. *Journal of the Faculty of Medicine Baghdad*. 2011 Jul; 53(2):171-4. doi.org/10.32007/jfacmedbagdad.532864
- [10] Siddall J, Mat CG. Guideline for the management of Thrombocytopenia in pregnancy. Royal Berkshire NHS Foundation Trust. 2017; 8(3):165-36.
- [11] Ramström S, Rånby M, Lindahl TL. The role of platelets in blood coagulation—effects of platelet agonists and GPIIb/IIIa inhibitors studied by free oscillation rheometry. *Thrombosis Research*. 2002 Jan; 105(2):165-72. doi: 10.1016/s0049-3848(02)00005-1.
- [12] Mohamed AO, Hamza KM, Babker AM. Physiological changes in some hematological and coagulation profile among Sudanese healthy pregnant women. *International Journal of Medical Science and Public Health*. 2016 Mar; 5(3): 525-8. doi.org/10.5455/ijmsph.2016.30092015149
- [13] Ijaz T, Atif M, Ullah M, Arshad S, Ashraf S, Munir S, et al. Prevalence of Anemia and thrombocytopenia in pregnant females of Lahore. *Life Sciences International Journal*. 2016 Jan; 10(01):38-42.
- [14] Tzur T, Weintraub AY, Sergienko R, Sheiner E. Can leukocyte count during the first trimester of pregnancy predict later gestational complications? *Archives of gynecology and obstetrics*. 2013 Mar; 287(3):421-7. doi: 10.1007/s00404-012-2603-0
- [15] Kaur S, Khan S, Nigam A. Hematological profile and pregnancy: a review. *International Journal of Advances in Medicine*. 2014 Jul; 1(2):68-70. DOI: 10.5455/2349-3933.ijam20140804
- [16] Yankowitz J, Weiner CP. Blood transfusion for haemolytic disease as a cause of leukocytosis in the fetus. *Prenatal Diagnosis*. 1996 Aug; 16(8):719-22. doi: 10.1002/(SICI)1097-0223(199608)16:8<719: AID-PD934>3.0.CO;2-O.
- [17] Khan H, Masood A, Wazir AK. Physiological changes in individual leukocytes in pregnancy. *Annals of Abbasi Shaheed Hospital and Karachi Medical and Dental College*. 2017; 22(1):60-3.
- [18] Bauer ME, Price LK, MacEachern MP, Housey M, Langen ES, Bauer ST. Maternal leukocytosis after antenatal corticosteroid administration: a systematic review and meta-analysis. *Journal of Obstetrics and Gynaecology*. 2018 Feb; 38(2):210-216. doi: 10.1080/01443615.2017.1342614.
- [19] Chandra S, Tripathi AK, Mishra S, Amzarul M, Vaish AK. Physiological changes in hematological parameters during pregnancy. *Indian Journal of Hematology and Blood Transfusion*. 2012 Sep; 28(3):144-6. doi: 10.1007/s12288-012-0175-6.
- [20] Pitkin RM, Witte DL. Platelet and leukocyte counts in pregnancy. *JAMA*. 1979 Dec; 242(24): 2696-8. doi.org/10.1001/jama.1979.03300240036023
- [21] Ciobanu AM, Colibaba S, Cimpoa B, Peltecu G, Panaitescu AM. Thrombocytopenia in Pregnancy. *A Journal of Clinical Medicine*. 2016 Mar; 11(1):55-60.
- [22] Mourad J, Elliott JP, Erickson L, Lisboa L. Appendicitis in pregnancy: new information that contradicts long-held clinical beliefs. *American Journal of Obstetrics and Gynecology*. 2000 May; 182(5):1027-9. doi: 10.1067/mob.2000.105396.
- [23] Dapper DV, Ibe CJ, Nwauche CA. Haematological values in pregnant women in Port Harcourt, Nigeria. *Nigerian Journal of Medicine*. 2006 Jul-Sep; 15(3):237-40. doi: 10.4314/njm.v15i3.37220.

- [24] Nazli R, Khan MA, Akhtar T, Mohammad NS, Aslam H, Haider J. Frequency of thrombocytopenia in pregnancy related hypertensive disorders in patients presenting at tertiary care hospitals of Peshawar. *Khyber Medical University Journal*. 2012 Jul; 4(3): 101-5.
- [25] İlhan M, İlhan G, Gök AF, Bademler S, Verit Atmaca F, Ertekin C. Evaluation of neutrophil-lymphocyte ratio, platelet-lymphocyte ratio and red blood cell distribution width-platelet ratio as early predictor of acute pancreatitis in pregnancy. *Journal of Maternal-Fetal and Neonatal Medicine*. 2016 May; 29(9):1476-80. doi: 10.3109/14767058.2015.1051026.
- [26] Bai P, Memon I, Ashfaq S, Sultan S, Irfan SM. Prevalence and etiology of thrombocytopenia in pregnant women in Southern Pakistan. *Journal of the Society of Obstetrics and Gynecologists of Pakistan*. 2018 Apr; 8(1):15-9
- [27] Ifeanyi OE, Ndubuisi OT, Deticia EB, Uche EC. Hematological profile of pregnant women in Umuahia, Arabia State, Nigeria. *Indian Journal of Current Microbiology and Applied Sciences*. 2014; 3(1):713-8.



Original Article

Evaluation Of Blood Flow in Superficial Arteries of Face by Doppler Ultrasound in Young Adults

 Izza Javaid^{1*}, Anjum Tazeen¹, Syeda Khadija Ul Sughra¹, Zareen Fatima¹, Muhammad Adeel Saleem, Mahreen Fatima¹ and Umm e Rubab

¹University Institute of Radiological Sciences & Medical Imaging Technologies, The University of Lahore, Pakistan

ARTICLE INFO

Key Words:

Superficial arteries, Doppler ultrasound, Facial artery, Temporal artery

How to Cite:

 Javaid, I., Tazeen, A., Khadija, S., Fatima, Z., Saleem, M. A., Fatima, M., & Rubab, U. (2022). Evaluation of blood flow in superficial arteries of face by Doppler ultrasound in young adults : Blood Flow in Superficial Arteries of Face by Doppler Ultrasound. *Pakistan BioMedicalJournal*,5(6).<https://doi.org/10.54393/pbmj.v5i6.540>

*Corresponding Author:

 Izza Javaid
 University Institute of Radiological Sciences & Medical Imaging Technologies (UIRSMIT), The University of Lahore, Pakistan
izzajavid86@gmail.com
Received Date: 13th June, 2022Acceptance Date: 27th June, 2022Published Date: 30th June, 2022

ABSTRACT

Acknowledgement: Knowledge of vascular hemodynamics of a particular region is essential to draw a fine line between normal and a pathological state. Face is highly vascular and little is known about normal blood flow characteristics of its superficial arteries. Thus there is a need to assess the normal blood flow characteristics of the face and to establish a normative database. This may later be helpful in planning of aesthetic procedures, face reconstruction following trauma or during surgery and in follow up examination of many skin diseases. To evaluate the blood flow of superficial arteries of face by Doppler ultrasound in young adults. **Methods:** A cross sectional descriptive study was conducted at University of Lahore Teaching Hospital and University Ultrasound Clinic Green Town, Lahore. Data was collected according to inclusion criteria. Sample size of 311 patients were included in this research comprising 112 (36%) females and 199(63.9%) were males. Data entry and analysis was done by using SPSS version-23. **Results:** Analysis of data showed that out of 311 patients 112 (36%) females and 199(63.9%) were males, According to the result analysis of the total number of 311 patients, facial artery had a mean diameter of 1.4 mm (0.14cm) and diameter of temporal artery at tragus was calculated 1.5mm (0.15cm) with SD 0.2. Facial and temporal artery average PSV among individuals was 26.8 ± 5.3 and 35.2 ± 11.9 respectively. Average RI value of facial artery was 0.81± 0.05 mm and for temporal was 1.0 ± 0.8 mm . **Conclusion:** The facial and temporal artery can be assessed on Doppler ultrasound for velocity and resistance parameters. No significant difference was seen in the parameters between males and females.

INTRODUCTION

Vascular supply is an important key for maintenance of healthy tissue conditions but also with regard to healing process following trauma or therapeutic interventions. Compromised vascularity is not only a leading cause of alterations in healthy tissues conditions but may also cause many blood borne diseases [1]. The human face is probably the most exposed and vascular region of the body. There are many diseases of the skin that may lead to change in the hemodynamics of the skin [2]. For instance acne is a common skin disease and often leads to scarring. Tissue and Collagen damage from the acne inflammation ends up causing permanent skin texture and vascular changes [3]. Acne is a widely affecting skin disease ranked

8th most common among other skin diseases Its worldwide prevalence (equal for ages) estimates about 9.38% [4]. Global disease study conducted in 2010 stated that prevalence of acne varies widely, with an estimate of 35% for 100% of adolescents having acne at some point of their life [5]. Atopic dermatitis (AD) is also quite common. It is the common chronic inflammatory skin disease with increased blood flow. It has a wide range of clinical presentations and symptoms. Estimate shows that prevalence of atopic dermatitis among children is 20% and 3% among adults yet it is still on an increase [6]. Changes in blood supply are also influenced by progressive age, diabetes mellitus, impediment, increased fatty acids, cigarette smoking and

so many other contributing factors. With many factors which can change blood supply to the skin, knowledge of the normal blood flow is essential to treat a unhealthy condition [7]. Surgical interventions of face are in high demand and rapidly increasing with time and so their need of arterial mapping. Knowledge of normal vascular architecture and flow parameters is essentials. Deviations from normal parameters can guide the surgical planning and even impair the patient's postoperative recovery. Various invasive and non-invasive procedures are used to estimate blood supply of face.. These procedures comprise venous occlusion plethysmography, Doppler ultrasonography, blood flow Doppler laser, thermostrom, Hertzman photoelectric plethysmography and radioactive isotopes. All of these methods have their own limitations. Among all Doppler ultrasonography is much common, easily available, non- invasive and radiation free mehod for estimating blood flow [8]. Doppler ultrasound enables assessment of hemodynamics, which includes dynamic features of both vascular architecture and blood flow and these features are a direct determinant of viability of a certain region[9]. In order to achieve maximum accuracy it is important to understand the meaning of the parameters of Doppler US and how to adjust them.

METHODS

It was a cross-sectional descriptive study conducted in 9 month as MS research at University of Lahore Teaching Hospital and University Ultrasound Clinic, Green town Lahore, Pakistan. A total of 310 healthy volunteers were included. The study was aimed to evaluate the blood flow in superficial arteries of face in young adults. Approval was taken from the institutional review board (IRB) and the Ethical Committee of the University of Lahore. Volunteers have been explained the procedure and also aim of the research therefore a written informed consent was signed.. Volunteers were asked for demographic details like age and gender, and measures like arterial diameter, PSV and EDV, RI, PI were recorded The results were summarized in the form of graphs and tables. Facial arteries were examined on grey scale and Doppler ultrasound with 7-10 MHz frequency transducer at the intersection border of mandible with the anterior border of masseter muscle, and superficial temporal arteries were interrogated at the level of the tragus. Data entry and analysis was done by using Med calc software. Descriptive analysis was done on all variables. Categorical variables were presented in the form of frequency and percentage. Data regarding artery diameter, PSV, EDV, RI and PI was reported in mean ± S.D. Kruskal-Wallis test and chi-square test was used to compare the results between male and female individuals.

RESULTS

Analysis of data showed that out of 311 patients 112 (36%) females and 199(63.9%) were males, According to the result analysis of the total number of 311 patients, facial artery had a mean diameter of 1.4 mm (0.14cm) and diameter of temporal artery at tragus was calculated 1.5mm (0.15cm) with SD 0.2. Facial and temporal artery average PSV among individuals was 26.8 ± 5.3 and 35.2 ± 11.9 respectively. Average RI value of facial artery was 0.81± 0.05 mm and for temporal was 1.0 ± 0.8 mm

Facial artery	Value	Confidence interval	Male	female	P-value
Peak systolic velocity (cm/s)	26.8±5.3	26.2-27.4	27	27	0.33
End diastolic velocity (cm/s)	5.1±1.6	4.9-5.2	5.6	5.5	0.98
Resistive index	0.9±0.4	0.8-0.9	0.7	0.7	0.4
Pulsatility index	2.1±0.6	2.1-2.2	2.0	1.8	0.60
Diameter	1.4 ± 0.2	1.44 -1.51	1.5	1.6	0.08

Table 1: Descriptive statistics of vascular status of facial artery

Temporal artery	Value	Confidence interval	Male	female	P-value
Peak systolic velocity	35.2±11.9	33.8-36.5	33	30	0.05
End diastolic velocity	4.7±2.6	4.4-5.0	4.1	4.1	0.5
Resistive index	1.0±0.8	1.0-1.1	1.0	1.0	0.5
Pulsatility index	2.5±0.5	2.4-2.5	2.6	2.7	0.89
Diameter	1.5±0.2	1.49-1.54	1.5	1.6	0.63

Table 2: Descriptive statistics of vascular status of temporal artery

DISCUSSION

This study was designed to evaluate the hemodynamic characteristics of superficial arteries of human face by color Doppler ultrasound in order to provide normative data base for future comparison with pathological states. In this study, attempt was made to determine normal ranges of different parameters of superficial arteries by using high frequency color Doppler ultrasound. Data was collected from 311 healthy volunteers, out of which 199 were males (63.9%) and 112 were females (36%). In our study the detection rate of facial artery and temporal artery in male and female individuals was 100%. In a previous study the detection rates of the main trunk of facial artery and it's all branches was 100% [10]. Another study found detection rate of main facial artery trunk was 77.6% [11]. Similarly, masseter branch of the facial artery was detected in 88% of the cases [12]. Temporal artery showed 100% detection rate in almost every case. Most of available data regarding superficial arteries of face is based on its examination in cadaveric studies. Difference in the detection rate of vessels could be due to the reason that cadaver procedures which includes latex injection may cause vessel dehydration and morphologic changes. In our study, the facial artery had a mean diameter of 1.4 mm (0.14cm). No

significance difference was found in the diameter of facial artery in males and females ($p=0.08$). A study found the mean diameter of right and left facial artery to be 1.6mm (0.16 cm) and 1.5mm (0.15 cm) respectively [7]. In another study it was 1.0 ± 0.4 mm (range: 0.4–2.2 mm) with no difference between face sides [13]. Other found facial artery mean diameter to be 1.8mm [11]. These studies provided a close agreement with the value as analyzed by our study. However, a study showed a mean diameter of 2.14mm (0.21cm) with the SD of 0.43 [14]. The diameter of the facial vessels in an anatomic study was determined and ranged from 1.7 to 3.6 mm (mean, 2.6 mm) [1]. We assume the difference found among these studies could be due to methods used and specific area analyzed. In our study diameter of temporal artery at tragus calculated was 1.5mm (0.15cm) with SD 0.2. Temporal artery diameter was consistent and showed no difference among males and females ($p=0.63$). A study published in literature stated the superficial temporal artery mean diameter 1.5 mm (95% confidence interval) [13]. In other study it was 1.6 mm (0.16 cm) SD 0.35 mm at the front of the tragus [15]. Another study found diameter of superficial temporal artery, 1.7 ± 0.43 mm [16]. Temporal artery diameter value showed a strong comparison with the values found earlier in literature. In our study facial and temporal artery average peak systolic velocity (PSV) among individuals was 26.8 ± 5.3 cm/sec with a range from 16.4 to 46.3 cm/sec and 35.2 ± 11.9 cm/sec with a range from 16.7 to 69.7cm/sec respectively. There was no significance difference of indices found among male and female individuals. In another study maximum peak systolic velocity (PSV) of 24.6 cm/s and minimum to be 5.1 cm/s [11]. Peak systolic values of facial artery and temporal artery provided a close agreement with the previous studies. In our study we found facial artery resistive index (RI) to be 0.9 ± 0.4 mm with a range from 0.7 to 2.8 and temporal artery resistive index (RI) recorded was 1.0 ± 0.8 mm with a range from 0.6 to 3.9 same for both genders. No significant difference was observed ($p= 0.497$). Tucunduva in his study observed the average value of resistive index (RI) of facial artery was 0.81 ± 0.05 mm. and of temporal artery 0.79 ± 0.11 mm [14]. In another study facial artery resistive index (RI) was 0.79 ± 0.05 mm. Other found resistive index (RI) of facial artery to be 0.08mm [11]. No statistically difference was present between male and female individuals in this index. Resistive index value provided a close agreement with the findings published in early literature. In this study the mean and Standard deviation of facial artery pulsatility index (PI) among individuals was 2.1 ± 0.6 . and temporal artery pulsatility index (PI) was 2.5 ± 0.5 . No statistical difference was observed between male and female in this regard. Arijji Y et al., found facial artery pulsatility index (PI) to be 2.51. 32

Both finding were in close agreement [11]. In a study published in literature facial artery peak systolic velocity (PSV) recorded was 21.38 ± 13.70 cm/sec and temporal artery peak systolic velocity (PSV) recorded was 42.09 ± 23.02 cm/sec [17]. Some literature has discussed these perspectives in great detail as book chapters [18–20] but no data regarding pulsatility index (PI) of temporal artery and end diastolic velocity of both vessels were found in literature and need further investigation.

CONCLUSION

The facial and temporal artery can be assessed on Doppler ultrasound for velocity and resistance parameters. No significant difference was seen in the parameters between males and female.

REFERENCES

- [1] Zhao Z, Li S, Xu J, Li Y, Huang W, Yang M, Mu L, Liu Y, Zhai H, Jin J, Li J, Li J, Fu X. Color Doppler flow imaging of the facial artery and vein. *Plast Reconstr Surg.* 2000 Nov; 106(6):1249–53. doi: 10.1097/00006534-200011000-00002
- [2] von Arx T, Tamura K, Yukiya O, Lozanoff S. The Face – A Vascular Perspective. A literature review. *Swiss Dent J.* 2018 May 14; 128(5):382–392.
- [3] Baran U, Li Y, Choi WJ, Kalkan G, Wang RK. High resolution imaging of acne lesion development and scarring in human facial skin using OCT-based microangiography. *Lasers Surg Med.* 2015 Mar; 47(3):231–8. doi: 10.1002/lsm.22339.
- [4] Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, Shibuya K, Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 2012 Dec 15; 380(9859):2163–96. doi: 10.1016/S0140-6736(12)61729-2
- [5] Stathakis V, Kilkenny M, Marks R. Descriptive epidemiology of acne vulgaris in the community. *Australas J Dermatol.* 1997 Aug; 38(3):115–23. doi: 10.1111/j.1440-0960.1997.tb01126.x.
- [6] Nutten S. Atopic dermatitis: global epidemiology and risk factors. *Ann Nutr Metab.* 2015; 66 Suppl 1:8–16. doi: 10.1159/000370220
- [7] Iqbal N, Shahid K, Imtiaz M, Yasser F, Ashraf A, Zain M. Determination of Blood Flow in Superficial Arteries of Human Face using Doppler Ultrasonography in Young Adults. *The International Journal of Frontier Sciences.* 2021 Jan 22. doi: 10.37978/tijfs.v5i1.339
- [8] Cho YW, Park SH. Use of ultrasound Doppler to determine tooth vitality in a discolored tooth after traumatic injury: its prospects and limitations.

- Restorative dentistry & endodontics. 2014 Feb 1;39(1):68-73./doi.10.5395/rde.2014.39.1.68
- [9] Bavitz JB, Harn SD, Homze EJ. Arterial supply to the floor of the mouth and lingual gingiva. *Oral surgery, oral medicine, oral pathology*. 1994 Mar 1;77(3):232-5. doi.10.1016/0030-4220(94)90290-9
- [10] Zhao YP, Arijji Y, Gotoh M, Kurita K, Natsume N, Ma XC, Arijji E. Color Doppler sonography of the facial artery in the anterior face. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2002 Feb 1;93(2):195-201. doi.10.1067/moe.2002.120054
- [11] Arijji Y, Kimura Y, Gotoh M, Sakuma S, Zhao YP, Arijji E. Blood flow in and around the masseter muscle: normal and pathologic features demonstrated by color Doppler sonography. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology*. 2001 Apr 1;91(4):472-82. doi.10.1067/moe.2001.111760
- [12] Won SY, Choi DY, Kwak HH, Kim ST, Kim HJ, Hu KS. Topography of the arteries supplying the masseter muscle: using dissection and Sihler's method. *Clinical anatomy*. 2012 Apr;25(3):308-13. doi.10.1002/ca.21205
- [13] Koziej M, Polak J, Wnuk J, Trybus M, Walocha J, Chrapusta A, Brzegowy P, Mizia E, Popiela T, Hołda M. The transverse facial artery anatomy: Implications for plastic surgery procedures. *PLoS One*. 2019 Feb 7;14(2):e0211974. doi: 10.1371/journal.pone.0211974.
- [14] Tucunduva MJ, Tucunduva-Neto R, Saieg M, Costa AL, de Freitas C. Vascular mapping of the face: B-mode and doppler ultrasonography study. *Medicina Oral, Patología Oral y Cirugía Bucal*. 2016 Mar;21(2):e135. doi: 10.4317/medoral.20754.
- [15] Pinar YA, Govsa F. Anatomy of the superficial temporal artery and its branches: its importance for surgery. *Surgical and Radiologic Anatomy*. 2006 Jun;28(3):248-53. doi: 10.1007/s00276-006-0094-z.
- [16] Bae JW, Yu H, Lee SC. Color Doppler Sonography of Patients with Temporal Arteritis: Comparison with Normal Superficial Temporal Artery. *Journal of Korean Society of Medical Ultrasound*. 2001 Sep 1;20(3):227-33
- [17] Oglat AA, Matjafri MZ, Suardi N, Oqlat MA, Abdelrahman MA, Oqlat AA. A review of medical doppler ultrasonography of blood flow in general and especially in common carotid artery. *Journal of medical ultrasound*. 2018 Jan;26(1):3. doi: 10.4103/JMU.JMU_11_17.
- [18] Lee W. General principles of carotid Doppler ultrasonography. *Ultrasonography*. 2014 Jan;33(1):11-7. doi: 10.14366/usg.13018.
- [19] Taylor KJ, Burns PN and Well PN. Clinical applications of Doppler ultrasound. 1988 Aug.8(2):206. doi.org/10.1016/0741-5214(88)90421-1
- [20] Pellerito J and Polak JF. Introduction to Vascular Ultrasonography E-Book. Elsevier Health Sciences.2012.6th Edition.



Original Article

Prevalence of Migraine and its Association with Neck Pain Among Students of the University of Lahore

Sapna Altaf¹, Iqra Mubeen¹, Fareeha Amjad^{1*}, Adnan Hashim¹, Muhammad Umer² and Mishab Zahur³¹University Institute of Physical Therapy, Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan²Sadiq Hospital, Sargodha, Pakistan³University institute of Diet and Nutritional Sciences, Faculty of Allied Health Sciences, The University of Lahore, Lahore, Pakistan

ARTICLE INFO

Key Words:

Hypothyroidism, End Stage Renal Disease, Hemodialysis

How to Cite:

Altaf, S., Mubeen, I., Amjad, F., Hashim, A., Umer, M., & Zahur, M. (2022). Prevalence of Migraine and its Association with Neck Pain Among Students of the University of Lahore : Migraine and its Association with Neck Pain. *Pakistan BioMedical Journal*, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.596>

*Corresponding Author:

Bhagwan Das
 Department of Nephrology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
dr_jairamani@hotmail.com

Received Date: 26th May, 2022

Acceptance Date: 20th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Headaches have been associated with a certain collection of mental difficulties, including sadness, anxiety, worries, and frenzied issues. If untreated, cranial discomfort and atypical headache attacks may cause nervousness and sorrow due to the victim's sense of helplessness brought on by the pain's irrationality **Objective:** To find out the prevalence of migraine attacks and its association with neck pain among students of the University of Lahore **Methods:** Data was collected from 217 students of The The University of Lahore, having migraine and neck pain by using questionnaire of Neck Disability Index and Numerical Pain rating scale for Migraine. The permission was taken from institute and the questions were asked after obtaining consent of student **Results:** Age distribution among students was 20.88±1.644 years with minimum age of 19yrs and maximum 25 yrs. Out of 217, males with the percentage 28.6 % and 71.4 % females. Students with no migraine were 17.1%, mild migraine were 36.9%, moderate migraine were 27.6% and severe migraine were 18.4%. Out of 217, 7(3.2%) had no neck pain, 6(2.8%) had mild neck pain, 115(53.0%) had moderate neck pain, 74(34.1%) had severe neck pain and 10(4.6%) had very severe neck pain **Conclusion:** An association between migraine attacks and neck pain was observed.

INTRODUCTION

Migraine and headaches have become frequent in recent times. Unease may be caused by the anguish that comes from atypical headache attacks, and depression may result [1,2]. Word 'headache', defined as attacks occurring less than 15 days of the month, may develop into persistent headache, defined as attacks occurring more than 15 days of the month. Attacks connected to persistent headaches satisfy the criteria for headaches without aura according to The International Classification of Headache Disorders-2 (ICHD-2) [3]. The pattern of headache is characterized by excruciating attacks, including migraine, separated by pain-free intervals known as interictal intervals. Even though there is no anguish during the interictal intervals

between attacks, there are still negative effects. Some sufferers grow anxious during these aggravation-free intervals, fully anticipating the next migraine [4,5]. These attacks may be triggered by declining converges of endogenous estrogen before menses or withdrawal of exogenous estrogen while using hormonal contraception. They are described as being of longer duration, more severe, and more difficult to treat than non-feminine migraines. Around half of female migraineurs have headaches related with feminine cycle, with 1.7-2.5-overlap expansion in headache risk during the period - 2 to +3 days comparative with the beginning of menses [6]. Headaches' etiology is not fully understood. The focused

sensory system logically initiates headache attacks, even if the aggravation during a headache assault arises from initiating afferent neurons that innervate the cerebral vasculature. Cortical spreading depression may be the cause of, for example, the adverse effects of the headache quality [7]. With an estimated point prevalence of 5.9-22.2% and a 1-year cumulative incidence of 14.6-17.9% in adults, neck pain may be one of the most common outer muscle problems. Although there are many recognized specific causes of neck pain (such as a herniated disc, a rheumatic infection), the majority of neck pain episodes have a mysterious origin and are typically described as vague neck ache [8,9]. The condition put out by Acheson and Jonsson has the following temporary meaning: Acute neck pain can cause 0-3 weeks of discomfort or perhaps disability. Sub-intense neck pain causes 4 to 12 weeks of suffering as well as disability. ongoing neck pain that has lasted for more than a year, resulting in both disability and agony. Patients seeking assistance after roughly a month of not seeking care or being placed on disability leave after at least a month of employment are examples of intermittent difficulties [10]. Explicit back analysis and prior debilitated leave due to back problems increased the chance for short- and long-term wiped-out leave; self-revealed pain and movement restrictions increased the chance for debilitated pass on and handicap benefits due to back and neck pain; and heavy actual responsibility, bowed or curved working position, and low work fulfilment increased the risk for both short- and long-term wiped-out leave [11]. Most cases of vague neck pain are addressed by a wide range of professionals with important consideration, and the most frequently used treatments are the "pensive" method, referral to physiotherapy, and referral to spinal control therapy [12]. In the traditional remedial classification of manual treatment, several systems are coordinated at the outer muscle tissues to alleviate mechanical pain [13]. The first subcategory includes manual foothold, control, and assembly. The second group comprises both core delicate tissue treatments like trigger point therapy, shiatsu, and pressure point massage as well as summed up delicate tissue treatments like the various types of back rubs. We used the various therapy categories of control, activation, manual footing, back rubs, and strain treatments for this audit [14]. The notion of segmenting headache patients into smaller groups in order to study organic and hereditary portrayal, characterize intriguing aggregates, improve headache visualization, and advance toward more successful treatment concepts is still up for discussion [15-18]. The existence of neck discomfort has received special attention among the concurrent and comorbid disorders and side effects found in headache patients. Neck pain has been identified as a common side

effect displayed by headache sufferers during attacks, before to attacks, and even in between attacks. Despite the lack of evidence for causal cervical spine neurotic disorders, 91% of patients with self-reported neck discomfort also experience headache attacks (categorized as a headache or probable headache) [19-23]. The goal of this study was to determine whether neck pain increases the risk of headache chronicity and whether neck pain-related impairments increase with increased frequency of headache attacks. Since headaches are a major cause of work absence and disability, they have a crippling effect on physical, social, and occupational tasks. These deficiencies lower personal happiness. Consciousness of neck pain as a common associated component of headache may influence patients' perspectives on medical service cycles and outcomes and aid in demonstrating accuracy while positively influencing treatment duration.

METHODS

Data was collected from 217 students of The University of Lahore, having migraine and neck pain. Data was collected by using questionnaire of Neck Disability Index and Numerical Pain rating scale for Migraine. The permission was taken from institute and the questions was asked from students after consent of student.

RESULTS

Students with no migraine were 17.1%, mild migraine were 36.9%, moderate migraine were 27.6% and severe migraine were 18.4% (Table 1).

N	Frequency	Percent
No Migraine	37	17.1
Mild Migraine	80	36.9
Moderate Migraine	60	27.6
Severe Migraine	40	18.4

Table 1: Descriptive statistics for Pain-NPRS (Migraine)

N	Frequency	Percent
No Neck Pain	7	3.2
Mild Neck Pain	6	2.8
Moderate Neck Pain	115	53.0
Severe Neck Pain	74	34.1
Very Severe Neck Pain	10	4.6

Table 2: Descriptive statistics for Neck disability index-NDI

Out of 217, 7(3.2%) have no neck pain, 6(2.8%) have mild neck pain, 115(53.0%) have moderate neck pain, 74(34.1%) have severe neck pain and 10(4.6%) have very severe neck pain (Table 2). Age distribution among students was 20.88±1.644 with minimum age of 19yrs and maximum 25 yrs (Figure 1).

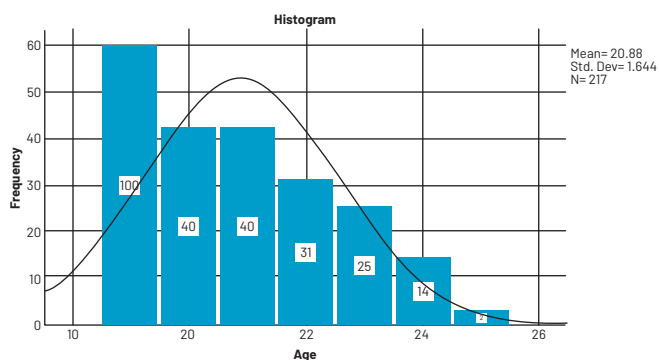


Figure 1: Graphical representation of age

DISCUSSION

According to current study, Age distribution among students was 20.88 ± 1.644 with minimum age of 19yrs and maximum 25 yrs. The gender distribution of students was as follows; males with the percentage 28.6 % and percentage of 71.4 % came out to be females. Students with no migraine were 17.1%, mild migraine were 36.9%, moderate migraine were 27.6% and severe migraine were 18.4%. According to a prior review, Zhe Yu et al. conducted a review in 2019 to examine the potential factors associated with EM neck pain and determine whether there were differences in peri cranial muscle delicacy between EM with and without neck pain. Enlisted personnel were given a headache incapacity score and a neck incapacity file. All patients' cranio-cervical muscle delicacy scores and mechanical torment edge were evaluated during the headache-free interval. Between EM with and without neck pain, there were no significant differences in migraine force ($p=0.44$), headache impairment ($p=0.71$), length ($p=0.44$), or recurrence ($p=0.85$). When compared to EM without neck pain, those who had it scored higher on both the cephalic and neck delicacy scales ($p=0.01$) [15]. According to the most recent evaluation, the percentage of students who are currently unbothered is 55 (25.3%), followed by those who are experiencing moderately intense anguish (39.0%), moderate torment (39.0%), truly extreme torment (25.1%), and serious torment (27.0%). (12.4%). 42 (19.4%) students can frequently take care of themselves without it adding to their stress, whereas 51 (23.5%) students can do so without it adding to their stress. There were 27 (12.4%) students who could take care of themselves, but they were cautious and slow. 28 (12.9%) require assistance frequently in many aspects of self-care, whereas 37 (17.1%) require some support but are able to manage the majority of their own affairs. 32 (14.7%) refuse to get dressed, wash their clothes with difficulty, and stay in bed. As in the previous review, Zenkevich AS et al. led a new review in 2016 to examine neck pain in patients with headache to identify potential comorbidity factors of these diseases. 50 people in total, including 9 men and 41 women,

were identified as having headaches for the review. 50 headache patients received information regarding the occurrence of neck side effects throughout various times of their assaults. Only 10.9 % of the patients reported having neck pain start at a different time than their headache or migraine, compared to the 89.1% of patients who said their cerebral discomfort and neck pain started and ended simultaneously (30 min before cerebral pain, 2 h previously or later than migraine and 12 h later than migraine). Based on our analysis, we have concluded that neck pain begins concurrently with headache attacks and may be necessary for headache to follow similarly [16]. According to a recent study, 33 (15.2%) students can lift heavy objects without experiencing further discomfort, 24 (11.1%) can lift heavy objects, but doing so causes further discomfort, 35 (16.1%) can do so without experiencing further discomfort, 29 (13.4%) can do so without experiencing further discomfort when lifting heavy objects, and 41 (18.9%) can lift exceptionally light objects. 34 (15.7%) students had the freedom to read as much as they wanted without experiencing any severe inconvenience. 23 (10.6%) students had the opportunity to read as much as they wanted despite experiencing some neck pain. 25 (11.5%) people with moderate pain can read as much as they need, 38 (17.5%) people with moderate pain can't read as much as they need, and 49 (22.6%) people with terrible pain can barely read at all. By all accounts, none of the 18 (8.3%) undergraduates had any form of brain pain. 9 (4.1%) people suffer infrequent, mild migraines. A mild migraine affects 13 (6.0%) people occasionally, a moderate brain pain affects 17 (7.5%) people frequently, and a severe cerebral pain affects 10 (4.6%) people frequently. According to a previous evaluation, Christian Lampl et al. directed an investigation in 2015 to determine whether neck pain (NP) is a prodromal headache side effect or if it is related to the headache attack. Information was evaluated from 487 people who suffer from wordy migraines (73.1% females; 77% had headache without quality). 338 patients (69.4%) disclosed NP at any point while experiencing a headache. 36 patients (bunch C; 7.4%) experienced NP between two and forty-eight hours prior to the cerebral pain stage, while 118 patients (bunch B; 24.2%) revealed NP within two hours before the migraine stage and 184 patients (bunch A; 54.4%) experienced NP at the start of the migraine stage. In bunch B, we discovered a significant amount of typical headache-related side effects, and in 82.2% of cases, NP proceeded into the relief of cerebral discomfort. These facts show that NP is a very common component of headache attacks and is therefore likely to be more significant for the attack itself than a prodromal headache side effect [17]. 34 (15.7%) had no trouble concentrating fully when studying, 36 (16.6%) people could

fully concentrate, when necessary, with some difficulty, 35 (16.1%) had a decent amount of difficulty focusing, 25 (11.5%) had a ton of difficulty concentrating, and 35 (16.1%) had a lot of difficulty concentrating. 25 (11.5%) students could complete any amount of work they need to, 15 (or 6.9%) could complete basic tasks, but not more, 16 (7.4%) could perform the majority of routine work but not more, 11 (5.1%) and 14 (6.5%) both struggled to complete even the most basic tasks. 47 (21.7%) students could operate a vehicle with barely any neck pain, 39 (18%) could do so for as long as they need with only a little discomfort, 33 (15.2%) could do so for as long as they need with moderate discomfort, 37 (17.1%) could not operate a vehicle for as long as they need due to moderate discomfort, and 26 (12%) could hardly operate a vehicle at all because of severe discomfort. 35 (16%) had no trouble falling asleep, 33 (15%) were little disturbed while they rest, 39 were somewhat disturbed while they rest, 30 were decently disturbed while they rest, and 37 were tremendously disturbed while they rest. While 27 (12.4%) were unable to engage in any form of entertainment activity, and 26 (12.0%) had the option to engage in all amusement activities with some neck discomfort, 43 (19.8%) had the opportunity to engage in all diversion activities without even the slightest amount of neck pain. Due to pain in their necks, 41 people (18.9%) were able to participate in the vast majority of common recreational activities, and 37 people (17.1%) were willing to partake in a few of these activities. Out of 217, 7 (3.2%) had no neck pain, 6 (2.8%) had mild neck pain, 115 (53.0%) had moderate neck pain, 74 (34.1%) had intense neck pain, and 10 (4.6%) had really severe neck pain. p value was less than 0.05, therefore we reject the unfounded hypothesis and accept the favoured hypothesis. As a result, it was stated that there is a relationship between migraine attacks and neck pain.

REFERENCES

- [1] Lantéri-Minet M, Radat F, Chautard MH, Lucas C. Anxiety and depression associated with migraine: influence on migraine subjects' disability and quality of life, and acute migraine management. *Pain*. 2005 Dec 5;118(3):319-326. doi: 10.1016/j.pain.2005.09.010.
- [2] Brandes JL. The migraine cycle: patient burden of migraine during and between migraine attacks. *Headache: The Journal of Head and Face Pain*. 2018 Mar;48(3):430-41. doi.org/10.1111/j.1526-4610.2007.01004.x
- [3] Lipton RB, Bigal ME, Steiner TJ, Silberstein SD, Olesen J. Classification of primary headaches. *Neurology*. 2004 Aug 10;63(3):427-35. doi: 10.1212/01.wnl.0000133301.66364.9b.
- [4] Cady RK, Schreiber CP, Farmer KU. Understanding the patient with migraine: The evolution from episodic headache to chronic neurological disease: A proposed classification of patients with headache. *Headache*. 2014; 44:426-435. doi.org/10.1111/j.1526-4610.2004.04094.x
- [5] Brandes JL, Poole AC, Kallela M, Schreiber CP, MacGregor EA, Silberstein SD, Tobin J, Shaw R. Short-term frovatriptan for the prevention of difficult-to-treat menstrual migraine attacks. *Cephalalgia*. 2019 Nov;29(11):1133-48. doi: 10.1111/j.1468-2982.2009.01840.x.
- [6] Hussain SI, Ahmad A, Amjad F, Shafi T, Shahid HA. Effectiveness of natural apophyseal glides versus grade I and II Maitland mobilization in nonspecific neck pain. *Annals of King Edward Medical University*. 2016 Feb 11;22(1):23-. doi.org/10.21649/akemu.v22i1.792
- [7] Sauro KM, Becker WJ. The stress and migraine interaction. *Headache*. 2009 Oct;49(9):1378-86. doi: 10.1111/j.1526-4610.2009.01486.x.
- [8] Fejer R, Kyvik KO, Hartvigsen J. The prevalence of neck pain in the world population: a systematic critical review of the literature. *Eur Spine J* 2006; 15:834-48. doi: 10.1007/s00586-004-0864-4.
- [9] Schellingerhout JM, Verhagen AP, Heymans MW, Pool JJ, Vonk F, Koes BW, de Vet HC. Which subgroups of patients with non-specific neck pain are more likely to benefit from spinal manipulation therapy, physiotherapy, or usual care? *Pain*. 2018 Oct 31;139(3):670-80. doi: 10.1016/j.pain.2008.07.015.
- [10] Amjad F, Mohseni-Bandpei MA, Gilani SA, Ahmad A, Hanif A. Effects of non-surgical decompression therapy in addition to routine physical therapy on pain, range of motion, endurance, functional disability and quality of life versus routine physical therapy alone in patients with lumbar radiculopathy: a randomized controlled trial. *BMC Musculoskelet Disord*. 2022 Mar 16;23(1):255. doi: 10.1186/s12891-022-05196-x.
- [11] Hansson T & Jensen I. Swedish Council on Technology Assessment in Health Care (SBU). Chapter 6. Sickness absence due to back and neck disorders. *Scandinavian Journal of Public Health*. Supplement 2014; 63: 109e151.
- [12] Vos C, Verhagen AP, Passchier J, Koes B. Management of acute neck pain in general practice: a prospective study. *Br J Gen Pract* 2017; 57:23-8.
- [13] Bergmann TF. Chiropractic technique. In: Gatterman MI, editor. *Foundations of chiropractic: subluxation*. 2nd ed. St. Louis (Mo): Elsevier Mosby; 2015.133-67.
- [14] Vernon H, Humphreys K, Hagino C. Chronic

- mechanical neck pain in adults treated by manual therapy: a systematic review of change scores in randomized clinical trials. *Journal of Manipulative and Physiological Therapeutics*. 2017 Mar 1;30(3):215-27. doi: 10.1016/j.jmpt.2007.01.014.
- [15] Pradhan S, Choudhury SS. Clinical characterization of neck pain in migraine. *Neurology India*. 2018 Mar 1;66(2):377. doi: 10.4103/0028-3886.227302.
- [16] Yu Z, Wang R, Ao R, Yu S. Neck pain in episodic migraine: a cross-sectional study. *Journal of pain research*. 2019; 12:1605-1613. doi: 10.2147/JPR.S200606.
- [17] Amjad F, Mohseni-Bandpei MA, Gilani SA, Ahmad A, Waqas M, Hanif A. Urdu version of Oswestry disability index; a reliability and validity study. *BMC musculoskeletal disorders*. 2021 Dec;22,311(2021):1-1. doi.org/10.1186/s12891-021-04173-0
- [18] Luedtke, K, May, A. Stratifying migraine patients based on dynamic pain provocation over the upper cervical spine. *J Headache Pain* 2017; 18: 97-101. doi: 10.1186/s10194-017-0808-0.
- [19] Lampl C, Rudolph M, Deligianni CI, Mitsikostas DD. Neck pain in episodic migraine: premonitory symptom or part of the attack? *J Headache Pain*. 2015;16:566. doi: 10.1186/s10194-015-0566-9.
- [20] Ashina S, Bendtsen L, Lyngberg AC, Lipton RB, Hajiyeva N, Jensen R. Prevalence of neck pain in migraine and tension-type headache: a population study. *Cephalalgia*. 2015 Mar;35(3):211-9. doi: 10.1177/0333102414535110.
- [21] Özer G, Benlier N. Neck pain: is it part of a migraine attack or a trigger before a migraine attack? *Acta Neurol Belg*. 2020 Apr;120(2):289-293. doi: 10.1007/s13760-018-1030-9.
- [22] Zarar M and Amjad F. Prevalence of Migraine (Headache) Among Physiotherapy Students and Its Impact on Daily Activities. *International Journal of Scientific & Engineering Research*, 2019,10(3):367-370.
- [23] Shahzadi K, Amjad F, Tanveer F, Ahmed A and Gilani SA. Frequency of migraine in students of university of Lahore. *Isra Medical Journal*, 2017; 9(6): 424-426.



Original Article

Prevalence of Hypothyroidism in Esrd Patients with Maintenance Hemodialysis

Haseeb Jameel Memon¹, Bhagwan Das^{2*}, Asma Naveed³, Rafia Memon¹, Sughand Memon⁴, Santosh Kumar⁵¹ Liaquat University Hospital, Hyderabad, Pakistan² Department of Nephrology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan³ Department of Nephrology, Bahria University of Medicine and Dental College (BUMMDC), Pakistan⁴ Department of Critical Care Medicine, Ziauddin University Hospital, Karachi, Pakistan⁵ Department of Nephrology, Jinnah Sindh Medical University, Karachi, Pakistan

ARTICLE INFO

Key Words:

Hypothyroidism, End Stage Renal Disease, Hemodialysis

How to Cite:

Jameel Memon, H. ., Das, B. ., Naveed, A. N. ., Memon, R. ., Memon, S. ., & Kumar, S. . (2022). Prevalence Of Hypothyroidism in Esrd Patients with Maintenance Hemodialysis: Hypothyroidism in Esrd Patients with Maintenance Hemodialysis. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.524>

*Corresponding Author:

Bhagwan Das
 Department of Nephrology, Liaquat University of Medical and Health Sciences, Jamshoro, Pakistan
dr_jairamani@hotmail.com

Received Date: 6th June, 2022Acceptance Date: 20th June, 2022Publihsed Date: 30th June, 2022

ABSTRACT

The kidney affects "the thyroid gland causing various derangements in its function whenever the kidney is impaired, even with a minor imperfection in its job, and this makes dialysis patients more prone to thyroid disorders with subsequent increase in mortality and morbidity.

Objective: To determine the frequency of hypothyroidism in ESRD patients who are on maintenance hemodialysis. **Methods:** A descriptive cross-sectional study was conducted at Department of Nephrology, Liaquat University of Medical and Health Sciences Jamshoro", upon a sample of 140 patients having age between 18 to 70 years presented with end stage renal disease with 3 months or more of maintenance hemodialysis were consecutively enrolled. Investigations was advised for TSH levels, T3, T4. The presence of hypothyroidism along with baseline and clinical characteristics were noted. **Results:** Of 140 patients, the mean age of the sample was 62.31± 9.78 years. Majority of the sample were males as compared to females, i.e., 93 (66.4%) and 47 (33.6%). History of thyroid disorder was observed in 83 (59.3%) patients. Comorbidity showed that type 2 diabetes mellitus was observed in 65(46.4%) and hypertension in 77(55%) patients. The mean TSH, T3 and T4 level was found to be 4.67± 0.20, 0.97± 0.37, and 5.33± 0.69 respectively. Frequency of hypothyroidism was found to be 53 (37.9%) patients. **Conclusion:** A considerably higher number of patients were presented with hypothyroidism in "ESRD patients who are on maintenance hemodialysis.

INTRODUCTION

Chronic kidney disease is an increasing disease of all age groups causing irreversible loss of kidney function [1]. It is divided into five stages on the basis of glomerular filtration rate. Stage V disease has glomerular filtration rate less than 15ml/min/1.73m, also called as End Stage Renal Disease (ESRD)[2]. The patients of chronic kidney disease stage 5 cannot sustain their life without renal replacement therapy either in the form of dialysis or renal transplant [3, 4]. A larger number of chronic kidney disease patients have high prevalence of unrecognized endocrine complication of thyroid dysfunction. Hypothyroidism is common in progressively deranged renal function in some large

population based studies [5]. The 3rd National Health and Nutrition Examination survey that includes data from 14,623 participants shows prevalence of hypothyroidism was 5.4%, 10.9%, 20.4%, 23.0%, and 23.1% among those with estimated glomerular filtration rates (eGFRs) of ≥90, 60-89, 45-59, 30-44, and <30ml/min/1.73m², respectively [5]. Primary hypothyroidism is common in CKD patients as the metabolism of thyroid hormones is disturbed due to effect on pituitary-thyroid axis [6]. The symptoms of chronic kidney disease (CKD) and hypothyroidism overlap in many aspects, making it difficult to recognize primary hypothyroidism in ESRD [7]. There is a high prevalence of

thyroid dysfunction in patients of advanced chronic kidney disease including those who are receiving dialysis [8]. Reduced levels of thyroid hormones i.e. Total and free serum thyrotropin are associated in patients on maintenance hemodialysis [9]. The derangements in thyroid function tests may be associated with cardiovascular morbidity and mortality in CKD and ESRD patients as shown in various data [10]. The presence of Hypothyroidism is associated with an increased risk of mortality from cardiovascular causes in the dialysis population. The study was conducted with an aim to determine the frequency hypothyroidism in the local hemodialysis population as local data on this topic was not available.

METHODS

Upon a sample of 140 patients (chosen via non-probability consecutive sampling). Patient having both gender and age between 18 to 70 years presented with end stage renal disease with 3 months or more of maintenance hemodialysis were recruited for the research after taking informed written consent. Investigations were advised for TSH levels, T3, T4. The presence of hypothyroidism along with baseline and clinical characteristics were noted. Descriptive statistics were analyzed by SPSS version 21

RESULTS

Of 140 patients, the mean age of the patients was 62.31±9.78 years. Most of the patients were males as compared to females, i.e., 93 (66.4%) and 47 (33.6%). Urban residence was observed in 62 (44.3%) patients while rural residence in 78 (55.7%). The mean height, weight, and BMI of the patients was found to be 1.55±0.06, 60.53±5.13 kg, 26.74±5.19 kg/m² respectively. There were 71 (50.7%) patients with >25 kg/m² BMI and 69 (49.3%) with ≤25 kg/m² BMI. The mean duration of ESRD was 5.92±1.39 months. There were 92 (65.7%) patients with ≤6 months duration of ESRD and 48 (34.3%) with >6 months duration of ESRD. The mean duration of hemodialysis was 4.41±1.99 months. There were 82 (58.6%) patients with ≤4 months duration of hemodialysis and 58 (41.4%) with >4 months duration of hemodialysis. History of thyroid disorder was observed in 83 (59.3%) patients. The mean TSH, T3 and T4 level was found to be 4.67±0.20, 0.97±0.37, and 5.33±0.69 respectively. Frequency of hypothyroidism was found to be 53 (37.9%) patients. A significant association of hypothyroidism was observed with duration of ESRD (p-value <0.001) and hypertension whereas age (p-value 0.695), gender (p-value 0.415), BMI (p-value 0.696), residence (p-value 0.853), duration of hemodialysis (p-value 0.988), history of thyroid disorder (p-value 0.360), and type 2 diabetes mellitus (p-value .627) were found to be insignificant.

Duration Of Esrd (in Months)	Hypothyroidism		Total	p-value
	Present	Absent		
≤6	23 (25.0)	69 (75.0)	92 (100)	<0.001
>6	30 (62.5)	18 (37.5)	48 (100)	
Total	53 (37.9)	87 (62.1)	140 (100)	

Table 1: Comparison of Hypothyroidism with Age of the Patients

DISCUSSION

A large number of chronic kidney disease patients have high prevalence of unrecognized endocrine complication of thyroid dysfunction [11]. Hypothyroidism is common in progressively deranged renal function in some large population based studies [12]. The 3rd National Health and Nutrition Examination survey that includes data from 14,623 participants shows prevalence of hypothyroidism was 5.4%, 10.9%, 20.4%, 23.0%, and 23.1% among those with eGFRs of ≥90, 60-89, 45-59, 30-44, and <30 ml/min/1.73m², respectively [13]. Primary hypothyroidism is common in CKD patients as the metabolism of thyroid hormones is disturbed due to effect on pituitary-thyroid axis [14]. The symptoms of CKD and hypothyroidism overlap in many aspects, making it difficult to recognize primary hypothyroidism in ESRD [15,16]. There is a high prevalence of thyroid dysfunction in patients of advanced chronic kidney disease including those who are receiving dialysis [17]. Reduced levels of thyroid hormones i.e., Total and free serum thyrotropin are associated in patients on maintenance hemodialysis [18]. The derangements in thyroid function tests may be associated with cardiovascular morbidity and mortality in CKD and ESRD patients as shown in various data [19]. According to the current study findings, the frequency of hypothyroidism was found to be 37.9% patients. Somewhat similar frequency was observed in a previous study as well. 5 Similarly, in Shantha et al., study, "in 137 hemodialysis patients tested for TSH and FT4, SCH prevalence was 24.8% [20]. Nevertheless, all agreed that dialysis patients had a high prevalence of hypothyroidism, and even confirmed in a larger-scale study of 8840 hemodialysis patients based on baseline TSH, they observed that 22% of them had hypothyroidism, but they did not test FT4, so they had no results about overt and subclinical hypothyroidism [21]. Thus, one can conclude that the prevalence of hypothyroidism defined as high TSH is similar in different population but varies in terms of its category (SCH and overt hypothyroidism). An important point to consider in this regard is that studies had different definitions for hypothyroidism, and this arises from the arguments about the accepted TSH level in dialysis, as some authors propose that levels between 5 and 20 IU/ml are considered normal in dialysis patients and so no treatment is required, though in studies that assessed mortality found that TSH even in high

normal range (3–5 μ IU/ml) was associated with a higher risk of mortality[22]. Limitation of this study is that it was a cross-sectional study; therefore, cause-effect relationships cannot be assessed. Moreover, we did not estimate the prevalence of low FT4 and FT3 since it was, especially low FT3, associated with mortality and worse prognosis. Furthermore, anti-thyroid antibodies were not tested in our study, which may help to find the etiology whether a primary thyroid abnormality or due to renal impairment. Finally, we did not have a comparison group of healthy controls to study the differences between them, but we compared with other studies in our population and different ones.

CONCLUSION

A considerably higher number of patients were presented with hypothyroidism in ESRD patients who are on maintenance hemodialysis”.

REFERENCES

- [1] Czarzasta K, Cudnoch-Jedrzejska A, Niemczyk L, Wrzesien R, Tkaczyk M, Puchalska L, et al. Effect of chronic kidney disease on changes in vasopressin system expression in the kidney cortex in rats with nephrectomy. *BioMed research international*. 2018 Jun 14; 2018.doi.org/10.1155/2018/2607928.
- [2] Shaikh GM, Khan DA, Khan FA, Ali MK. Validation of modified estimated glomerular filtration rate in chronic kidney disease patients. *J Coll Physicians Surg Pak*. 2013 Nov;23(10):793-7.
- [3] Sharma K, Slawski B. renal disease and the surgical patient: Minimizing the impact. *Cleve Clin J Med*. 2018 Jul;85(7):559-67.doi.org/10.3949/ccjm.85a.17009
- [4] Anees M, Butt G, Gull S, Nazeer A, Hussain A, Ibrahim M. Factors affecting dermatological manifestations in patients with end- stage renal disease. *J Coll Physicians Surg Pak*. 2018 Feb;28(2):98-102. doi: 10.29271/jcsp.2018.02.98.
- [5] Rhee CM, Zadeh KK, Ravel V, Streja E, You AS, Brunelli SM, et al. Thyroid status and death risk in U.S. veterans with chronic kidney disease. *Mayo Clin Proc*. 2018 May;93(5):573-585.doi.org/10.1016/j.mayocp.2018.01.024
- [6] Bajaj S, Purwar N, Gupta A, Gupta P, sirivastava A. Prevalence of hypothyroidism in nondiabetic chronic kidney disease and effect of thyroxine replacement on estimated glomerular filtration rate. *Indian J Nephrol*. 2017 Mar - Apr; 27(2): 104 - 107.doi.org/10.4103/0971-4065.181464
- [7] Paudel K. Prevalence and clinical characteristics of hypothyroidism in a population undergoing maintenance hemodialysis. *J ClinDiagn Res*. 2014 Apr; 8(4): MC01-MC04. doi.org/10.7860/JCDR/2014/7821.4246
- [8] You AS, Sin JJ, Kovesdy CP, Streja E, nguyen DV, Brent GA, et al. Association of thyroid status prior to transition to end stage renal disease with early dialysis mortality. *Nephro dial transplant*. 2018 oct 2018. doi.org/10.1093/ndt/gfy289
- [9] Jusufovic S, Hodzic E. Functional thyroid disorders are more common in patients on chronic hemodialysis compared with the general population. *Mater Sociomed*. 2011; 23(4): 206 - 209.doi.org/10.5455/msm.2011.23.206-209
- [10] Rhee CM, Brent GA, Kovesdy CP, Soldin OP, Nguyen D, Budoff MJ, Brunelli SM, Kalantar-Zadeh K. Thyroid functional disease: an under-recognized cardiovascular risk factor in kidney disease patients. *Nephrol Dial Transplant*. 2015 May;30(5):724-37. doi: 10.1093/ndt/gfu024.
- [11] Pakfetrat M, Dabbaghmanesh MH, Karimi Z, Rasekhi A, Malekmakan L, Hossein Nikoo M. Prevalence of hypothyroidism and thyroid nodule in chronic hemodialysis Iranian patients. *Hemodial Int*. 2017 Jan;21(1):84-89. doi: 10.1111/hdi.12453.
- [12] Naseem F, Mannan A, Dhrolia MF, Imtiaj S, Qureshi R, Ahmed A. Prevalence of subclinical hypothyroidism in patients with chronic kidney disease on maintenance hemodialysis. *Saudi J Kidney Dis Transpl*. 2018 Jul-Aug;29(4):846-851. doi: 10.4103/1319-2442.239646.
- [13] Rhee CM, Kim S, Gillen DL, Oztan T, Wang J, Mehrotra R, et al. Association of thyroid functional disease with mortality in a national cohort of incident hemodialysis patients. *J Clin Endocrinol Metab*. 2015 Apr;100(4):1386-95. doi: 10.1210/jc.2014-4311.
- [14] Xu H, Brusselaers N, Lindholm B, Zoccali C, Carrero JJ. Thyroid Function Test Derangements and Mortality in Dialysis Patients: A Systematic Review and Meta-analysis. *Am J Kidney Dis*. 2016 Dec;68(6):923-932. doi: 10.1053/j.ajkd.2016.06.023.
- [15] Cuna V, Menghi V, Comai G, Cappuccilli M, Cianciolo G, Raimondi C, et al. Functional Abnormalities and Thyroid Nodules in Patients with End-stage Renal Disease. *In Vivo*. 2017 Nov-Dec;31(6):1203-1208. doi: 10.21873/invivo.11191.
- [16] Rhee CM, Chen Y, You AS, Brunelli SM, Kovesdy CP, Budoff MJ, et al. Thyroid Status, Quality of Life, and Mental Health in Patients on Hemodialysis. *Clin J Am Soc Nephrol*. 2017 Aug 7;12(8):1274-1283. doi: 10.2215/CJN.13211216.
- [17] Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, et al. American Association of Clinical Endocrinologists and American Thyroid Association Taskforce on Hypothyroidism in Adults. *Clinical*

- practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Endocr Pract.* 2012 Nov-Dec;18(6):988-1028. doi: 10.4158/EP12280.GL.
- [18] Pearce SH, Brabant G, Duntas LH, Monzani F, Peeters RP, Razvi S, et al. 2013 ETA Guideline: Management of Subclinical Hypothyroidism. *Eur Thyroid J.* 2013 Dec;2(4):215-28. doi: 10.1159/000356507.
- [19] Amro N, Halahla A, Znaid I, Masalmah A. General assessment of thyroid stimulating hormone (TSH) levels among people living in south of Hebron, Palestine. *International Journal of Information Research and Review.* 2017; 4:4934-4937.
- [20] Shantha GP, Kumar AA, Bhise V, Khanna R, Sivagnanam K, Subramanian KK. Prevalence of Subclinical Hypothyroidism in Patients with End-Stage Renal Disease and the Role of Serum Albumin: A Cross-Sectional Study from South India. *Cardiorenal Med.* 2011;1(4):255-260. doi: 10.1159/000332757.
- [21] Rhee CM, Kim S, Gillen DL, Oztan T, Wang J, Mehrotra R, et al. Association of thyroid functional disease with mortality in a national cohort of incident hemodialysis patients. *The Journal of Clinical Endocrinology & Metabolism.* 2015 Apr 1;100(4): 1386-95. doi.org/10.1210/jc.2014-4311
- [22] Xu H, Brusselaers N, Lindholm B, Zoccali C, Carrero JJ. Thyroid function test derangements and mortality in dialysis patients: a systematic review and meta-analysis. *American Journal of Kidney Diseases.* 2016 Dec 1;68(6):923-32. doi.org/10.1053/j.ajkd.2016.06.023



Original Article

Incidence of Biliary Leakage and Spilled Gallstones in Laparoscopic Cholecystectomy

 Khawar Iqbal¹, Saadia Nawaz Durrani², Faiz ur Rahman^{3*}, Imranuddin Khan⁴, Kanwal⁵, Muhammad Attique Sadiq⁶
Muhammad Attique Sadiq⁶¹Department of Surgery, Sheikh Khalifa Bin Zaid Hospital (PGMI), Quetta, Pakistan²Department of Surgery, Naseer Teaching Hospital, Gandhara Medical University, Peshawar, Pakistan³Department of Surgery, Gaju Khan Medical College Swabi, Pakistan⁴Department of Surgery, Hyatabad Medical Complex, Peshawar, Pakistan⁵Department of Surgery, Jinnah Postgraduate and Medical Center, Karachi, Pakistan⁶Department of Surgery, Foundation University Medical College, Fauji Foundation Hospital, Rawalpindi, Pakistan

ARTICLE INFO

Key Words:

Biliary Leakage, Laparoscopic Cholecystectomy and Spillage of Gallstone

How to Cite:

 Iqbal, K., Nawaz Durrani, S., Rahman, F. ur., Khan, I., .., K., .. & Attique Sadiq, M. (2022). Incidence of Biliary Leakage and Spilled Gallstones in Laparoscopic Cholecystectomy: Biliary Leakage and Spilled Gallstones Incidence. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.519>

*Corresponding Author:

 Faiz ur Rahman
 Department of Surgery, Gaju Khan Medical College,
 Swabi, Pakistan
drfaizdagai@gmail.com
Received Date: 2nd June, 2022Acceptance Date: 20th June, 2022Published Date: 30th June, 2022

ABSTRACT

Gallstones (GS) are a major health problem worldwide. Its prevalence in the adult population of the United States is about 10%, which reaches 30% in the age group over 70 years. The incidence of GS in Pakistan is 15%, which represents 22% of surgical admissions. Laparoscopic cholecystectomy is accepted worldwide as the 1st line of treatment for symptomatic gallstone disease. **Objective:** To assess the occurrence of spilled gallstones and biliary leakage during laparoscopic cholecystectomy. **Methods:** A prospective descriptive study was conducted in the Surgical Department of Hayatabad Medical Complex Peshawar for six months duration from 15 June, 2021 to 15 November, 2021. Patients with gallstones were hospitalized via outpatient department. They were admitted for the analysis after procurement of knowledgeable consent in written form. All related investigations have been performed. Eligibility for anesthesia was assessed using the ASA scoring system. Patients endured laparoscopic cholecystectomy and the data was secured in a previously designed form. **Results:** During the period under analysis, 150 patients underwent laparoscopic cholecystectomy. 40.10 years \pm 10.74 years was the mean age. The main complication in 18 cases (12%) where the largest number of stones were removed during surgery, was gallstone spillage from whom 3 (17.6%) patients were 19-29 years old, 8 patients (47.1%) were 30-40 years old, 5 (29.4%) patients were 41-50 years old and 1 patient (5.9%) was 51-60 years old and 1 (5.9%) patient were 61-70 years old. The rate of gallstone spillage was 7 (4.7%) for men and 1 (7.3%) for women. Biliary leakage occurred in 5 patients (3.3%) aged 30-40 years and in 1 (0.7%) of patients aged 41-50 years. **Conclusion:** Laparoscopic cholecystectomy is effective and safe method in our environment and brings improved outcomes in the hands of specialists.

INTRODUCTION

Gallstones are a major health problem worldwide. Its prevalence in the adult population of the United States is about 10%, which reaches 30% in the age group over 70 years [1]. The incidence of GS in Pakistan is 15%, which represents 22% of surgical admissions [2,3]. Laparoscopic cholecystectomy is accepted worldwide as the 1st line of treatment for symptomatic gallstone disease. Karl-Langerbach accomplished the first open cholecystectomy in 1882, and Philip Mort executed the first Laparoscopic cholecystectomy in 1987 in Lyon, France [4,5]. In 1991, 1st

laparoscopic cholecystectomy was performed in Pakistan [6]. Globally, Laparoscopic cholecystectomy has believed to be a typical treatment for gallstone disease and open cholecystectomy has been substituted [7]. In the United States alone, 75% of the 600,000 gallstone surgeries performed annually are performed laparoscopically [8]. Laparoscopic cholecystectomy gives the subject, the assistances of minimally invasive surgery (MIS), counting better postoperative healing, cosmetic surgery scarring and earlier arrival to daily routine. Though, it is associated

with some of the rare complications reported in open cholecystectomy [9]. The laparoscopic cholecystectomy complications comprise primary or late complications. Primary complications include port entrance complications, intestinal trauma, bleeding, and late complications including gallstones, biliary leakage, and biliary trauma. Gallstone spillage is common during laparoscopic cholecystectomy [10]. The estimated incidence is between 3 and 33%. The incidence of complications due to stones that are not removed is approximately 0.3%. Biliary leakage is observed in 0.3-2.7% of patients after laparoscopic cholecystectomy. Although most spilled intraperitoneal gallstones are negligible by the surgeons, result in postoperative adhesions, peritonitis, intra and extra-abdominal abscesses, enterocutaneous, and entero vesical fistulas have been reported. Laparoscopic cholecystectomy is a new method of treating gallstone disease in Pakistan [11]. There is a tendency to prefer laparoscopic cholecystectomy in place of open cholecystectomy [12]. The laparoscopic cholecystectomy complications have been investigated in several hospitals. Though, since no systematic facts has been printed from our center, they should be reproduced [13]. Further studies should be conducted to change future development for the treatment and prevention of complications after laparoscopic cholecystectomy. The aim of this analysis was to assess the occurrence of spilled gallstones and biliary leakage during laparoscopic cholecystectomy.

METHODS

A prospective descriptive study was performed at the Surgical Department of Hayatabad Medical Complex Peshawar for six months duration from 15 June, 2021 to 15 November, 2021 on 150 patients approved by the Hospital Ethics Committee Patients with obstructive jaundice, gallbladder cancer, comorbidities and history. Upper abdominal surgery was ruled out due to confounding factors and study biasness. Patients with gallstones were hospitalized via outpatient department. They were admitted for the analysis after procurement of knowledgeable consent in written form. All related investigations have been performed. Eligibility for anesthesia was assessed using the ASA scoring system. Patients endured laparoscopic cholecystectomy and the data were secured in a previously designed form.

RESULTS

During the period under analysis, 150 patients underwent laparoscopic cholecystectomy. 40.10 years \pm 10.74 years was the mean age. Most patients 68(45.3%) were 30-40 years old, 39(26%) were 50-41 years old, 35 patients(23.3%) were under 30 years old and 7 patients (4.7%) were older >

60 years. The M:F ratio was 1: 2.40. As shown in Figure 1, 39 (26%) were male and 111(74%) were female.

Genderwise distribution

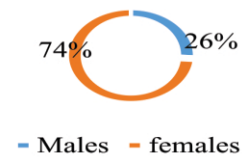


Figure 1: Gender-wise Distribution

The main complication in 18 cases (12%) where the largest number of stones were removed during surgery was gallstone spillage from whom 3 (17.6%) patients were 19-29 years old, 8 patients (47.1%) were 30-40 years old, 5 (29.4%) patients were 41-50 years old and 1 patient (5.9%) was 51-60 years old and 1 (5.9%) patient were 61-70 years old, shown in Table 1. Gallstone's spillage was more common in women than men. The rate of gallstone spillage was 7 (4.7%) for men and 11 (7.3%) for women. Biliary leakage occurred in 5 patients (3.3%) aged 30-40 years and in 1 (0.7%) of patients aged 41-50 years. Of all patients, 1 (0.7%) biliary leak was in male and 5 (3.3%) were female. Also, 12 patients (8%) underwent open cholecystectomy and laparoscopic cholecystectomy was successfully performed in 138 patients (92%). There were no deaths in our study.

Gall stone spillage	N=18
Age wise distribution	
19-29 years	3 (17.6%)
30-40 years	8 (47.1%)
41-50 years	5 (29.4%)
51-60 years	1 (5.9%)
61-70 years	1 (5.9%)
Gender wise distribution (18/150)	
Males	7 (4.7%)
females	11 (7.3%)
Biliary leakage (n=6)	
30-40 years	5 (3.3%)
41-50 years	1 (0.7%)
open cholecystectomy	12 (8%)
laparoscopic cholecystectomy	138 (92%)

Table 1: Patients' distributions of complication according to Age

DISCUSSION

Laparoscopic cholecystectomy has developed to be the first line of treatment for chronic cholecystitis and symptomatic gallstones and has replaced traditional open cholecystectomy [13,14]. In acute cholecystitis, maximum specialists now prefer laparoscopic cholecystectomy. Laparoscopic procedure has many benefits, but incidence of morbidity is somewhat advanced, especially in educational settings [15]. This study aim was to focus specifically on biliary leakage and spilled gallstones, two common complications of LC. 40.10 years \pm 10.74 years was

the mean age. Most patients 68(45.3%) were 30-40 years old, 39(26%) were 50-41 years old, 35 patients(23.3%) were under 30 years old and 7 patients (4.7%) were older > 60 years. In the study of Müftü et al., 40.30 years was the mean age and the maximum of patients (31.66%) were in the 30-40 years of age group. However, in the CL study in acute cholecystitis, 43.7 years was the mean age of patients and 4.5: 1 was the female to male ratio [16,17]. Alternative study was on 280 LC cases involving 140 males and 140 females with 56.9 years (89-23 years) mean age [18]. In all cases, we used the classic 4-port approach in our work. Though, a 3-port technique, and more freshly 2 cholecystectomy ports, using 3 mm miniature instruments, is possible and can improve aesthetic and surgical outcomes [19]. In this study a varus needle is used to produce pneumoperitoneum, but in an LC study, direct placement of a trocar without pneumoperitoneum proved to be a safe, effective, and time-saving alternative with fewer procedural complications [20,21]. Gallbladder injury is a life-threatening and serious complication of LC, and numerous analyses stated 0.6% to 1.5% of biliary duct injury. Biliary duct injury during LC is worrisome and can lead to benign biliary duct obstruction after surgery several months later, increased complications, and postoperative mortality [22]. Late postoperative stenosis is often the result of overuse of electrical coagulation in the vicinity of the common biliary duct or late problem of biliary reconstruction due to injuries after cholecystectomy. In this analysis, severe biliary duct injury happened in 1(0.7%) case [23]. ERCP and MRCP were performed to show lateral biliary duct damage. Stenting was also performed with successful results in the same session. 1.94 days was the average hospital stay, comparable to a local study at the Khyber Teaching Hospital, which recorded 2.06 days compared with Vagenas K et al., 2.29 days were reported in a center study [24]. Despite the complications mentioned, the inclusive result was acceptable, with improved reception of the operation by the patient [25].

CONCLUSION

LC is the most common method for symptomatic gallstones. In experienced hands, this is a safe and effective method in our environment. Most of the complications were due to inexperience and excessive enthusiasm. Adequate preoperative work, low conversion thresholds, and adequate training and equipment make this surgery a safe procedure with good results.

REFERENCES

- [1] Taki-Eldin A, Badawy AE. Outcome of laparoscopic cholecystectomy in patients with gallstone disease at a secondary level care hospital. ABCD. Arquivos Brasileiros de Cirurgia Digestiva (São Paulo). 2018 Jun; 31. doi.org/10.1590/0102-672020180001e1347.
- [2] van Dijk AH, van der Hoek M, Rutgers M, van Duijvendijk P, Donkervoort SC, de Reuver PR, et al. Efficacy of Antibiotic Agents after Spill of Bile and Gallstones during Laparoscopic Cholecystectomy. Surg Infect (Larchmt). 2019 May/ Jun; 20(4):298-304. doi: 10.1089/sur.2018.195.
- [3] Agarwal S, Joshi AD. Perioperative complications of laparoscopic cholecystectomy: a cross-sectional observational study. International Surgery Journal. 2020 Apr; 7(5):1490-5. doi.org/10.18203/2349-2902.isj20201857.
- [4] Tonolini M, Ierardi AM, Patella F, Carrafiello G. Early cross-sectional imaging following open and laparoscopic cholecystectomy: a primer for radiologists. Insights into imaging. 2018 Dec; 9(6):925-41. doi.org/10.1007/s13244-018-0663-9.
- [5] Faruquzzaman Q, Hossain SM. Overall operative outcomes of laparoscopic cholecystectomy and our experience in statistics. Arch Clin Gastroenterol. 2017 May; 3(2):33-6. DOI: 10.17352/2455-2283.000035.
- [6] Maitra TK, Ullah ME, Mondol SK. Operative and postoperative complications of laparoscopic cholecystectomy: experience from a Tertiary Care Hospital of Bangladesh. Bangladesh Critical Care Journal. 2017 May; 5(1):116. doi.org/10.3329/bccj.v5i1.32536.
- [7] Gerkema MH. Deep learning for identification of gallbladder leakage during laparoscopic cholecystectomy (Master's thesis, University of Twente). 2020.
- [8] Qamar SA, Jamil M, Salim K. Laparoscopic cholecystectomy for gall stone disease. A single center experience. The Professional Medical Journal. 2020 Sep; 27(09):19838. doi.org/10.29309/TPMJ/2020.27.09.5969.
- [9] Chauhan VS, Kariholu PL, Saha S, Singh H, Ray J. Can post-operative antibiotic prophylaxis following elective laparoscopic cholecystectomy be completely done away with in the Indian setting? A prospective randomised study. Journal of Minimal Access Surgery. 2018 Jul; 14(3):192. doi.org/10.4103/jmas.JMAS_95_17.
- [10] Vedamanickam PR. Complications of laparoscopic cholecystectomy performed by junior surgeon in resource-restricted settings. International Surgery Journal. 2019 Aug; 6(9):34703. doi.org/10.18203/2349-2902.isj20194102.
- [11] Asim Niaz MM, Hameed FM, Zahid M. Laparoscopic Cholecystectomy: A Study of Demographic, Morphological Factors and Iatrogenic Occurrences.

- Pakistan Armed Forces Medical Journal. 2020 Aug; 70(4).
- [12] Alexander HC, Bartlett AS, Wells CI, Hannam JA, Moore MR, Poole GH et al. Reporting of complications after laparoscopic cholecystectomy: a systematic review. *HPB*. 2018 Sep; 20(9):78694. doi.org/10.1016/j.hpb.2018.03.004.
- [13] Choudhury P. Fail to retrieve gallstones in laparoscopic cholecystectomy—a study. *Journal of Evolution of Medical and Dental Sciences*. 2017 Sep; 6(71):5035-40. doi.org/10.14260/Jemds/2017/1095.
- [14] Ibrahim AH, Abdel Wahab AW, Ali KA. Use of Drain in Laparoscopic Cholecystectomy. *The Egyptian Journal of Hospital Medicine*. 2018 Oct; 73(9):7615-21. doi.org/10.21608/ejhm.2018.19790.
- [15] Kadhim AM, Altaraikhim MH. Short Term Effect of Spilled Bile & Gallstone During Laproscopic Cholecystectomy on Clinical Outcome. *Indian Journal of Public Health*. 2019 Jun; 10(6):499. doi.org/10.5958/0976-5506.2019.01323.8.
- [16] Taki-Eldin A, Badawy AE. Outcome of Laparoscopic Cholecystectomy in Patients with Gallstone Disease at A Secondary Level Care Hospital. *Arq Bras Cir Dig*. 2018 Jun; 31(1):e1347. doi: 10.1590/0102-672020180001e1347.
- [17] Musa DH. Laparoscopic Cholecystectomy: Athree-Year Retrospective Study. *Duhok Medical Journal*. 2018 Dec; 12(2):8191. doi.org/10.31386/dmj.uod.18.12.2.7.
- [18] Begum S, Khan MR, Gill R. Cost effectiveness of glove endobag in laparoscopic cholecystectomy: Review of the available literatur. *The Journal of the Pakistan Medical Association*. 2019; 69(Supl. 1):S58.
- [19] Ridha AP, Kandil M. Clinical Outcomes of Gall Bladder Perforation During Laparoscopic Cholecystectomy. *Annals of Tropical Medicine and Public Health*. 2019 Dec; 22:190206. doi.org/10.36295/ASRO.2019.221220.
- [20] Arbogast M, Nebiker CA. Misleading Diagnostics After a Presumed Recovery of Gallstone Spillage. *Journal of Surgery and Research*. 2020 Aug; 3(3):297-300. doi.org/10.26502/jsr.10020084.
- [21] Alghamdi AB, Alzahrani ZA, Almutairi MD, Alotaibi NN, Alzahrani AY. Patient compliance in laparoscopic cholecystectomy versus open cholecystectomy. *The Egyptian Journal of Hospital Medicine*. 2018 Jan; 70(1):171-6. doi.org/10.12816/0042980.
- [22] Gupta OP, Khan S. Incidents and complications in laparoscopic cholecystectomy: a retrospective analysis of 336 cases. *Int J Contemporary Med Surg Radiol*. 2019; 4:1-5. doi.org/10.21276/ijcmsr.2019.4.2.1.
- [23] Biswasa S, Gognab S, Patelb P. Delayed Presentation of Actinomycotic Intra-Abdominal Abscess Following Laparoscopic Cholecystectomy Complicated by Empyema: Dropped Gallstone to Blame?. DOI: 10.14740/cii74e.
- [24] Gupta S, Singh R, Singh K, Singh K, Tiwana H, Thind A. Extra Biliary Complications Of Laparoscopic Cholecystectomy: A Prospective Analysis Of 100 Cases. *Journal of Advanced Medical and Dental Sciences Research*. 2017 Oct; 5(10):42-5. Doi: 10.21276/jamdsr.2017.5.10.11
- [25] Vidal GP, Davidov T. Gallbladder. In *The Internist's Guide to Minimally Invasive Gastrointestinal Surgery 2019* (pp. 79-92). Humana Press, Cham. doi.org/10.1007/978-3-319-96631-1_6.



Original Article

Role of Vitamin B6 and Folic Acid in Decreasing Diabetic Peripheral Sensory and Motor Neuropathy

Nasar Iqbal Ranjha¹, Muhammad Azeem¹, Muhammad Khan Malik¹, Khalil Ahmed^{2*}¹District Head Quarter (DHQ) Teaching Hospital, Sargodha, Pakistan²Niazi Medical and Dental College, Sargodha, Pakistan

ARTICLE INFO

Key Words:

Diabetes, Peripheral neuropathy, Vitamin B6, Folic acid, Homocysteine

How to Cite:

Iqbal Ranjha, N., Azeem, M., Khan Malik, M., & Ahmed, K. (2022). Role of Vitamin B6 and Folic Acid in Decreasing Diabetic Peripheral Sensory and Motor Neuropathy : Role of Vitamin B6 and Folic Acid in Decreasing Diabetic Peripheral Sensory and Motor Neuropathy. *Pakistan BioMedical Journal*, 5(6), 182-185. <https://doi.org/10.54393/pbmj.v5i6.573>

*Corresponding Author:

Khalil Ahmed
Niazi Medical and Dental College, Sargodha, Pakistan
khalilahmedmirza@gmail.comReceived Date: 20th June, 2022Acceptance Date: 25th June, 2022Published Date: 30th June, 2022

ABSTRACT

Diabetic peripheral neuropathy is a disease of diabetic patients in which nerves of peripheral nervous system got degenerated and unable to transmit any signals. Diabetic peripheral neuropathy occurs due to decreased serum level of B type vitamins in the body among which vitamin B6 and folic acid are more important. **Objective:** To determine the role of Vitamin B6 and folic acid in decreasing peripheral neuropathy. **Methods:** This study was conducted in the Hospital of Sargodha from 2018 to 2020. This study was carried on 250 type 2 diabetic patients. Both males and females were included. Subjects were submitted to detailed medical history about the duration of diabetes and symptoms of peripheral neuropathy. Complete examination of nervous system was conducted. Laboratory examination was done to find out mean fasting glucose. The control group comprised of 50 potentially healthy males and females was made. Serum level of vitamins was checked before and after treatment. **Results:** The main symptom which was present in all the patients was severe pain in lower legs Distal numbness was reported in 200 patients. Distal sensory neuropathy was reported in 150 patients. Distal motor neuropathy was reported in 52 patients. 157 patients had demyelinating neuropathy, 57 had axonal and 44 had mixed neuropathy. Peripheral diabetic neuropathy decreased after supplementations of homocysteine, folic acid and vitamin b6. **Conclusions:** Vitamin B6 and folic acid are known for their role to support healthy nervous system. Vitamin B6 and folic acid improved glycemic control through decreasing homocysteine. B6 relieves nerve pain and transmits nerve impulses correctly. The risk of peripheral neuropathy increased as serum folate decreased. Their supplementations are effective strategies for the treatment of peripheral diabetic neuropathy.

INTRODUCTION

Diabetic mellitus (DM) is a disease in which there is higher concentration of glucose in the blood than usual. DM occurs due to disturbance in production and release of insulin. Insulin is a hormone which decreases the concentration of glucose in the body. Due to low production of insulin, concentration of glucose in blood increases. According to WHO, almost 9-10% population of this world is diabetic. Neuropathy is a disorder of nervous system in which transmission of signals from brain to spinal cord or from spinal cord to brain got disturbed [1]. In this disorder, nerves of central and peripheral nervous system got damaged and unable to transmits signal [2]. Peripheral neuropathy is a disorder in which nerves of peripheral

nervous system got damaged. Almost 30% patients of peripheral neuropathy are positive to diabetes as well. It means diabetes is related to destructive and damage of nerves of peripheral nervous system. Peripheral neuropathy has many symptoms among which most common are restless leg syndrome and burning foot syndrome [3]. Diabetic peripheral neuropathy is a disease of diabetic patients in which nerves of peripheral nervous system got degenerated and unable to transmit any signals. As we discussed, diabetes is a disorder related to hyperglycaemia (high concentration of glucose in blood). Hyperglycaemia causes increased deposition of protein kinase C and polyol (compound that contains multiple

hydroxyl groups) in neurons. It leads to damage of neurons. It also leads to oxidative stress. One third of patients of diabetic peripheral neuropathy shows symptoms (Burning, Lancing, paraesthesia) that are extremely painful [4]. After several studies, researchers stated that vitamins had strong effect on the normal functioning of brain [5]. It was also observed that due to surgeries, level of many vitamins got decreased in the body and it led to disorders of nervous system [6]. For the treatment of diabetic peripheral neuropathy, several vitamins and nutrients are required.

METHODS

In this case control study, 250 diabetic patients of both genders were enrolled in the hospital of Sargodha from 2018 to 2020. Data was collected from the record sheets of each verified case. Following procedures were done on the admitted patients: A detailed medical history about the duration of diabetes, Complete examination of nervous system, Symptoms of peripheral neuropathy present in the patients, Electro physiological studies were conducted Laboratory examination to find out blood group and mean fasting glucose. Control group of 50 healthy males and females was made. Their age ranged from 28-58 years. The mean and standard values of vitamins before and after treatment. Both male and females who are positive to diabetic peripheral neuropathy with age 20 years or above was included. Pregnant women, patients with psychiatric disorders, patients with contraindications to folic acid, pyridoxine, methylcarbylamine were removed from our study.

RESULTS

The main symptom which was present in all the patients was severe pain in lower legs Distal numbness was reported in 200 patients. Distal sensory neuropathy was reported in 150 patients. Distal motor neuropathy was reported in 52 patients (Table 1). Total 157 patients had demyelinating neuropathy, 57 had axonal and 44 had mixed neuropathy. Peripheral diabetic neuropathy decreased after supplementations of homocysteine, folic acid and vitamin b6 (Table 1). Serum level of homocysteine, pyridoxine and folic acid in diabetic patients before and after treatment is shown in table 2.

Characteristics	Diabetic Patients, N=250	Control Group, N=50
Gender		
1.Males	110	25
2.Females	140	25
Age	35-60	28-58
Characteristics:		
1.Distal numbness	200	nil
2.Distal sensory neuropathy	150	nil
3.Distal motor neuropathy	52	nil

4.Demyelinating neuropathy	157	nil
5.Axonal neuropathy	57	nil
6.Mixed neuropathy	44	nil
7. Fasting blood glucose mg/L	110-260	70-102
8.Post prandial blood glucose mg/L	157-360	90-118
Serum level of various vitamins in diabetic patients or control group		
9.Glycosylated haemoglobin	5-10%	3-5%
10. Serum level of homocysteine umol/L1	2.3-2.6	2.5-6.4
11.Serum level of vitamin B6 nmol/L	6-25	6-50
12. Serum level of folic acid nmol/L	3-12.5	3-14.5

Table 1: Comparison of characteristics between diabetic patients and control group

Variables	Before treatment Mean ± SD	After treatment Mean± SD	p- value
Homocysteine umol/L	8.46 ± 5.18	7.55±4.51	0.604
Vitamin B6 nmol/L	24.2± 0.52	51± 2.52	24.8
Folic acid ng/L	5.17± 1.41	6.720± 2.76	0.196

Table 2: Serum level of homocysteine, pyridoxine and folic acid in diabetic patients before and after treatment

DISCUSSION

Diabetic neuropathy is analogous to neuropathy which occurs due to chemotherapy [7] and peripheral neuropathy which occurs due to high concentration of glucose in diabetic patients [8]. Sources of this vitamin are carrots, spinach, peas, potatoes, milk, cheese, eggs, fish, meat, and wheat. Isoniazid is a drug which causes deficiency and decreased serum level of this vitamin in the body [9,10]. When deficiency of this vitamin occurs in the body, then ability of body to convert tryptophan to nicotinic acid will be lost. In this way, peripheral neuropathy occurs. Folic acid plays a very important role in one carbon metabolism. It is used to produce several compounds in our body. Its active form is tetrahydrofolate. It plays crucial role in metabolism of cell [11]. It leads to differentiation of stem cells of neurons of nervous system and lengthening of their axons as well [12]. Regular intake of folic acid prevents neural tube defects in pregnant women and diabetic peripheral neuropathy as well [13,14]. Folic acid is required for the proper and rapid growth of Schwann cells. Researchers observed that when the nerves of peripheral nervous system got damaged, Schwann cells returned to its early parent state. Then Schwann cells formed some specific bands which had ability to grow axons [15]. Harma et al. observed that when proper supplementation of folic acid was given to the injured model of sciatic nerve, then this nerve became able to increase the volume of its axon and its viscosity and myelination as well. It means this vitamin is able to cause healing of nerves of peripheral nervous system [16]. Hyperhomocysteinemia is a disorder which

occurs due to decreased serum level of vitamin b6 and b9. This disorder is responsible for diabetic peripheral neuropathy as well [17]. Oxidative stress also causes demyelination of neurons and leads to neuronal damage [18]. For the treatment of diabetic peripheral neuropathy, aldose reductase inhibitors are used [19,20]. It is very difficult to understand the exact pathophysiology of pain which happens in patients of neuropathy. But there are several central and peripheral mechanisms that try to explain the pathophysiology of this pain [21].

CONCLUSIONS

Vitamin B6 and folic acid play crucial role in normal and proper functioning of nervous system. These vitamins decrease the serum level of homocysteine. They also maintain normal concentration of glucose in blood. Pyridoxine causes proper transmission of nerve impulses. The risk of peripheral neuropathy increased as serum level of folic acid decreased. Proper and regular intake of vitamin B6 and B9 are required to treat diabetic peripheral neuropathy.

REFERENCES

- [1] Costigan M, Scholz J, Woolf CJ. Neuropathic pain: a maladaptive response of the nervous system to damage. *Annu Rev Neurosci.* 2009;32:1-32. doi: 10.1146/annurev.neuro.051508.135531.
- [2] Cojocaru IM et al. Peripheral nervous system manifestations in systemic autoimmune diseases. *Mædica*, 2014, 9(3):289.
- [3] Kassab MY. Peripheral Neuropathy: Differential Diagnosis and Management. *American Family Physician*, 2010, 81, 887-892.
- [4] Tesfaye S. Recent advances in the management of diabetic symmetrical polyneuropathy. *J Diabetes Invest*, 2010; 2: 33- 42. doi: 10.1111/j.2040-1124.2010.00083.x.
- [5] Hammond N, Wang YX, Dimachkie MM and Barohn RJ. Nutritional Neuropathies. *Neurologic Clinics*, 2013, 31, 477-489. doi: 10.1016/j.ncl.2013.02.002.
- [6] Rudnicki SA. Prevention and Treatment of Peripheral Neuropathy after Bariatric Surgery. *Current Treatment Options in Neurology*, 2010, 12, 29-36. doi: 10.1007/s11940-009-0052-2.
- [7] Lees JG et al. Immune-mediated processes implicated in chemotherapy-induced peripheral neuropathy. *Eur J Cancer*, 2017, 73:22-29. doi: 10.1016/j.ejca.2016.12.006.E
- [8] Rasouljan B et al. Neuroprotective and antinociceptive effects of rosemary (*Rosmarinus officinalis* L.) extract in rats with painful diabetic neuropathy. *J Physiol Sci*, 2018, 61(10):1-8. doi: 10.1007/s12576-018-0620-x.
- [9] Bell DS. Metformin-Induced Vitamin B12 Deficiency Presenting as a Peripheral Neuropathy. *Southern Medical Journal*, 2010, 103, 265-267. doi: 10.1097/SMJ.0b013e3181ce0e4d.
- [10] Ito T and Jensen RT. Association of Long-Term Proton Pump Inhibitor Therapy with Bone Fractures and Effects on Absorption of Calcium, Vitamin B12, Iron, and Magnesium. *Current Gastroenterology Reports*, 2010, 12, 448-457. doi: 10.1007/s11894-010-0141-0.
- [11] Henry CJ, Nemkov T, Casas-Selves M, Bilousova G, Zaberezhnyy V, Higa KC et al. Folate dietary insufficiency and folic acid supplementation similarly impair metabolism and compromise hematopoiesis. *Haematologica*. 2017 doi: 10.3324/haematol.2017.171074.
- [12] Liu H, Cao J, Zhang H, Qin S, Yu M, Zhang X et al. Folic acid stimulates proliferation of transplanted neural stem cells after focal cerebral ischemia in rats. *J Nutr Biochem.* 2013; 24: 1817-1822. doi: 10.1016/j.jnutbio.2013.04.002.
- [13] De-Regil LM, Pena-Rosas JP, Fernandez-Gaxiola AC, Rayco-Solon P. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database Syst Rev.* 2015, doi: 10.1002/14651858.
- [14] Ganesh D, Sagayaraj BM, Barua RK, Sharma N, Ranga U. Arnold Chiari malformation with spina bifida: a lost opportunity of folic Acid supplementation. *J Clin Diag Res.* 2014;8:0d01-0d03. doi: 10.7860/JCDR/2014/11242.5335.
- [15] Napoli I, Noon LA, Ribeiro S, Kerai AP, Parrinello S, Rosenberg LH, Collins MJ, Harrisingh MC, White IJ, Woodhoo A, Lloyd AC. A central role for the ERK-signaling pathway in controlling Schwann cell plasticity and peripheral nerve regeneration in vivo. *Neuron.* 2012;73:729-742. doi: 10.1016/j.neuron.2011.11.031.
- [16] Harma A, Sahin MS, Zorludemir S. Effects of intraperitoneally administered folic acid on the healing of repaired tibial nerves in rats. *J Reconstr Microsurg.* 2015;31:191-197. doi: 10.1055/s-0034-1395414.
- [17] Luo JJ, Sivaraaman K, Nouh A and Dun NJ. Elevated Plasma Level of Homocysteine Is an Independent Risk Factor for Peripheral Neuropathy. *British Journal of Medicine & Medical Research*, 2014, 4, 161-169. doi: 10.9734/BJMMR/2014/5206.
- [18] ARETi A, Yerra VG, Naidu VGM and Kumar A. Oxidative Stress and Nerve Damage: Role in Chemotherapy Induced Peripheral Neuropathy. *Redox Biology*, 2014, 2, 289-295. doi: 10.1016/j.redox.2014.01.006.

- [19] 19. Maladkar M, Saggi N, Moralwar P, Mhate AA, Zemse D and Bhoraskar A. Evaluation of Efficacy and Safety of Epalrestat and Epalrestat in Combination with Methylcobalamin in Patients with Diabetic Neuropathy in a Randomized, Comparative Trial. *Journal of Diabetes Mellitus*, 2013, 3, 22-26. doi: 10.4236/jdm.2013.31004
- [20] 20. Maladkar M, Srividya S and Parmi P. Post-Marketing Surveillance of Epalrestat and Methylcobalamin– Game Changer in the Management of Diabetic Neuropathy: An Indian Perspective. *The Indian Practitioner*, 2013, 66, 683-688. doi:10.4236/jdm.2014.42019.
- [21] 21. Tesfaye S, Vileikyte L, Rayman G et al. Painful diabetic peripheral neuropathy: consensus recommendations on diagnosis, assessment and management. *Diabetes Metab Res Rev* 2011; 27 629–638. doi: 10.1002/dmrr.1225.



Original Article

Maternal Obesity & Feto-Maternal Outcomes

Shazia Rani¹, Farhana Anjum², Ambreen Amna Siddique², Sarosh Khan³, Khalil Kazi⁴, Sindhu Almas⁵¹.Gynecology & Obstetrics, Liaquat University of Medical & Health Sciences, Jamshoro².Gynecology & Obstetrics, Isra University Hyderabad³.Surrey and Sussex Healthcare NHS Trust, United Kingdom⁴.Department of Community Medicine, Indus Medical College - Tando Muhammad Khan⁵.Department of Community Medicine & Public Health Sciences, Liaquat University of Medical & Health Sciences, Jamshoro

ARTICLE INFO

Key Words:

Maternal Obesity; BMI; Foeto-maternal outcome, macrosomia

How to Cite:

Rani, S. ., Anjum, F., Amna Siddique, A. ., Khan, S. ., Kazi, K. ., & Almas, S. (2022). Maternal Obesity & Feto-Maternal Outcomes: Maternal Obesity & Feto-Maternal Outcomes. Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.588>

*Corresponding Author:

Shazia Rani
Liaquat University of Medical & Health Sciences,
Jamshoro
drshaziakhan2003@yahoo.com

Received Date: 22nd June, 2022

Acceptance Date: 28th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Obesity has become a "silent epidemic and its prevalence is increasing in pregnant women.

Objective: This study aims to highlight the impact of maternal obesity on the fetal and maternal outcome. **Methods:** The study was conducted on 320 pregnant women in their first trimester with viable singleton pregnancy at Department of Gynecology & Obstetrics, Liaquat University of Medical & Health Sciences, Jamshoro. The obese group (BMI > 25) of 160 women, were compared for feto-maternal outcome, with parity matched 160 women in non-obese group (BMI < 25). **Results:** There was increased incidence of antepartum, intrapartum and fetal complications in obese group as compared to non-obese group. Preeclampsia was seen in 42.1% vs 14.1%, GDM in 14.5% vs 10.3%, induction of labor in 31.9% vs 13.3%, in obese as compared to non-obese respectively. Lower segment caesarean second (37.5% vs 13.8%), macrosomia (22.4% vs 1.3%), shoulder dystocia (18.4% vs 3.8%), birth asphyxia (11.8% vs 5.1%) and neonatal intensive care unit (NICU) admission (12.7% vs 6.6%) were more common in obese as compared to non-obese. **Conclusion:** Maternal obesity is a risk factor for many antepartum, intrapartum, postpartum and fetal complications. All attempts should be made to prevent obesity in women of childbearing age" and to encourage weight loss before pregnancy.

INTRODUCTION

Obesity has become "a silent epidemic, a major public health issue and is likely to remain so for the foreseeable future. It has become a worldwide phenomenon cutting across regional and economic barriers. It contributes to the development of several chronic diseases including type 2 diabetes mellitus, hypertension, coronary heart disease, and stroke. As per WHO, it is a "killer disease" at par with HIV and malnutrition. The rate of obesity in the general population is increasing drastically. The WHO estimated that in 2016, more than 1.9 billion adults, 18 years and older, were overweight. Of these over 650 million were obese [1]. In developing countries like India, obesity often co-exists

with under nutrition leading to double burden [2]. Body mass index (BMI) is the most commonly used parameter for measuring obesity at population level. WHO defines obesity as BMI > 30 for the world population [1]. However, this value could be misleading when comparing the Western countries to Asian Pakistani population. This is because of the difference in the phenotype and general body structure of the two diverse set of people in East and West. Pakistani people are obese at a lower BMI than specified for Western people. Recent studies have also shown that Asian Pakistani have more pre-disposition for truncal obesity and the risk of complications for Asians is

well below the cut-off values of BMI recommended by WHO, and thus for the Pakistani population, BMI > 25 is defined as obesity [3]. Many studies have observed that maternal obesity can result in adverse outcomes for both women and fetuses like increase in the risk of miscarriage, gestational diabetes mellitus (GDM), gestational hypertension and preeclampsia [4]. It has also been associated with prolonged pregnancies, prolonged labor, two-fold increased risk for a caesarean delivery, increased incidence of post-natal infections with prolonged hospital stay [5, 6]. Obesity is often associated with a high risk of adverse neonatal outcomes including stillbirth, birth defects like neural tube defects, abdominal wall defects etc., neonatal intensive care admissions and perinatal mortality rates [7, 8]. Furthermore, long term studies demonstrate that having an obese mother increases the risk of child growing up to be obese themselves, thereby possibly inducing a transgenerational effect [9]. With alarmingly increasing prevalence of obesity in India, the need to determine its effect on maternal and fetal outcome is increasing. This study aimed to highlight the impact of maternal obesity on the outcome of singleton pregnancy in otherwise uncomplicated singleton women in Pakistani population.

METHODS

The study was conducted on 320 pregnant women in their first trimester with viable singleton pregnancy. Women with pre-existing hypertension, diabetes, heart disease, thyroid disorders or any other chronic illness; bad obstetrics history or prior caesarean second were excluded from the study. They were categorized into two groups: obese group comprising of 160 women with BMI > 25 and non-obese group comprising of 160 women with BMI < 25. They were followed up for feto-maternal outcome. Routine antenatal care was given as per hospital protocol. Maternal outcome variables included were antepartum complications (miscarriages, GDM, pre-eclampsia, eclampsia), onset of labor (spontaneous, induced), mode of delivery (vaginal, caesarean, instrumental) and postpartum complications (postpartum hemorrhage, wound sepsis, prolonged hospital stay). Perinatal outcome variables included were birth weight, intrauterine deaths (IUDs), stillbirth, macrosomia and NICU admissions. All results were analyzed statistically with the help of parametric and non-parametric tests, wherever applicable. A p-value of < 0.05 was considered as statistically significant.

RESULTS

Table 1 shows the mean age was slightly higher in obese group (26.7 years) as compared to non-obese group (24.55 years), p-value 0.001. Obesity may cause reduced fertility that may be a probable cause of obese women being older

than non-obese ones. Parity was similar in both the groups (p-value 0.223).

Parameters	Non-obese group	Obese group	p-value
BMI (Mean+ SD)	22.4 +1.45	30.9+1.48	
Mean age	24.55 years	26.7 years	
Primary	35%	30%	
Multiparity	65%	70%	0.001
Non Vegetarian	83.8%	87.5%	0.223
Vegetarian	16.2%	12.5%	0.499
Lipid Profile Deranged	2.5%	10%	0.05

Table 1: Profile of women in both groups

Table 2 show that there was increased incidence of antepartum complications in obese group as compared to non-obese group. The occurrence of gestational hypertension and preeclampsia was significantly more in the obese group (p-value < 0.001). The proportion of miscarriage (p-value 0.246), APH (p-value 0.225) and gestational diabetes mellitus (p-value 0.426) were more in the obese group; though it was not statistically significant.

Parameters	Non-obese group	Obese group	p-value
Spontaneous abortion	4(2.5%)	10 (6.2%)	0.246
Preeclampsia	22(14.1%)	64(42.1%)	<0.001
GDM	16(10.3%)	22(14.5%)	0.426
Intrauterine growth restriction (IUGR)	10(6.4%)	8(5.3%)	0.777
Antepartum hemorrhage (APH)	4(2.6%)	10 (6.7%)	0.225

Table 2: Antenatal complications in both groups

Table 3 show the difference in the onset of labor as well as mode of delivery, between the two groups was significant. Proportion of pregnant women having induced labor was more in the obese group as compared to non-obese group. The p-value was 0.007 making this correlation significant. Also, the rate of caesarean second was significantly higher in the obese group (37.5%) when compared to the non-obese group (13.8%), p-value < 0.001. The complication of shoulder dystocia was observed significantly more in obese group (18.4%) than in non-obese group (3.8%), p-value 0.004. Postpartum complications, like postpartum hemorrhage was more in obese group (16%) than in non-obese group (9%). But it was statistically not significant; p-value = 0.188. The wound sepsis was significantly higher in obese group (28%) than in non-obese group (9.5%), p-value 0.009. Thus, prolonging hospital stay in the obese group. It was found that the obese group had significantly longer duration of stay in the hospital (mean stay 3.34 + 2.04) than the non-obese group (2.44 + 1.65), p-value was 0.002.

Parameters	Non-obese group	Obese group	p-value
Induction of Labour	20(13.3%)	44(31.9%)	0.007
LSCSS	22(13.8%)	60(37.5%)	0.006
houlder dystocia	06(3.8%)	28(18.4%)	0.004
Maternal injury	18(11.5%)	30(20.0%)	0.150
Wound sepsis	08(5.1%)	28(18.7%)	0.009
PPH	14(9.0%)	24(16.0%)	0.188
Mean hospital stay	2.44 + 1.65	3.34 + 2.04	0.002

Table 3: Intrapartum complications in both groups

Table 4 shows that in perinatal outcomes, the mean birth weight in the obese group (3.29 + 0.4603 Kg) was significantly more than in the non-obese group, (2.75 + 0.5960) ($p < 0.001$). The proportion of macrosomia babies were observed significantly more in the obese group (p -value < 0.001). Thirteen percent neonates, obese group required NICU admission compared to 6.6% neonates in non-obese group, the difference was not statistically significant (p -value 0.19). In obese group, there were three (4%) IUDs while in non-obese group, there were two (2.6%) IUDs. The proportion of IUDs was more in obese group than non-obese group; but p -value was 0.62 making this difference insignificant.

Parameters	Non-obese group	Obese group	p-value
Mean Baby Weight	2.756 + 0.460	3.291 + 0.5960	< 0.001
IUDs	34(2.6%)	6(3.9%)	0.628
Macrosomia	2(1.3%)	34(22.4%)	< 0.001
Birth asphyxia	8(5.1%)	18(11.8%)	0.134
NICU admission	10(6.6%)	18(12.7%)	0.208

Table 4: Perinatal outcomes in both groups.

DISCUSSION

This study demonstrates that maternal obesity can result in adverse outcomes for both mother and fetuses like increase in the risk of miscarriage, gestational diabetes, gestational hypertension, preeclampsia, sudden IUD, macrosomia, shoulder dystocia, and higher caesarean rates. The rate of miscarriage was seemingly more in obese group (6.2% vs 2.5%) though not statistically significantly. Recent evidence indicate that obese women undergoing infertility treatment are at increased risk of spontaneous miscarriage [10]. However, this point is controversial. Roth et al conducted a study in 494 patients to ascertain whether BMI affects first- trimester pregnancy outcome in patients with infirmity [11]. It is concluded that the likelihood of a spontaneous abortion in singleton gestations in the first trimester, after treatment for infertility, was not affected by BMI. In this study, the number of pregnant women developing gestational hypertension and preeclampsia remained significantly high in obese group (42.1%) as compared to non- obese group (14.1%), p -value < 0.001 . Similarly, Dasgupta et al., in his prospective cohort study found that the incidence of gestational

hypertension and pre-eclampsia/eclampsia was significantly higher in obese (36.9%) compared to normal subjects (16.1%) [12]. Walsh et al., concluded both obesity and preeclampsia are associated with increased markers of inflammation such as C-reactive protein and inflammatory cytokines, tumor necrosis factor- α , interleukin-6, and interleukin-8 [13]. These findings suggest that obesity is a risk factor for pre-eclampsia because of pre-existing inflammation. This study does not show significant correlation between obesity and GDM, but still GDM cases were found more in obese category (14.5%) than non-obese (10.3%), p - value was 0.426. This may be because of smaller sample size and increased number of GDM complicated pregnancies in non-obese group than previous studies. Chu SY et al., in a meta-analyses estimated the risk of GDM in maternal obesity and their findings indicate that high maternal weight is associated with a substantially higher risk of GDM [14]. Obesity is considered to be an insulin resistant state, and thus accentuates the insulin resistance of normal pregnancy. Obese women with GDM are more likely to need insulin to achieve optimum glycemic control, as compared to women with normal BMIs, and the use of insulin in these pregnant women is also associated with better pregnancy outcome. In present study, although the proportion of pregnant women having genital infection remained high in the obese group but the p -value was 0.062 making this correlation insignificant. Sebire et al., also concluded from their study that genital tract infections are more common in obese compared to non-obese pregnant women [15]. Obesity is associated with higher incidence of induction of labor, as seen with many studies conducted earlier. Proportion of pregnant women having induced labor were more in the obese group (31.9%) as compared to non-obese group (13.3%), p -value was 0.007. The indication was mainly hypertension, post-datism and diabetes related complications. Robinson et al., also found increased rates of labor induction in obese group when compared to non-obese groups (32.1% in obese and 19.3% in non-obese) [16]. Similarly, Athukorala et al., in their study found that the overweight and obese women were more likely to be induced than women with a normal BMI (RR: 1.33 [95%CI 1.13, 1.57], $p = 0.001$ and RR 1.78 [95%CI 1.51, 2.09], $p < 0.0001$ respectively). 17 S Arrowsmith and colleagues in their study found that with increase in maternal BMI there was a dose dependent increase in number of women having induction of labor [18]. Results of study showed much higher rates of caesarean second in obese women as compared to non-obese (37.5% vs 13.8%). Although, the rates of operative vaginal delivery were lower in the obese groups. This is likely due to the higher caesarean delivery rates in the obese groups and the reluctance to perform operative

vaginal deliveries in this population because of the increased risk of shoulder dystocia. Similarly, Robinson et al., also found that obese women had a higher rate of caesarean delivery, with the adjusted OR increasing with increased maternal weight (moderate obesity: adjusted OR 1.60, 95% CI 1.66–1.83; severe obesity: adjusted OR 2.46, 95% CI 2.11–2.85) [16]. Obese women were less likely to have operative vaginal deliveries. Also, in a population-based study conducted by Sheiner et al., the association between maternal obesity and caesarean section remained significant [19]. In an observational study conducted by Barau et al., it was found that there is a linear association (X2 for linear trend, $P < 0.001$) between maternal corpulence and risk of caesarean deliveries, the leanest mothers having the best rate of vaginal delivery [20]. The obese women in our study are more than twice likely to deliver by caesarean due to various reasons like labor dystocia, macrosomia and poor myometrium contractility. In this study, the complication of shoulder dystocia was observed significantly more in obese group (18.4%) than in non-obese group (3.8%), p -value-0.004. Similarly, Majouni et al., concluded in their retrospective study that maternal obesity (OR; 95% CI: 3.6; 2.1–6.3) was a predictive of shoulder dystocia [21]. Also, Usha Kiran et al., found that the women in obese group were four times more likely to have shoulder dystocia [22]. The macrosomia associated with obesity being the main contributing factor. It has also been suggested that obesity leads to an increase in maternal so issue inside the pelvis, which narrows the birth canal. Regarding maternal injuries, we did not find any significant association of high BMI with maternal injuries in our study. Dasgupta et al., also found no significant increase in perineal tears, C-section angle extensions and other maternal injuries among obese women in their study ($p > 0.05$) [12]. Similarly, Beyer et al., 2011 showed that there was no difference between the obese and non-obese group in the rate of injuries during delivery though foetal birth weight increased significantly with higher BMI [23]. The high rate of caesarean delivery may be a contributory factor in obese group as the vaginal delivery is avoided with the resultant less likelihood of injuries. Obesity was also associated with higher incidence of wound sepsis and episiotomy infection and had significantly longer duration of stay in the hospital. Hence, increasing BMI was associated with an increased risk of wound complications. Similarly, Athukorala et al., concluded in their study that obese women were more likely than women with a normal BMI to require antibiotics for a wound infection (RR 2.77 [95% CI 1.11, 6.96], $p = 0.03$) [17]. Fetal complications are also observed to be increased in obese pregnant women. The mean birthweight was significantly increased for the obese group compared to the non-obese group. Similarly,

Mamun et al 2011, [24] found that women who were obese prior to pregnancy and women who gained excess weight during pregnancy were at greater risk for higher birth weight difference. In this study, the proportion of macrosomic babies was observed more in the obese group (p -value < 0.001). Dasgupta et al., also found that there was a significant association between macrosomia and morbid obesity [12]. Sheiner et al., concluded that after having adjusted for diabetes mellitus, no significant association was found between macrosomia and obesity alone [19]. In this study, there was a significant association between macrosomia and obesity. Also many women who delivered macrosomic babies; had developed GDM. Incidences of perinatal mortality were relatively high in the obese group as compared to non-obese group, though statistically insignificant. Sebire et al., [15] found that maternal obesity was associated with a higher foetal death rate. In this study the cause of IUD in the non-obese group was PIH with foetal growth restriction in one case and the other was probably because of post-datism with meconium aspiration. In the obese group, the probable causes of IUDs were preeclampsia, GDM, deranged Doppler, etc. The cause of stillbirth was birth asphyxia in two cases and one case had unexplained aetiology". From this study, we can't conclude that obesity is an independent risk factor for IUD and stillbirth; but we can say that due to more emphasis of adequate antenatal checkups and routine investigations, the rates of IUD and stillbirth have declined compared to the previous studies.

CONCLUSIONS

Present study supports that "obesity is associated with deleterious effect on feto-maternal outcome. In spite of the limitations of this study in terms of small sample size and short span of me it can be concluded that obesity is a risk factor for many antepartum, intrapartum, postpartum and fetal complications. In order to minimize the adverse effects of obesity on both mother and fetus, appropriate multidisciplinary management should be done.

REFERENCES

- [1] <https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight> Error! Hyperlink reference not valid.
- [2] Mendez MA, Monteiro CA, Popkin BM. Overweight exceeds underweight among women in most developing countries. *Am J Clin Nutr.* 2005 Mar;81(3):714–21. doi: 10.1093/ajcn/81.3.714.
- [3] Strebkova EA, Alekseeva LI. OSTEOARTHRITIS AND METABOLIC SYNDROME..
- [4] Sahu MT, Agarwal A, Das V, Pandey A. Impact of maternal body mass index on obstetric outcome. *J Obstet Gynaecol Res.* 2007 Oct;33(5):655–9. doi:

- 10.1111/j.1447-0756.2007.00646.x.
- [5] Cedergren MI. Maternal morbid obesity and the risk of adverse pregnancy outcome. *Obstet Gynecol.* 2004 Feb;103(2):21924. doi:10.1097/01.AOG.0000107291.46159.00.
- [6] Kabiru W, Raynor BD. Obstetric outcomes associated with increase in BMI category during pregnancy. *Am J Obstet Gynecol.* 2004 Sep;191(3):928-32. doi: 10.1016/j.ajog.2004.06.051.
- [7] Callaway LK, Prins JB, Chang AM, McIntyre HD. The prevalence and impact of overweight and obesity in an Australian obstetric population. *Med J Aust.* 2006 Jan 16;184(2):56-9. doi: 10.5694/j.1326-5377.2006.tb00115.x.
- [8] Deierlein AL, Siega-Riz AM, Adair LS, Herring AH. Effects of pre-pregnancy body mass index and gestational weight gain on infant anthropometric outcomes. *J Pediatr.* 2011 Feb;158(2):221-6. doi: 10.1016/j.jpeds.2010.08.008.
- [9] James WP. WHO recognition of the global obesity epidemic. *Int J Obes (Lond).* 2008 Dec;32 Suppl 7:S120-6. doi: 10.1038/ijo.2008.247.
- [10] Wang JX, Davies M, Norman RJ. Body mass and probability of pregnancy during assisted reproduction treatment: retrospective study. *BMJ.* 2000 Nov 25;321(7272):13201. doi:10.1136/bmj.321.7272.1320.
- [11] Roth D, Grazi RV, Lobel SM. Extremes of body mass index do not affect first-trimester pregnancy outcome in patients with infertility. *Am J Obstet Gynecol.* 2003 May;188(5):1169-70. doi: 10.1067/mob.2003.285.
- [12] Dasgupta A, Harichandrakumar KT, Habeebullah S. Pregnancy outcome among obese Indians—a prospective cohort study in a tertiary Care Centre in South India. *International journal of scientific study.* 2014;2(2):13-8.
- [13] Walsh SW. Obesity: a risk factor for preeclampsia. *Trends Endocrinol Metab.* 2007 Dec;18(10):365-70. doi: 10.1016/j.tem.2007.09.003.
- [14] Chu SY, Callaghan WM, Kim SY, Schmid CH, Lau J, England LJ, Dietz PM. Maternal obesity and risk of gestational diabetes mellitus. *Diabetes Care.* 2007 Aug;30(8):2070-6. doi: 10.2337/dc06-2559a
- [15] Sebire NJ, Jolly M, Harris JP, Wadsworth J, Joffe M, Beard RW, Regan L, Robinson S. Maternal obesity and pregnancy outcome: a study of 287,213 pregnancies in London. *Int J Obes Relat Metab Disord.* 2001 Aug;25(8):1175-82. doi: 10.1038/sj.ijo.0801670.
- [16] Robinson HE, O'Connell CM, Joseph KS, McLeod NL. Maternal outcomes in pregnancies complicated by obesity. *Obstet Gynecol.* 2005 Dec;106(6):1357-64. doi: 10.1097/01.AOG.0000188387.88032.41.
- [17] Athukorala C, Rumbold AR, Willson KJ, Crowther CA. The risk of adverse pregnancy outcomes in women who are overweight or obese. *BMC Pregnancy Childbirth.* 2010 Sep 17;10:56. doi: 10.1186/1471-2393-10-56.
- [18] Arrowsmith S, Wray S, Quenby S. Maternal obesity and labour complications following induction of labour in prolonged pregnancy. *BJOG.* 2011 Apr;118(5):578-88. doi: 10.1111/j.1471-0528.2010.02889.x.
- [19] Sheiner E, Levy A, Menes TS, Silverberg D, Katz M, Mazor M. Maternal obesity as an independent risk factor for caesarean delivery. *Paediatr Perinat Epidemiol.* 2004 May;18(3):196-201. doi: 10.1111/j.1365-3016.2004.00557.x
- [20] Barau G, Robillard PY, Hulsey TC, Dedecker F, Laffite A, Gérardin P, Kauffmann E. Linear association between maternal pre-pregnancy body mass index and risk of caesarean section in term deliveries. *BJOG.* 2006 Oct;113(10):1173-7. doi: 10.1111/j.1471-0528.2006.01038.x.
- [21] Mazouni C, Porcu G, Cohen-Solal E, Heckenroth H, Guidicelli B, Bonnier P, Gamberre M. Maternal and anthropomorphic risk factors for shoulder dystocia. *Acta Obstet Gynecol Scand.* 2006;85(5):567-70. doi: 10.1080/00016340600605044.
- [22] Usha Kiran TS, Hemmadi S, Bethel J, Evans J. Outcome of pregnancy in a woman with an increased body mass index. *BJOG.* 2005 Jun;112(6):768-72. doi: 10.1111/j.1471-0528.2004.00546.x.
- [23] Beyer DA, Amari F, Lüdders DW, Diedrich K, Weichert J. Obesity decreases the chance to deliver spontaneously. *Arch Gynecol Obstet.* 2011 May;283(5):981-8. doi: 10.1007/s00404-010-1502-5.
- [24] Mamun AA, Callaway LK, O'Callaghan MJ, Williams GM, Najman JM, Alati R, Clavarino A, Lawlor DA. Associations of maternal pre-pregnancy obesity and excess pregnancy weight gains with adverse pregnancy outcomes and length of hospital stay. *BMC Pregnancy Childbirth.* 2011 Sep 6;11:62. doi: 10.1186/1471-2393-11-62.



Original Article

Relationship Between Microalbuminuria and Activity of the Disease in Patients Suffering from Ulcerative colitis

Murad Ali¹, Maryam Ashfaq², Tariq Tahir Butt³, Bushra Gohar Shah^{4*} and Hammad Ur Rehman Bhatti⁵

¹Department of Medicine, Bacha Khan Medical College, Mardan, Pakistan

²Pakistan Institute of Medical Sciences, Islamabad, Pakistan

³Department of Medicine, Sialkot Medical College, Sialkot, Pakistan

⁴Department of Physiology, Sahara Medical College, Narowal, Pakistan

⁵Department of Medicine, Islam Medical and Dental College, Sialkot, Pakistan

ARTICLE INFO

Key Words:

Heart Health, Healthy Diet, Coronary Artery, Bypass, Patients

How to Cite:

Ali, M. ., Ashfaq, M. ., Tahir Butt, T. ., Gohar Shah, B. ., & Bhatti, H. U. R. (2022). Relationship Between Microalbuminuria and Activity of The Disease in Patients Suffering from Ulcerative Colitis: Microalbuminuria and Activity of the Disease in Patients Suffering from UC. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.531>

***Corresponding Author:**

Bushra Gohar Shah

Department of Physiology, Sahara Medical College, Narowal, Pakistan
arbhushragoharshah@gmail.com

Received Date: 8th June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Ulcerative Colitis (UC) is a gastrointestinal issue, in which inflammation of the tract takes place. The disease level may be severe, moderate, or mild, so the detection method was selected according to the disease level. Finding the disease level and diagnostic method of UC is challenging. **Objective:** To find out a non-interfering way for the assessment of the activity of the disease, which is particularly important for the detection of UC. Therefore, the main goal of this study is to find a safe method for the determination of disease severity in the patients suffering from UC. **Methods:** For this study, 93 patients were selected suffering from UC (UC). For the assessment of all the specific parameters, C-Reactive Protein (CRP), Rate of erythrocytes sedimentation (ESR) and calprotectin in fecal, commonly used turbidimetric-immunoassay, Enzyme-linked immunosorbent assay (ELISA) and Westergren technique was used. A partial clinical score was used for the estimation of disease severity and the level of microalbuminuria was used determined by the immuno-turbidimetric way. **Results:** Among 93 patients suffering from UC, 37 patients were male and 56 patients were female. The average age of the patients was 40 plus. Microalbuminuria was present in more than 52 % of the patients. The presence of microalbuminuria depends upon the severity level of the disease, the most severe patients with Inflammatory bowel disease (IBD) have a large amount of microalbuminuria. The CRP, rate of sedimentation of erythrocytes, and other proteins level also vary with disease level. **Conclusion:** To measure the activity or severity level of the UC, microalbuminuria is considered a safe or non-interfering marker.

INTRODUCTION

Ulcerative colitis (UC) is caused by inflammation, some parts of the tract may rupture. The level of the disease varies, it may be severe, moderate, or mild. For the treatment of UC, the disease level is considered first. It is quite difficult to estimate the activity level of the disease. For the estimation of disease, biopsy and endoscopy can be done, it can also be used for diagnostic purposes [1-4]. Several different other factors are studied for the estimation of disease progression levels. Among these factors, C-reactive protein (CRP), rate of erythrocytes sedimentation (ESR), and calprotectin are most common.

As a result of microalbuminuria, inflammation takes place in different parts of the gastrointestinal tract, the inflammation of these parts indicates the malfunction of the vascular system and initiation of many kidney-related issues. Sometimes, rheumatoid arthritis is also considered an indication of UC. When the disease caused by microalbuminuria became severe, it leads to the condition termed inflammatory bowel disease (IBD). Microalbuminuria has a link with the histopathology of the intestine [5-9]. The level of microalbuminuria varies in different disease levels, different methodologies are tried

and a number of research groups are trying to find the best possible method for the identification of the progression level of the disease [10]. Different other non-toxic confirmatory characteristic indicators are also estimated to find the inflammatory region within the gastrointestinal tract and to find out the relation between inflammation and microalbuminuria. Only at a limited level, these studies are being done in different labs, but still, more work is needed to find out the non-invasive methods for the identification of the severity level of the disease as well as to find out the more related methods for the identification of UC more accurately [11-15].

METHODS

It was a retrospective study conducted at medicine department of Sialkot Medical College for the duration of six months from December 2020 to May 2021. To proceed with this study 93 patients were selected, all of the patients were suffering from an infection of the gastrointestinal tract, and further, their infection was confirmed by an available diagnostic test which reveals that all of them are suffering from UC with the different disease severity level. Among these 93 patients, 37 were males and 56 females. The age of the patients was also considered, all of the patients had an average age of more than forty years. Some of the patients also had inflammatory bowel disease, and some of the patients have a number of diseases associated with the gastrointestinal tract such as microalbuminuria, which also comprised of diabetes, thrombosis, and the number of disorders related to the kidney such as nephrotic disease, amyloidosis, and renal vein inflammation. 94 % confidence level was considered for the estimation of sample specimen size. For microalbuminuria level 0.8 standard difference was kept for the different groups. For 93 patients, attrition rate was 30 % for the patients having more severe disease levels. All the related parameters were calculated for all patients. Verbal and written information was taken from the patients on the behalf of their consent. To measure the UC activity rate, a partial clinic score was used. The respective score for each patient was calculated on the basis of different factors like bleeding through the rectum, frequency of stool, and physician prediction about the severity level of the disease. Each of the levels was given a score from 0 to 3. The lowest score was 0 for mild, 1 for moderate, 2 for severe, and 3 for more acute levels. The disease score was predicted by estimation of all the related factors, usually, 3 factors are considered mainly as mentioned above. For the estimation of the level of the microalbuminuria immunoturbidimetric method was used. The level of microalbuminuria was measured two times in two days consecutively, then the average of both values were taken

for the estimation of microalbuminuria. CRP level and ESR were also calculated for the prediction of final results by using different immune-based assays like ELISA. Then for the prediction of the final results, statistical tests were applied. For different values, the average was taken as well as standard deviation was also calculated, and the one-way ANOVA was also performed to compare microalbuminuria level and its association with the progression of the disease. The p-value of 0.05 was selected to obtain significant results.

RESULTS

Table 1 shows the characteristics of all patients participated in this study. There were total 93 patients that contributed in this study. Among 93, 37 (39%) were male and 56 (60%) were female. The average age of the patients was 40 years \pm 13 years. Among the 56 female, 53% had albuminuria. The rate of this disease was much high in patients that had active illness in comparison with patients that had inactive form of IBD.

Characteristics	Total participants (93)	Active (47)	Inactive (46)	p- value
Age in years	40 years \pm 13	44 \pm 13	4100 \pm 14	0.6
Sex of patients				
Male	37 (39%)	17 (36%)	19 (40%)	0.9
Female	56 female (60%)	29 (61.2%)	28 (59%)	
Microalbuminuria				
Disease cases	46 (50%)	47 (100%)	8 (7%)	0.005
Negative	44 (48%)	0 (0%)	43 (92%)	
Extra intestinal manifestation				
Positive patients	3 (25%)	15 (31%)	8 (17%)	0.14
Healthy	67 (76%)	33 (70%)	38 (83%)	

Table 1: characteristic features of participants

Characteristics	Total participants (mean \pm SD)	Active (mean \pm SD)	In-active (mean \pm SD)	p- value
CRP (in ng / L)	4.2 \pm 3.2	5.87 \pm 1.08	0.37 \pm 0.33	< 0.005
ESR (mm / hr)	36.52 \pm 34.5	560.2 \pm 14.9	5.77 \pm 3.09	< 0.001
Urinary albumin mg / L	99 \pm 110.1	198.1 \pm 76	12.1 \pm 13.2	< 0.55
Urine creatinine mg / dL	950.1 \pm 20	970.1 \pm 193.3	934 \pm 261.3	< 0.05
Serum calprotectin in ng / ml	0.1331 \pm 370.1	650 \pm 261.1	13.1 \pm 11.1	< 0.001

Table 2: Laboratory characteristic comparison between active and inactive participants suffering from UC

Table 2 shows the values of laboratory profiling comparison done between the patients that contributed in this study. It was observed that there were quite high significance noted among patients with active and patients with inactive disease. (p= 0.05) exception was seen in case of urine creatinine (p=0.05).

Characteristics	N	Mean
Remission score	32	11.0 ± 13.11
Mild and moderate activity	26	95.1 ± 15.1
Intense activity	27	219.1 ± 18

Table 3: Urine albumin level comparison with the severity of UC

DISCUSSION

In this study, the rate of microalbuminuria is checked in patients with UC and it is then correlated with the activity of the disease. As per our studies, there were 53 patients that were included in the study that suffered from albuminuria. According to some previous studies, 52 % of the patients that had IBD also had proteinuria [16-18]. Babayeva and his fellows found that in 60% of their patients with UC, the incidence of albuminuria was seen. In a study carried out by Mahmud and his fellow workers, there were 100% patients that had microalbuminuria and IBD at the same time. The different observations found by scientist in these studies may be because of different degree of severity of the disease, like the marker of proteinuria, Crohn's illness vs UC and the use of any other form of drug by the person [19]. As per previous findings the level of CRP and the condition of microalbuminuria are strongly linked to each other in case of UC patients. However, in a study carried out by Muhmud and his fellows they found that there is need to check the link between microalbuminuria and the activity of the disease in case of UC patients [17]. In another study carried out by Herrlinger and his colleagues, they found that there exists prominent sort of link between proteinuria and the activity of disease in patients that are suffering from IBD [18]. Derici and his fellows later on reported that there is present a very strong variation in the albumin levels in the urine among the patients that are suffering from active form of UC if its compared with the control [10]. Moreover, they also told that the differences that were found between the patients actively suffering from disease and the patients that have in active disease are not statistically significant [19]. The differences that were found between different studies are mainly due to variations in a lot of parameters like drug administration, activity of the disease and the status of the inflammation in case of patients. There are a number of mechanisms that can help explain why such variations exists among patients [20].

One of the proposed assumption says that the mechanism that will causes association between activity of disease and microalbuminuria in UC patients is may be due to enhanced levels of cytokines. These cytokines can play a significant role in disturbing the mucosal sulphated compounds glycosaminoglycan that are present in the renal microvasculature where they speed up the vascular permeability of the albumin [21-23]. According to these studies, there are some of the limitations that could be improved to get better results. One of the limitations is that

in the mentioned study the activity of the disease was measured by using a MC score (mayo clinic score). Though there is no doubt that this is one of the most reliable and valid methods which can tell us about the activity of the disease but still if we could use a more reliable method, or more valid ways that can help provide us information about the disease activity in UC patients then the results could be improved in a much better way. Like if histological grading was done for the patients it can help decide results with more precision [24]. Also in this study one more point to consider was that the effect or response of different sort of drugs on level of microalbuminuria should also be checked. In this study the data was analyzed by using immunoturbidimetric ways. First sample was checked in the morning repeatedly for two days. Then mean was considered as a value reported as urinary level of albumin. On the basis of National Renal association criteria, the serum calprotectin level, CRP, ESR were calculated by using the conventional ways of immunoassays. To check the significance of non-invasive lab characteristics that can predict about the degree of the disease and the rate of inflammation and then the strong link between disease activity and microalbuminuria in UC patients ESR and CRP were used. The aim was to look for the disease activity index and the degree of albuminuria in persons suffering from UC.

CONCLUSION

The findings show that the microalbuminuria can be used as a marker for finding the activity of the disease in case of UC patients. However, there is need for further longitudinal studies for further confirmation.

REFERENCES

- [1] Khosla N, Sarafidis PA, Bakris GL. Microalbuminuria. *Clin Lab Med.* 2006 Sep;26(3):635-53, vi-vii. doi: 10.1016/j.cll.2006.06.005.
- [2] Mahmud N, Stinson J, O'Connell MA, Mantle TJ, Keeling PW, Feely J, et al. Microalbuminuria in inflammatory bowel disease. *Gut.* 1994 Nov;35(11):1599-604. doi:10.1136/gut.35.11.1599.
- [3] Mahmud N, McDonald GS, Kelleher D, Weir DG. Microalbuminuria correlates with intestinal histopathological grading in patients with inflammatory bowel disease. *Gut.* 1996 Jan;38(1):99-103. doi: 10.1136/gut.38.1.99.
- [4] Masnadi Shirazi K, Khayati S, Baradaran Binazir M, Nikniaz Z. Relationship between Microalbuminuria and Disease Activity in Patients with UC. *Middle East J Dig Dis.* 2020 Jan;12(1):34-38. doi: 10.15171/mejdd.2020.161.
- [5] Marvisi M, Bassi E, Bonassi R, Civardi G, Delsignore R. DLCO correlates with intestinal inflammation in UC,

- but albuminuria does not. *Minerva Gastroenterol Dietol.* 2007 Dec;53(4):321-7.
- [6] Nakamura T, Kawagoe Y, Matsuda T, Ueda A, Ueda Y, Takahashi Y, et al. Effect of granulocyte and monocyte adsorption apheresis on urinary albumin excretion and plasma endothelin-1 concentration in patients with active UC. *Blood Purif.* 2004;22(6):499-504. doi: 10.1159/000081896.
- [7] Mahmud N, O'Toole D, O'Hare N, Freyne PJ, Weir DG, Kelleher D. Evaluation of renal function following treatment with 5-aminosalicylic acid derivatives in patients with UC. *Aliment Pharmacol Ther.* 2002 Feb;16(2):207-15. doi: 10.1046/j.1365-2036.2002.01155.x.
- [8] Szigeti N, Markó L, Molnár GA, Fábián G, Cseh J, Mohás M, et al. Microalbuminuria in inflammatory bowel diseases using immunoturbidimetry and high-performance liquid chromatography. *Acta Gastroenterol Belg.* 2009 Oct-Dec;72(4):394-401.
- [9] Stepina EA, Kuposova KA, Khlynova OV, Tuev AV, Vasilets LV. [Systemic Inflammation Markers and Microalbuminuria in Inflammatory Bowel Diseases]. *Eksp Klin Gastroenterol.* 2016;(3):15-9.
- [10] Derici U, Tuncer C, Ebinç FA, Mutluay R, Yakaryılmaz F, Kulaksizoglu S, et al. Does the urinary excretion of alpha1-microglobulin and albumin predict clinical disease activity in UC? *Adv Ther.* 2008 Dec;25(12): 1342-52. doi: 10.1007/s12325-008-0109-8.
- [11] Loddo I, Romano C. Inflammatory Bowel Disease: Genetics, Epigenetics, and Pathogenesis. *Front Immunol.* 2015 Nov 2; 6:551. doi: 10.3389/fimmu.2015.00551.
- [12] Gracie DJ, Ford AC. Evidence-based management of UC. *Minerva Gastroenterol Dietol.* 2012 Jun;58(2):87-99.
- [13] Meier J, Sturm A. Current treatment of UC. *World J Gastroenterol.* 2011 Jul 21;17(27):3204-12. doi: 10.3748/wjg.v17.i27.3204.
- [14] Walsh AJ, Bryant RV, Travis SP. Current best practice for disease activity assessment in IBD. *Nat Rev Gastroenterol Hepatol.* 2016 Oct;13(10):567-79. doi: 10.1038/nrgastro.2016.128.
- [15] Glasscock RJ. Is the presence of microalbuminuria a relevant marker of kidney disease? *Curr Hypertens Rep.* 2010 Oct;12(5):364-8. doi: 10.1007/s11906-010-0133-3.
- [16] Niederstadt C, Happ T, Tatsis E, Schnabel A, Steinhoff J. Glomerular and tubular proteinuria as markers of nephropathy in rheumatoid arthritis. *Rheumatology (Oxford).* 1999 Jan;38(1):28-33. doi: 10.1093/rheumatology/38.1.28.
- [17] Mahmud N, Stinson J, O'Connell MA, Mantle TJ, Keeling PW, Feely J, et al. Microalbuminuria in inflammatory bowel disease. *Gut.* 1994 Nov;35(11):1599-604. doi: 10.1136/gut.35.11.1599.
- [18] Herrlinger KR, Noftz MK, Fellermann K, Schmidt K, Steinhoff J, Stange EF. Minimal renal dysfunction in inflammatory bowel disease is related to disease activity but not to 5-ASA use. *Aliment Pharmacol Ther.* 2001 Mar;15(3):363-9. doi: 10.1046/j.1365-2036.2001.00940.x.
- [19] Babayeva GH, Babayev ZM. Frequency of detection of some markers of endothelial dysfunction in patients with inflammatory bowel diseases. *Ter Arkh.* 2018 Apr 19;90(4):12-16. doi: 10.26442/terarkh201890412-16.
- [20] Klein NJ, Shennan GI, Heyderman RS, Levin M. Alteration in glycosaminoglycan metabolism and surface charge on human umbilical vein endothelial cells induced by cytokines, endotoxin and neutrophils. *J Cell Sci.* 1992 Aug;102 (Pt 4):821-32. doi: 10.1242/jcs.102.4.821.
- [21] Murch SH, MacDonald TT, Walker-Smith JA, Levin M, Lionetti P, Klein NJ. Disruption of sulphated glycosaminoglycans in intestinal inflammation. *Lancet.* 1993 Mar 20;341(8847):711-4. doi: 10.1016/0140-6736(93)90485-y.
- [22] Rankine-Mullings AE, Knight-Madden JM, Reid M, Ferguson TS. Gangrene of the digits of the right lower limb in a patient with homozygous sickle cell disease and UC. *Clin Pract.* 2014 Apr 3;4(1):610. doi: 10.4081/cp.2014.610.
- [23] Hasosah M, Matrafi A, Jastaniah W, Alsahafi A, Sukkar G, Satti M, et al. Pediatric Inflammatory Bowel Disease and Hereditary Hemolytic Anemia: A Retrospective Analysis. *Inflamm Bowel Dis.* 2016 Sep;22(9): E34-7. doi: 10.1097/MIB.0000000000000887.
- [24] Qin X. Increased Milk Consumption but Decreased Risk of Crohn's Disease (CD): Critical Evidence Negated Causative Role of *Mycobacterium avium* Subspecies *paratuberculosis* (MAP) in CD. *Inflamm Bowel Dis.* 2016 Sep;22(9): E37-8. doi: 10.1097/MIB.0000000000000892.



Original Article

Awareness Level and Practices of Heart Healthy Diet of Patients Undergoing Coronary Artery Bypass Grafting

 Mujahid ul Islam¹, Imtiaz Ahmad¹, Azam Jan¹, Muhammad Shahid, Bahauddin Khan², Rafat Shakil², Noor Ali Shah¹ and Faizan Ahmad Ali¹
¹Rehman Medical Institute, Peshawar, Pakistan

ARTICLE INFO

Key Words:

CRP, ESR, Microalbuminuria, IBD, UC, Calprotectin

How to Cite:

Islam, M. U. ., Ahmad, I. ., Jan, A. ., Shahid, M., Khan, B. ., Shakil, R. ., Ali Shah, N. ., & Ahmad Ali, F. . (2022). Awareness Level and Practices of Heart Healthy Diet of Patients Undergoing Coronary Artery Bypass Grafting : Heart Healthy Diet of Patients Undergoing Coronary Artery Bypass Grafting . Pakistan BioMedical Journal, 5(6), 195-199. <https://doi.org/10.54393/pbmj.v5i6.577>

*Corresponding Author:

 Mujahid Ul Islam
 Department of Cardiothoracic Surgery, Rehman Medical Institute, Peshawar, Pakistan

 Received Date: 21st June, 2022
 Acceptance Date: 25th June, 2022
 Published Date: 31st June, 2022

ABSTRACT

Change in dietary habits with reduction in specific type of foods with heavy calories may help in prevention of many types of primary and secondary Cardiovascular Diseases (CVD). Coronary artery disease (CAD) is the most common cause of death all over the world and mostly treated by Coronary Artery Bypass Grafting (CABG). The recommended diet according to the guidelines, is high in fruits, vegetables and whole grains and is low in high fats and processed foods. The factors involved in consumption of low-quality diet mainly are lack of public awareness about the role of dietary style in development of CVD, lack of food due to low socioeconomic conditions, cultural and traditional differences of food preparation and availability of poor-quality food in markets. **Objectives:** To assess the level of awareness amongst the patients of coronary artery bypass grafting in its worst form. **Methods:** The study was performed on 91 patients of CAD, admitted for CABG in tertiary care hospital. A questionnaire-based survey was conducted for a period of eight months. All patients admitted for revascularization for CAD were included. Details of patients co morbidities were collected and their socioeconomic status was confirmed from the medical record. They were scored on their general education, knowledge about heart healthy diet according to American Heart Association (AHA) dietary guidelines and their dietary practices were scored healthy or non-healthy based on their answers. **Results:** Among the patients, approximately, 75.82% were males, 96.7% had age above 49 years, half of the patients had some sort of awareness regarding heart healthy diet, 37% were following healthy diet, 50% were partially following and 4.4% were not following at all. **Conclusion:** The awareness of participants regarding heart healthy diet was over all poor and also their dietary practices were even worse and not in accordance to the medical recommendations. There is a need to increase awareness in heart patients regarding healthy diet choices so that their risk of disease progression can be reduced

INTRODUCTION

The greatest cause of death worldwide is cardiovascular disease (CVD) [1]. Every third person in the United States has a CVD of some kind [2]. Nations experience a significant health burden due to CVD. The most widespread kind of CVD is coronary artery disease (CAD), which is also the third most common reason for heart disease-related death [3]. Incidence of the disease is rising day by day because of rapidly changing lifestyles. It has been proved through various studies in different parts of the world that CAD is getting prevalent in US, China, Middle east as well as far east regions [4]. Prevalence of CAD is significantly higher in Pakistan, according to a study conducted at Karachi [5]. The common risk factors for CAD are growing

age, gender, family history of associated co morbid conditions like diabetes, obesity and hypertension (HTN) [6]. Along with all these non-modifiable factors, the significant role of diet could not be neglected. Health outcomes associated with dietary pattern is seen in lots of observational studies which are challenging in a way that measuring the quantity of daily intake and type of food intake in different families cannot be assessed subjectively [7]. Maintenance of caloric balance is the key factor of healthy eating. For cardio- metabolic benefit caloric restricted diet is supported by large number of published reports recently [8]. Dietary composition, quality of food along with avoiding the overconsumption of every nutrient

are important consideration as suggested by emerging evidence. Low-carbohydrate and superior to low-fat diets in maintaining healthy weight balance [9]. Thus, current dietary recommendations primarily based primarily on eating whole food items like total fruits and vegetable intake has been associated with much reduced risk factor of CAD. However, few of the fruits and vegetables like potatoes especially if taken as French fries has no benefits as a subgroup, in prevention of CVD. Role of fibers, folate and potassium containing foods are less studied. Use of whole grain is associated with a lower risk of CVD, whereas refined grain is deficient in many nutrients which are lost during milling process [10]. Modification of dietary intake habits need awareness amongst larger populations which is only possible if the knowledge of impact of food on CAD is thoroughly conveyed to the public. Moreover, the patient's particular knowledge of their own cardiovascular status and risk level match up with the compliance to drug treatment and adjustment to heart friendly lifestyle [11]. However, the awareness of CVD and its risk factors are still low in both primary and secondary prevention practices. Diet and exercise have been promoted as the "best buy" by the WHO to combat the rise in non-communicable diseases (NCDs) worldwide [16]. Therefore, adopting a healthy lifestyle and changing one's behavior are critical preventative measures for many primary and secondary cardiovascular problems. Vegetables, fruits, nuts, whole grains, lean animal protein, and fish should all be part of a balanced diet. Additionally, it reduces consumption of trans fats, red meat, processed red meats, refined carbs, and beverages with added sugar [17]. This study was carried out to help develop recommendations for health practitioners to expand their practice of educating patients about nutrition, specifically for the prevention of CVD.

METHODS

A questionnaire-based survey was conducted in a tertiary care hospital for a period of eight months. All patients admitted for revascularization for CAD were included. They were scored on their general education, knowledge about heart healthy diet according to AHA dietary guidelines and their dietary practices were scored healthy or non-healthy based on their answers. There were two parts of questionnaire. First was, Awareness Section that included 12 questions (Table 1) and the other was practice section that included 13 questions. Patients were asked in their own language. In awareness section, if patient was aware of more than 8 questions they were labeled as AWARE, between 8-6 PARTIALLY AWARE, and if replied to lesser than 6 then labeled as UNAWARE.

Awareness Section: This section was designed with

following questions:

No.	Questions for Awareness of Heart Healthy Diet
1	Do you know what calories are?
2	Do you know the method of calculation of calories?
3	Do you know about the BMI or Ideal Body weight?
4	What should be your ideal body weight according to your height or BMI?
5	Are you aware how much salt to be consume daily?
6	Are you aware of saturated fats and Trans fats or different types of good or bad cholesterol?
7	What is the recommended amount of Trans/saturated fats to be consume daily?
8	Is alcohol good for health or not?
9	Do you know what constitute heart healthy diet?
10	Which grain is good for health?
11	Which type of milk is good for heart health?
12	What is your opinion about soft drink for heart health, Is it good or bad?

Table 1: Questions regarding awareness of heart healthy diet

The second section of questionnaire was labelled as Practices Section (Table 2), in this the level of practices of daily eating habits of patients were assessed by scoring and labelling them 'PRACTICING' if more than 8 points were replied positively, while 'PARTIALLY PRACTICING' label was given if reply falls between 6-8 and in case of less than 6 responses the patient was categorized as 'NON PRACTICING'.

Practice questions: following were the questions in this section:

No.	Questions regarding practices of heart healthy diet by patients
1	Have you ever calculated calories?
2	Have you ever tried to lose weight (BMI)?
3	Your intake of salt? Do you eat eggs?
4	What kind of meat do you eat?
5	Do you drink alcohol?
6	Do you eat vegetables every day?
	Do you eat nuts every day?
7	Do you eat legumes every day?
8	Do you eat fruits every day?
9	Your intake of grain? Do you drink milk?
10	Do you drink soft drinks?

Table 2: Questions regarding practices of heart healthy diet by patients

RESULTS

Total of 91 patients were analyzed these included both males 69 (75.82%) and females 22 (24.17%). Most of the patients were above 40 years i.e. 88 (96.7%). Almost 6.6% participants were fully aware of healthy diet. 41.8% were partially aware and 51.6% had no awareness (Table 1). Regarding practices, only 40.7% were following heart healthy diet practices, 54.9% were partially following healthy diet and 4.4% were not following healthy diet (Table

3). As far as occupation among the patients was observed, 31 patients were having professional jobs, 32 were labors and 28 were unemployed (Table 2). The economic status of the patient was also varied, monthly income of 30 patients were between PKR 12,000-30,000, 34 patients were earning PKR 30k-60K monthly and per month income of 24 patients was above PKR 60,000 (Table 2). 48 (52.7%) were uneducated, 27 (29.7%) did matriculation, 11 (12.1%) did graduation, 5 (5.5%) did postgraduation. 56 patients were doing sedentary jobs while 35 patients were performing laborious jobs (Table 4). One or more of the studied chronic diseases were present as follows i.e., Diabetes 53(58.24%), Hypertension 33(36.26%) and Hyperlipidemia 13(14.28%).

Variables	Frequency	Percentage
Level of Awareness		
Fully Awareness	06	6.6
Partially Awareness	38	41.8
Unaware	47	51.6
Diet Practice		
Healthy Diet	37	40.7
Partially Healthy Diet	50	54.9
Unhealthy Diet	04	4.4

Table 3: Diet Awareness and practice

Variables	Frequency	Percentage
Occupation		
Professional	31	34.1
Labors	32	35.2
No Job	28	30.8
Income		
Up to 6000 Per Month		1.1
6000-12000 Per Month		1.1
12000-30000 Per Month		33.3
30000-60000 Per Month		37.8
More Than 60000 Per Month		26.7
Education		
Illiterate		52.7
Matriculation		29.7
Graduation		12.1
Post-Graduation		5.5
Job Nature		
Office work		51.6
Labor		48.4
Level of Activity		
1-5 per Week	35	38.5
Sedentary	56	61.5

Table 4: Demographic variables of studies population

DISCUSSION

The American Heart Association (AHA) suggests following a balanced dietary pattern that priorities a range of fruits and vegetables, whole grains, low-fat dairy products, skinless poultry and fish, nuts and legumes, and non-tropical vegetable oils in order to maintain optimal heart

health. The group also stresses eating fish high in omega-3 fatty acids (such salmon and trout) at least twice a week, watching portion sizes, and consuming alcohol moderately (i.e., no more than one serving per day for women and no more than two drinks per day for men). The American Heart Association presently advises minimizing sodium, red meat, sweets, and beverages with added sugar. Numerous research investigated the variables linked to patients' ignorance about CVD risk factors. Patients with a body mass index below 24 kg/m², those with a family history of dyslipidemia, older patients, and retirees were all shown to be more conscious of dyslipidemia, according to research by He et al. A lower level of awareness of dyslipidemia was linked to alcohol consumption, cigarette smoking, and physical activity [9]. Patients with a family history of diabetes mellitus and those who regularly exercise were more likely to be aware of the condition, according to research by Wang et al. Smokers and those who consume alcohol were also less likely to be aware of their blood glucose levels [10]. Men and smokers were shown to be less conscious of arterial hypertension, according to Méndez-Chacón et al. Patients' knowledge of arterial hypertension was correlated with a history of ischemic heart disease, stroke, diabetes mellitus, and obesity. Patients were less likely to be unaware of their hypertension if community health workers had visited them at home [20]. Studies conducted in the United States on adults between the ages of 18 and 26 and American Indian women who had previously experienced gestational diabetes revealed a high knowledge score for weight loss (78.5%) and stressed the impact of food and cholesterol on the risk of CVDs. Additionally, women in the French West Indies cited consuming fewer fats (42%), as well as consuming fewer alcoholic beverages (26%), as contributing factors to heart health. Only 50% of Malaysian participants in the study recognized obesity as a risk factor for heart attacks [24-27]. Spreading awareness may be substantially correlated with the differences in knowledge ratings between nations. For instance, the governments of Kuwait and the United Arab Emirates (UAE) make large investments in educating the populace about healthy lifestyles and cardiovascular risk factors. Although some nations, like Malaysia, have started a number of health education efforts, they still require successful, well-thought-out awareness campaigns, particularly with cardiovascular risk factors [24,28,29]. Participants with advanced degrees and jobs had higher knowledge ratings. This result is in line with earlier research [30] that showed rising levels of education, employment, and financial security were associated with greater CVD knowledge. This inference can be clarified by supposing that people with higher education are more cognizant of and capable of

comprehending health-related

CONCLUSIONS

The knowledge of participants regarding heart healthy diet was over all poor and also their dietary practices were even worse and not in accordance to medical recommendations. There is a need to increase awareness in heart patients regarding healthy diet choices so that their risk of disease progression can be reduced.

REFERENCES

- [1] Zhong VW, Ning H, Van Horn L, Carnethon MR, Wilkins JT, Lloyd-Jones DM, et al. Diet Quality and Long-Term Absolute Risks for Incident Cardiovascular Disease and Mortality. *Am J Med.* 2021 Apr;134(4):490-498.e24. doi: 10.1016/j.amjmed.2020.08.012.
- [2] Mendy VL, Vargas R, Cannon-Smith G, Payton M, Enkhmaa B, Zhang L. Food Insecurity and Cardiovascular Disease Risk Factors among Mississippi Adults. *Int J Environ Res Public Health.* 2018 Sep 15;15(9):2016. doi: 10.3390/ijerph15092016.
- [3] Prasad S, Mishra MK, Yadav T. Coronary Artery Disease Awareness: Levels of Socioeconomic Status and Dietary Restriction. *Nepal Journal of Health Sciences.* 2021 Jul 30;1(1): 37-42. doi.org/10.3126/njhs.v1i1.38726
- [4] Volgman AS, Palaniappan LS, Aggarwal NT, Gupta M, Khandelwal A, Krishnan AV, et al. Atherosclerotic cardiovascular disease in South Asians in the United States: epidemiology, risk factors, and treatments: a scientific statement from the American Heart Association. *Circulation.* 2018 Jul 3;138(1): e1-34. doi: 10.1161/CIR.0000000000000580.
- [5] Shaheen A, Fatima A, Saleem Z, Arshad H, Khan TM, Khan S, et al. How Fast Foods Impact Coronary Artery Disease Incidence: A Cross-Sectional Study. *European Journal of Medical and Health Sciences.* 2021 Oct 14;3(5):52-5. doi.org/10.24018/ejmed.2021.3.5.1033
- [6] Wang X, Gao M, Zhou S, Wang J, Liu F, Tian F, Jin J, et al. Trend in young coronary artery disease in China from 2010 to 2014: a retrospective study of young patients ≤ 45 . *BMC Cardiovasc Disord.* 2017 Jan 7;17(1):18. doi: 10.1186/s12872-016-0458-1.
- [7] Al-Nozha M M, Arafah MR, Al-Mazrou Y Y, Al-Maatouq MA, Khan NB, Khalil MZ, et al. Coronary artery disease in Saudi Arabia. *Saudi med J* 25(9):1165-71, 2004.
- [8] Yu E, Malik VS, Hu FB. Cardiovascular Disease Prevention by Diet Modification: JACC Health Promotion Series. *J Am Coll Cardiol.* 2018 Aug 21;72(8):914-926. doi: 10.1016/j.jacc.2018.02.085.
- [9] Jafar TH, Qadri Z, Chaturvedi N. Coronary artery disease epidemic in Pakistan: more electrocardiographic evidence of ischaemia in women than in men. *Heart.* 2008 Apr;94(4):408-13. doi: 10.1136/hrt.2007.120774.
- [10] Bowen KJ, Sullivan VK, Kris-Etherton PM, Petersen KS. Nutrition and Cardiovascular Disease—an Update. *Curr Atheroscler Rep.* 2018 Jan 30;20(2):8. doi: 10.1007/s11883-018-0704-3.
- [11] Reamy BV, Williams PM, Kuckel DP. Prevention of Cardiovascular Disease. *Prim Care.* 2018 Mar;45(1):25-44. doi: 10.1016/j.pop.2017.11.003.
- [12] Magnani JW, Mujahid MS, Aronow HD, Cené CW, Dickson VV, Havranek E, et al. Health literacy and cardiovascular disease: fundamental relevance to primary and secondary prevention: a scientific statement from the American Heart Association. *Circulation.* 2018 Jul 10;138(2): e48-74. doi: 10.1161/CIR.0000000000000579.
- [13] Registrar General of India Report on Medical Certification of Cause of Death 2013 Office of the Registrar General, New Delhi, India (2015) [Available at: www.censusindia.gov.in/2011-document/mccd_2013.pdf (Last cited April 13, 2016)] R. Gupta, I. Mohan, J. Narula. Trends in Coronary heart disease epidemiology in India
- [14] Aydın F, Akşit E, Yıldırım ÖT, Hüseyinoğlu Aydın A, Samsa M. Assessment of secondary prevention awareness among patients with coronary artery disease: A survey including patients from 3 centers. *Turk Kardiyol Dern Ars.* 2021 Oct;49(7):556-567. doi: 10.5543/tkda.2021.32302.
- [15] Tokgözoğlu L, Kaya EB, Erol C, Ergene O; EUROASPIRE III Turkey Study Group. EUROASPIRE III: a comparison between Turkey and Europe. *Turk Kardiyol Dern Ars* 2010; 38:164-72.
- [16] World Health Organization. Best Buys' and Other Recommended Interventions for the Prevention and Control of Noncommunicable Diseases. Geneva: World Health Organization; 2017.
- [17] Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *J Am Coll Cardiol.* 2019;74(10): e177-232. doi.org/10.1016/j.jacc.2019.03.010
- [18] He H, Yu YQ, Li Y, Kou CG, Li B, Tao YC, et al. Dyslipidemia awareness, treatment, control and influence factors among adults in the Jilin province in China: a cross-sectional study. *Lipids Health Dis.* 2014 Aug 3;13:122. doi: 10.1186/1476-511X-13-122.

- [19] Wang C, Yu Y, Zhang X, Li Y, Kou C, Li B, et al. Awareness, treatment, control of diabetes mellitus and the risk factors: survey results from northeast China. *PLoS One*. 2014 Jul 28;9(7): e103594. doi: 10.1371/journal.pone.0103594.
- [20] Méndez-Chacón E, Santamaría-Ulloa C, Rosero-Bixby L. Factors associated with hypertension prevalence, unawareness and treatment
- [21] Kelly-Irving M, Mulot S, Inamo J, Ruidavets JB, Atallah A, Lang T. Improving stroke prevention in the French West Indies: Limits to lay knowledge of risk factors. *Stroke*. 2010;41(11):2637-44. doi.org/10.1161/STROKEAHA.110.592659
- [22] Winham DM, Jones KM. Knowledge of young African American adults about heart disease: A cross-sectional survey. *BMC Public Health*. 2011;11(1):248. doi.org/10.1186/1471-2458-11-248
- [23] Jones EJ, Appel SJ, Eaves YD, Moneyham L, Oster RA, Ovalle F. Cardiometabolic risk, knowledge, risk perception, and self-efficacy among American Indian women with previous gestational diabetes. *J Obstet Gynecol Neonatal Nurs*. 2012;41(2): 246-57. doi.org/10.1111/j.1552-6909.2012.01339.x
- [24] Ahmed AA, Al-Shami AM, Jamshed S, Zawiah M, Elnaem MH, Ibrahim MI. Awareness of the risk factors for heart attack among the general public in Pahang, Malaysia: A cross-sectional study. *Risk Manag Healthc Policy*. 2020; 13:3089-102. doi.org/10.2147/RMHP.S281285.
- [25] Haron H, Kamal NF, Yahya HM, Shahar S. Knowledge, attitude and practice (KAP) of Malay elderly on salt intake and its relationship with blood pressure. *Front Public Health*. 2020; 8:559071. doi.org/10.3389/fpubh.2020.559071
- [26] Khan NS, Shehnaz SI, Guruswami GK, Ibrahim SAM, Mustafa SAJ. Knowledge of warning signs, presenting symptoms and risk factors of coronary heart disease among the population of Dubai and Northern Emirates in UAE: A cross-sectional study. *Nepal J Epidemiol*. 2017; 7(2): 670-80. doi.org/10.3126/nje.v7i2.17973
- [27] Awad A, Al-Nafisi H. Public knowledge of cardiovascular disease and its risk factors in Kuwait: A cross-sectional survey. *BMC Public Health*. 2014;14(1):1131. doi.org/10.1186/1471-2458-14-1131
- [28] Aminde LN, Takah N, Ngwasiri C, Noubiap JJ, Tindong M, Dzudie A, et al. Population awareness of cardiovascular disease and its risk factors in Buea, Cameroon. *BMC Public Health*. 2017;17(1): 1-10. doi.org/10.1186/s12889-017-4477-3
- [29] Ministry of Health and Prevention-United Arab Emirates. "Healthy Heart" Campaign: Ministry of Health and Prevention- United Arab Emirates; 2014. Available from: <https://www.moh.gov.ae/en/mediacenter/news/pages/1346.aspx>. [Last accessed on 2021 Jul 12].
- [30] Waśniowska A, Kopeć G, Szafraniec K, Misiowiec W, Waligóra M, Brózda M, et al. Assessment of knowledge on cardiovascular disease risk factors by postal survey in residents of Małopolska Voivodeship: Małopolska Cardiovascular Preventive Intervention Study (M-CAPRI). *Ann Agric Environ Med*. 2017;24(2):201-6. doi.org/10.5604/12321966.1228400



Original Article

Socioeconomic Burden of Major Rheumatic Diseases in A Tertiary Care Facility

 Muhammad Sharif¹, Muhammad Sufyan Khan¹, Tayyeba Khursheed Ahmed¹, Somaya Shah¹, Saira Tahir¹ and Avinash Punshi¹
¹Department of Rheumatology, PIMS, Islamabad, Pakistan

ARTICLE INFO

Key Words:

SES, Rheumatoid Arthritis, Rheumatic diseases, Musculoskeletal

How to Cite:

 Sharif, M. ., Sufyan Khan, M. ., Khursheed Ahmed, T. ., Shah, S. ., Tahir, S. ., & Punshi, A. . (2022). Socioeconomic Burden Of Major Rheumatic Diseases In A Tertiary Care Facility: Socioeconomic Burden of Major Rheumatic Diseases. Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.575>

*Corresponding Author:

 Muhammad Sharif
 Department of Rheumatology, PIMS, Islamabad, Pakistan
 msharif111@yahoo.com

 Received Date: 20th June, 2022
 Acceptance Date: 25th June, 2022
 Published Date: 30th June, 2022

ABSTRACT

Rheumatic diseases can have serious socioeconomic implications in a developing country like Pakistan. With dwindling resources in the healthcare sector, decision makers are forced to prioritize treatment between patients. **Objective:** To assess the socio-economic burden of major rheumatic diseases in a tertiary care hospital. **Methods:** 171 patients were enrolled in the study prospectively. Patients were selected through specially designed questionnaires. Diagnosis of the disease and patient's socioeconomic status were recorded and analyzed using SPSS ver. 25.0. **Results:** The mean age of the participants was 38.65 ± 13.20 years. A higher ratio of female patients (78.4 %) as compared to the male patients (21.6 %) was seen. The majority of the patients were not well educated as 79 % of the patients were below matric, 9 patients were graduated and only 2 patients were postgraduates. Most of patient fall in low socioeconomic background ($30,924.8 \pm 19,107.3$). Out of all the rheumatic diseases, Rheumatoid Arthritis 96 (56.1 %) was the most commonly found autoimmune disease. **Conclusion:** Rheumatic disease outcomes in Pakistan are influenced significantly by socioeconomic status. A comprehensive treatment plan for rheumatic disease is needed, especially for those with low education levels and poor quality of life.

INTRODUCTION

Rheumatic diseases can have serious socioeconomic implications in a developing country like Pakistan. With dwindling resources in the healthcare sector, decision makers are forced to prioritize treatment between patients. These decisions require accurate assessments of healthcare intervention costs and effectiveness. Nearly 30% of sick days are attributed to back, neck, and shoulder pain [1]. There is a prevalence between 0.5% -1% of rheumatoid arthritis (RA), and a rate of occurrence of 25-50 per 100 000 each year [2]. Studies have shown that prevalence of rheumatoid arthritis in northern Pakistan was 0.55% and 0.142% in urban areas of Karachi, although exact epidemiological statistics are not yet available for developing countries [3,4]. Health services and people with RA are both believed to bear a substantial economic burden. Compared to other disease groups,

musculoskeletal disorders impose a significant burden on society concerning morbidity, long-term disability and costs, but their mortality rate is low [5]. According to Rice [6], cost of illness (COI) assessments include three types of cost components: direct costs, indirect costs, and psychosocial costs. The term direct cost refers to those that are actually payable. These costs include medical costs such as hospital costs and treatment, as well as personal expenses like transportation to the physician and specialist aids. Indirect costs are incurred when resources are lost without direct payment. The costs of morbidity and mortality can be divided into two categories: morbidity costs related to productivity losses suffered by an individual, his or her family, society, and employer, and mortality costs related to lost production due to premature death caused by illness. The third category of costs is

intangible or psychosocial. These costs reduce the quality of life for patients as well as their families and friends. For example, individuals with RA may experience disability, pain, low self-esteem, and a lack of well-being. These costs are difficult to quantify and therefore are often left out of economic studies [7]. Among developing world countries, Pakistan ranks 84th on the social composite index [8]. The majority in Pakistan is of low or middle socioeconomic status; only a small fraction has high socioeconomic status. Pakistan's economy is largely reliant on its agriculture sector. Over the last decade, the country's urbanization rate has increased by 5.6%, which has a negative impact on agriculture. In turn, this has led to unemployment and poverty in the country [9]. The Social Economic Status (SES) of individuals, households, and census tracts is defined as the level at which they are able to produce and consume goods valued by society [8]. SES is difficult to assess, and the tools used to measure it vary from study to study. Some studies assess SES by measuring an individual's educational level, while others consider occupation or income as more reliable indicators. Using census data, such as job levels in the area or poverty indices, it is possible to determine the socioeconomic status of an area [9,10]. The rationale of this study was to investigate the socio-economic burden of major rheumatic diseases in leading tertiary care hospital of Pakistan.

METHODS

Inclusion Criteria: Patients 13 years of age or older with rheumatic diseases. **Exclusion Criteria:** Patients aged less than 13 years and with a diagnosis other than the rheumatic diseases spectrum. The sample size was calculated as 142 cases with the WHO sample size calculator using the following parameters; expected prevalence 24% [11], precision level 5%, and confidence level 95%. A total of 171 patients were enrolled in the study after a complete medical history and written consent was obtained. A questionnaire was used to select the patients. Information on socio-demographic variables such as age, gender, level of education, marital status and socioeconomic status was extracted from questionnaires. A number of health characteristics were considered, such as disease duration, disease activity, and quality of life. Expenses related to travel, transportation, medication, and the sources of medication as well as the diagnosis of different forms of rheumatic diseases were noted. The clinical history of every patient was noted. The data were recorded and analyzed using SPSS version 25 (Statistical Package for Social Sciences). The mean and standard deviation were calculated for continuous data, while frequency and percentage were calculated for categorical data.

RESULTS

After providing informed consent, 171 participants were enrolled in the study. The mean age of the participants was 38.65 ± 13.20 years. We observed a higher ratio of female patients (78.4%) than male patients (21.6%).

Features	N = 171
Age	38.65 ± 13.20
Gender	
1.Male	37 (21.6 %)
2.Female	134 (78.4 %)
Marital Status	
1.Married	119 (69.6 %)
2.Un-Married	42 (24.6%)
3.Divorced	5 (2.9 %)
4.Widow	5 (2.9 %)
Education	
1.Illiterate	46 (26.9 %)
2.Primary School	26 (15.2 %)
3.Middle School	1 (0.6 %)
4.Matriculation	62 (36.3 %)
5.Intermediate	25 (14.6 %)
6.Graduate	9 (5.2 %)
7.Postgraduate	2 (1.2 %)
Income (PKR)	30,924.8 ± 19,107.3

Table 1: Demographic characteristics of Patients

There were 119 married patients (69.6%), 42 unmarried patients (24.6%), and also divorced and widowed individuals (2.9% each) included in the study. In this study, 79 % of the patients had less than matriculated, 9 patients graduated and only 2 patients had postgraduate degrees. A massive income gap was seen between the patients ($39,941.8 \pm 50,563.7$) as shown in Table - I.

Disease Diagnosed	Cases n = 171
1.Rheumatoid Arthritis (RA)	96 (56.1 %)
2.Ankylosing spondylitis (AS)	17 (9.1 %)
3.Psoriatic Arthritis (PA)	5 (2.9 %)
4.Axial Spondyloarthritis	14 (8.2 %)
5.Systemic lupus erythematosus (SLE)	18 (10.5 %)
6.Juvenile Idiopathic Arthritis (JIA)	9 (5.3 %)
7.Systemic Sclerosis (SSc)	2 (1.2 %)
8.Mixed Connective Tissue Disease (MCTD)	5 (2.9 %)
9.Osteoarthritis	2 (1.2 %)
10.Polymyalgia Rheumatica	1 (0.6 %)
11.Scleroderma	1 (0.6 %)
Vasculitis	1 (0.6 %)

Table 2: Different Autoimmune Diseases Diagnosed in Patients

A variety of different autoimmune diseases were seen in the cases. Out of all the autoimmune diseases Rheumatoid Arthritis was seen most frequently 96 (56.1 %). Some rare diseases like Polymyalgia Rheumatic, MCTD and JIA were also recorded as shown in Table 2. The mean duration of diagnosis in patients was 8.35 ± 7.2 year and the mean duration of symptoms was 9.833 ± 7.95 year. Out of the 171 patients enrolled, the majority visited with a family member 123 (71.9 %) and traveled in local transport 128 (74.9 %). Out of 171 patients, only 5 patients got reimbursements from

their companies and 32 (18.7 %) patients got support from Bait-ul-Mal for medication costs as shown in Table 2.

Features	Cases n= 171
Clinical History	
1.Duration of diagnosis (Years)	8.35 ± 7.2
2.Duration of symptoms (Years)	9.833±7.95
3.First Visited Clinic (Years)	7.62± 6.71
Clinical Visit	
1.Alone	48 (28.1 %)
2.Family	123 (71.9 %)
MemberTransport	
1.Local/Public	128 (74.9 %)
2.Self-Transport	43 (25.1 %)
3.RentedTravel	-
1.Travel Time (hours)	2.5 ± 3.4
2.Travel Cost (PKR)	1946.3 ± 3514.5
Medication Cost (PKR)	
Source of Medication Cost	5464.7 ± 6778.7
1.Self	134 (78.4 %)
2.Bait-ul-Mal	32 (18.7 %)
3.Company Reimbursement	5 (2.9 %)

Table 3: Clinical History and Socio-Economic Status

DISCUSSION

The purpose of this study was to investigate the impact of socioeconomic status on rheumatic diseases in developing countries like Pakistan. Rheumatic diseases are caused by genetic, socioeconomic and environmental factors, but which environmental factors because rheumatic diseases are still a matter of debate [9]. An individual's socioeconomic status is typically determined by their educational level, occupation (e.g., their own or their partner's occupation), and income (either individual or household income). In previous studies, obtaining information on income was difficult because a great number of people were reluctant to declare their individual or family incomes [10]. The mean age of the participants was similar to that found in other studies. Studies have shown that females are more likely to suffer from rheumatic diseases [11]. A recent European cohort study has revealed that women are more likely than men to develop rheumatic diseases [12]. According to the study, symptoms of rheumatic diseases in females appear later than those in males. We found similar results in terms of gender proportion and duration of symptoms in our study. This difference is most likely due to the difference in physical workload between genders [16]. The link between SES and rheumatic diseases is multidimensional as evidenced by previous studies. Case-control or cross-sectional studies have shown that there is sometimes disagreement between association between SES and disease activity and patient-reported outcomes [13]. RA, for example, can result in very serious economic consequences for people, as they have to reduce their working hours or become work disabled due to the pain of

this condition, resulting in reduced income and low socioeconomic standing. In our study, people relying on daily wages or doing physical labor were found to be at risk due to the mean monthly income of workers in the labour class. In general, people from lower socioeconomic backgrounds have higher smoking and obesity rates. These individuals also have more nutritional deficiencies [14,17]. SES is also associated with the risk of developing autoimmune diseases and should be considered when investigating the independent relationship between SES and disease. In our study, we found that patients with low SES show up at the hospital long after their symptoms appear because of a lack of education. This can be seen from the difference between mean time between diagnosis and onset of symptoms (8.35 ± 7.2 vs. 9.833±7.95). Pakistan is a nation with strong family ties, so most of our cohort came to the hospital with a relative (n=123, or 71.9%). In developing countries, access to transport is an issue as Pakistan has 20.2 vehicles per 1000 people making it number 150 globally; while the United States has 785.6 vehicles per 1,000 people making it number 4 [15,18]. In our study, we found that more people use public or local transportation (n=128, 74.9%). Using our study population as an example, the average cost of a single visit to the hospital with the patient and caretaker and monthly medication expenses was about 1946.3±3514.5 and 5464.7±6778.7 (PKR) which is 25% of the mean monthly income. Several studies conclude that patients with a low socioeconomic status are worse off than patients with a high socioeconomic status. Patients with lower and higher SES had significantly different health outcomes [19]. SES must be explored further as a risk factor for developing autoimmune diseases and as a factor that might affect self-reported and disease activity outcomes. In turn, authorities will be able to improve management strategies with this type of information[20].

CONCLUSION

Socioeconomic status significantly impacts the rheumatic disease outcomes of Pakistani patients. Based on the results, it is imperative for authorities to formulate an integrated approach for treating rheumatic diseases, especially for those with low education levels and poor quality of life.

REFERENCES

- [1] Kuijpers T, van der Windt DA, van der Heijden GJ, Twisk JW, Vergouwe Y, Bouter LM. A prediction rule for shoulder pain related sick leave: a prospective cohort study. *BMC Musculoskelet Disord*. 2006 Dec 6; 7:97. doi: 10.1186/1471-2474-7-97.
- [2] Guo Q, Wang Y, Xu D, Nossent J, Pavlos NJ, Xu J. Rheumatoid arthritis: pathological mechanisms and

- modern pharmacologic therapies. *Bone Res.* 2018 Apr 27; 6:15. doi: 10.1038/s41413-018-0016-9.
- [3] Farooqi A, Gibson T. Prevalence of the major rheumatic disorders in the adult population of north Pakistan. *Br J Rheumatol.* 1998 May; 37(5):491-5. doi: 10.1093/rheumatology/37.5.491.
- [4] Imran MY, Saira Khan EA, Ahmad NM, Farman Raja S, Saeed MA, Ijaz Haider I. Depression in Rheumatoid Arthritis and its relation to disease activity. *Pak J Med Sci.* 2015 Mar-Apr; 31(2):393-7.
- [5] Cooper NJ. Economic burden of rheumatoid arthritis: a systematic review. *Rheumatology (Oxford).* 2000 Jan; 39(1):28-33. doi: 10.1093/rheumatology/39.1.28.
- [6] Rice DP. Estimating the cost of illness. *Am J Public Health Nations Health.* 1967 Mar; 57(3):424-40. doi: 10.2105/ajph.57.3.424.
- [7] Larg A, Moss JR. Cost-of-illness studies: a guide to critical evaluation. *Pharmacoeconomics.* 2011 Aug; 29(8):653-71. doi: 10.2165/11588380-000000000-0-00000.
- [8] Cruz-Castillo Y, Montero N, Salazar-Ponce R, Villacís-Tamayo R. Quality of Life in Ecuadorian Patients with Rheumatoid Arthritis: A Cross-sectional Study. *Reumatol Clin (Engl Ed).* 2019 Sep-Oct; 15(5):296-300. English, Spanish. doi: 10.1016/j.reuma.2017.08.012.
- [9] Russell O, Lester MS, Black R, Hill C. Socioeconomic status (ses) and medication use in rheumatoid arthritis (ra): a scoping review. *In Internal Medicine Journal* 2020; 50:20-23.
- [10] Chen HH, Lin CH, Wang CY, Chao WC. Association of Hospitalised Infection with Socioeconomic Status in Patients with Rheumatoid Arthritis Receiving Biologics or Tofacitinib: A Population-Based Cohort Study. *Front Med (Lausanne).* 2021 Jul 12; 8:696167. doi: 10.3389/fmed.2021.696167.
- [11] Haq SA, Darmawan J, Islam MN, Uddin MZ, Das BB, Rahman F, et. al. Prevalence of rheumatic diseases and associated outcomes in rural and urban communities in Bangladesh: a COPCORD study. *J Rheumatol.* 2005; 32(2):348-53.
- [12] Yang DH, Huang JY, Chiou JY, Wei JC. Analysis of Socioeconomic Status in the Patients with Rheumatoid Arthritis. *Int J Environ Res Public Health.* 2018 Jun 7; 15(6):1194. doi: 10.3390/ijerph15061194.
- [13] Song H, Fang F, Tomasson G, Arnberg FK, Mataix-Cols D, et al. Association of Stress-Related Disorders with Subsequent Autoimmune Disease. *JAMA.* 2018 Jun 19; 319(23):2388-2400. doi: 10.1001/jama.2018.7028.
- [14] Harrison SR, Li D, Jeffery LE, Raza K, Hewison M. Vitamin D, Autoimmune Disease and Rheumatoid Arthritis. *Calcif Tissue Int.* 2020 Jan; 106(1):58-75. doi: 10.1007/s00223-019-00577-2.
- [15] <http://mecometer.com/compare/pakistan+united-states/vehicles-per-thousand-people/>
- [16] Cuijpers P, Ebert DD, Acarturk C, Andersson G, Cristea IA. Personalized psychotherapy for adult depression: a meta-analytic review. *Behavior Therapy.* 2016 Nov 1; 47(6): 966-80. doi.org/10.1016/j.beth.2016.04.007
- [17] Zampeli E, Vlachoyiannopoulos PG, Tzioufas AG. Treatment of rheumatoid arthritis: unraveling the conundrum. *Journal of autoimmunity.* 2015 Dec 1; 65:1-8. doi.org/10.1016/j.jaut.2015.10.003
- [18] Filipovic I, Walker D, Forster F, Curry AS. Quantifying the economic burden of productivity loss in rheumatoid arthritis. *Rheumatology.* 2011 Jun 1; 50(6):1083-90. doi.org/10.1093/rheumatology/keq399
- [19] Zhang W, Anis AH. The economic burden of rheumatoid arthritis: beyond health care costs. *Clinical rheumatology.* 2011 Mar; 30(1):25-32. doi.org/10.1007/s10067-010-1637-6
- [20] Furneri G, Mantovani LG, Belisari A, Mosca M, Cristiani M, Bellelli S, et al. Systematic literature review on economic implications and pharmacoeconomic issues of rheumatoid arthritis. *Clinical and Experimental Rheumatology-Incl Supplements.* 2012 Jul 1; 30(4): S72



Original Article

A Comparison of Sonourethrography and Retrograde Urethrography in Evaluation of Anterior Urethral Strictures

Zubair Janan Orakzai¹, Sumera Nighat², Sana Sharif³ and Mahwish Zahra⁴¹Department of Radiology, MTI Mardan Medical Complex, Mardan, Pakistan² Department of Diagnostic Radiology, Bakhtawar Amin Memorial and Trust Hospital, Multan, Pakistan³BUMDC, PNS Shifa Karachi, Pakistan⁴Children Hospital, Multan, Pakistan

ARTICLE INFO

Key Words:

Sonourethrography, urinary pathway, RGU, sensitivity, specificity

How to Cite:

Janan Orakzai, Z. ., Nighat, S. ., Sharif, S. ., & Zahra, M. . (2022). A Comparison of Sonourethrography and Retrograde Urethrography in Evaluation of Anterior Urethral Strictures: Sonourethrography and Retrograde Urethrography in Evaluation of Anterior Urethral Strictures. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.576>

***Corresponding Author:**

Zubair Janan Orakzai
 Department of Radiology, MTI Mardan Medical Complex, Mardan, Pakistan
zjaurakzai@hotmail.com

Received Date: 21st June, 2022Acceptance Date: 26th June, 2022Published Date: 30th June, 2022

ABSTRACT

The urinary tract has restrictions in its lower parts. This problem can be detected by two different methods. Obstruction in the anterior portion of this tract can be diagnosed by some available standard methods. **Objective:** To assess the general problems in the male urethra specifically in the anterior portion. **Methods:** It is a prospective and comparative study with a statistical approach, conducted at Bakhtawar Amin Memorial and Trust Hospital, Multan and MTI Mardan Medical Complex, Mardan for the duration of one year from December 2020 to December 2021. The study was done by using ultrasound of high resolution. Then the comparison of the operative conclusions has to be done with retrograde urethrography (RGU) to find out the efficiency of RGU. For this study work, seventy-seven patients were selected. All these patients had some restrictions in the urinary pathway confirmed by retrograde urethrography. Different characteristics of the patients were studied and matched with the available standard methods. By both tests specificity, sensitivity, and overall accuracy of the protocol were also assessed. Different statistical analyses were performed to find out the results. **Results:** All the seventy-seven patients were having some restriction of urinary pathway, which were detected by sonourethrography and further confirmation was done by other previously verified methods. The retrograde urethrography shows almost very low sensitivity of this particular problem detection. This test was about 60 to 80% sensitive for this diagnosis. This sensitivity is specific for the length of about 1 to 5 cm. These results were compared with the results of sonourethrography. The problem termed as spongiofibrosis was also diagnosed with sensitivity about 76 to 82 %. A number of other problems were also detected by this method like calculi and further confirmation was done at the time of surgery. The probability was greater than 0.001 and difference in frequency was also not so significant. It was less than 0.5. **Conclusions:** Both of the methods have equal efficiency for the detection of different restrictions in urinary tract. When other parameters were assessed; it was inferred that sonourethrography is more efficient method.

INTRODUCTION

The urinary tract has restrictions in its lower parts, this problem can be detected by two different methods. Obstruction in the anterior portion of this tract can be diagnosed by some available standard methods. The two most commonly used methods are retrograde and antegrade methods for urethrography [1,2]. Retrograde methods are commonly used by the assistance of penile clamps. Catheter can also be used in case of women to detect obstructions. But for the diagnosis of male urethra,

different other techniques are used for detection of obstruction due to larger length of tract, such as different radiations and other anatomy related methods [3, 4]. Every diagnostic method has number of advantages as well as some limitations in sensitivity and specificity for the detection of a particular disease. In case of retrograde methods, strictures appeared within tract, there is difficulty in the measurement of exact position of stricture within penis [5]. In the case of other method, like sono-

urethrography, which is considered as a standard method for the detection of different restrictions within urinary pathway, it can scan the urethra from posterior side as well as from the urinary bladder from the Trans side of the rectum [6, 7]. When sensitivity of both retro and antegrade method was compared, both have same level of efficiency for the diagnosis of restriction in the urethra but other parameters like length of urinary pathway which is different in case of male and female were considered, then it seems a difference in measuring capacity of both tests [8-10]. A new method of detection of restriction in urinary pathway was introduced in 1988. This method was quite useful for the detection in case of longer urinary pathway as in case of males. The new method has high resolving power ultrasound waves for the detection. The name of this method was sono-urethrography [11]. Firstly, ultrasound waves of 6 MHz were used and inducted on penis from dorsal side and images were obtained from all sides. In case of normal person, the walls of the urethra were elastic, spongy and blood filled veins were present but in case of any obstruction or stricture, the elasticity of urethral wall is lost. Collagen content gets reduced from the wall. To measure the efficiency, specificity and sensitivity of the both retrograde and sono-urethrography, all patients undergo detection by both methods [12]. The main objective of this study is to find the better method for the detection of different problems in urinary pathway.

METHODS

It is a prospective and comparative study with a statistical approach, conducted at Bakhtawar Amin Memorial and Trust Hospital, Multan and MTI Mardan Medical Complex, Mardan for the duration of one year from December 2020 to December 2021. To proceed with this study, about 77 patients were selected, all these patients were having obstructions in urinary pathway. Patients had acute symptoms were not included in this study. Some patients had history of urinary tract infection or some kind of trauma related to urinary pathway were also included. The patients were analyzed completely by noticing and analyzing all the attributes like length of urinary tract, symptoms, dilatation of urethra, and discharge from urinary pathway, diversification and all the related parameters. All this information was taken from the patients by their own consent. Disease level of the patient was detected by using prescribed protocols of retrograde method. Patients were not allowed to drink water 5 to 6 hours before test. A radiogram of the penis was taken by using catheter as well. The radiogram was analyzed by experts by considering all the parameters described above. The quality level of stricture with urinary pathway was determined. Then the same patient was further analyzed by using

sonourethrography test by using ultrasound waves of 9 MHz and images were taken. All the related parameters were analyzed by experts. Sensitivity and specificity were measured. Comparison of the results was done by using some statistical tools, such as Chi-square. The significant difference was observed in the detection level of both of the tests. Kappa values and probability was measured to find out the significant differences between both of the methods. The studies were carefully analyzed by expert team for the prediction of final results.

RESULTS

The study was carried out in 77 male patients. The most frequent symptom that they showed was thin streamed urine flow in case of 73 (94%) patients. Almost 68 (88%) of the patients complained about micturition straining problems, 14 (18%) patients had past history that they were suffering from urethritis. Most of the patients were showing symptoms within less than 13 months. 19 (24%) patients had already carried out surgery previously, 16 (20%) patients were already suffering from urethritis. Some of the patients also reported previous signs and symptoms like trauma for example assault, electric burns etc. Extent and characteristics of spongiofibrosis are showed in table 1. All the cases of the disease that include detection by RGU also got scanned by sonourethrography (SUG) and it was confirmed at the time of surgery. In the determination of site of strictures at the position of urethra, SUG showed better results than RGU. The sensitivity and working of RGU was almost 61-67% in detecting the overall length of the available stricture (Table 2). For the similar reasons the SUG showed very promising results of 67% with an average accuracy of 98%. The estimation of the diameter of detected stricture was analyzed by RGU and it showed a sensitivity of 49-78% (Table 3). There was a case of bulbar urethral stricture that had a filling problem observed near to it by RGU. Peri-urethral fibrosis was also detected by using SUG with prominent accuracy and precision. The SUG eliminated the idea of spongiofibrosis significantly as the negative prediction value can be observed from the data. Using kappa statistical analysis, the level of agreement was determined between SUG and RGU, and it was revealed that a very strong agreement was observed (table 3). Intravasation of contrast occurred in 5% of the patients during RGU, which created problems.

Extent of spongiofibrosis	Less Intense	medium	Intense
Color of the detected urethral mucosa	Pink colored	grey	White colored
Resistance in causing incision	mild	medium	severe

Table 1: Characteristics for the complete assessment of spongiofibrosis

Disease	Length (mm)	Sensitivity %	Specificity %	PPV%	NPV%	Accuracy %
RGU	<11	84	95	78	97	93
	1-21	61	99	91	91	91
	22-33	62	97	62	97	95
	34-44	67	94	54	96	92
	45-55	99	98	52.2	99	98
	diffuse	94	96	94	95	98
SUG	<11	85	98.2	96	96	93
	11-21	63	99	76	92	91.7
	22-33	62.4	98.9	66.4	96.5	95.1
	34-44	65	99	100	93.6	92
	45-55	100	100	95	99	98.4
	diffuse	92	92	93	97	96

Table 2: RUG and SUG comparison to estimate strictures length

Disease	Diameter (mm)	Sensitivity %	Specificity %	PPV%	NPV%	Accuracy %
RGU	0-3	75	89	78.1	81	93.1
	4-7	68	85	75	82	81
	7-10	62.9	79	62.4	84.1	85
	10-13	67.3	86	25.5	97.2	83
SUG	0-3	82	95	95	81	93.1
	4-7	86.2	96.5	86	82.6	88.5
	7-10	69	98	65	94.1	95.2
	10-13	82	97.5	33.9	97.2	83.4

Table 3: RUG and SUG comparison to estimate strictures diameter

DISCUSSION

In order to detect and view anterior urethra, RGU in addition with cystourethrography was used as it was considered as a standard procedure for this purpose. According to recent studies, the use of urethrography was not only to decrease the primary stricture so that the source of the patient's stricture can be located [13]. Studies were required to show what sort of procedure will be suitable for the patient to know the location, length and the correct diameter of the stricture of the patient. The overall complete idea of the severity of the disease like the presence of false tract, polyps, fistula will surely help the radiologist to find the cure of the disease. By making use of a negative contrast, this technique is used to achieve all the features [14]. The complications that were showed in this study included trauma (18%), infection (21%) and surgery (26%). Nash et al., detected a blunt trauma in almost 45% of the patients that had history of this sort of infection [9]. Most of the patients of Wagner et al., studies had these strictures because of infection that occurs after using catheter for too long [15]. Albers et al., found that after repeatedly using the procedure of urethrotomy, the urethral strictures become a critical factor causing complications. In the present study, the SUG presented a higher sensitivity while determining the length of stricture so that overall better findings can be done. When the grouping was done on the

basis of anatomical areas, both these procedures showed almost equal sensitivity and length was also similar in both cases. However, it was found that RGU had poorer ability to determine the length of the stricture [16]. According to the previous studies the correlation between SUG and RGU showed poor results in determining the length of the bulbar urethral stricture. Gupta et al., did a study on 30 patients and showed that the both techniques had low correlation in determining the length of the stricture. It is very important to precisely determine the exact length of the stricture as this is something that will determine what sort of treatment and scanning procedure should be used for the patient. Urethral ultrasound is the right way that can help to determine accurate length and diagnosis can be made easier [17]. Gluck et al., showed that the reconstructive treatment provided by sonourethrography was very much different from that of RGU [12]. The detection of length and diameter of stricture plays a very important role in assessing the degree of narrowing as compared to RGU. However, in our study we showed that the sensitivity was less and the sonourethrography showed similarities with operative results. As per studies, there was poor correlation between the diameter of the lumen detected by RGU and that of operative data, but they didn't mention statistical evidence. If we have information about diameter of the lumen, then it can help to decide the possible dimensions for the reconstruction of penile flap. Peri-urethral fibrosis is also one of the critical factors that play important role in determining the possible therapy and the final result. As it was observed that critical case of fibrosis is the main cause of recurrence. Urethral ultrasound is also important as you can also detect spongiofibrosis while using it. If the spongiofibrotic tissue has a lot of scars that appear in form of reflective zones, then there are chances that it appeared because of elevated collagen content. When showed in form of a shadow the spongiofibrosis is very critical which will appear in form of highly dense images and shadowed view. It is mostly seen near the traumatic event [18, 19]. No doubt SUG does not tell about the depth of spongiofibrosis but it provides enough information that can help to classify the form of disease. The risk factors that are associated included urethral bleeding and pain during RGU. It was also found that after SUG some patients complained about bleeding. There was no discomfort that was reported by any patient during RGU and SUG. Other than that, in SUG the complications like haematuria and urinary infection were observed. As compared to RGU, SUG was more comfortable for patients so it can be used if discomfort is reported in case of SUG [20-22].

CONCLUSION

Concluding it, the study showed that the sonourethrography is a very effective and easy way to evaluate and detect male urethra as it is a combination of normal saline and high resolution B-mode sonography. It can provide information about the depth and length of strictures that can help to decide what sort of treatment can be used for treatment of this medical condition.

REFERENCES

- [1] 10.1111/j.1464-410X.2010.09800.x
- [2] Lumen N, Hoebeke P, Willemsen P, De Troyer B, Pieters R, Oosterlinck W. Etiology of urethral stricture disease in the 21st century. *J Urol.* 2009 Sep;182(3):983-7. doi:10.1016/j.juro.2009.05.023.
- [3] Santucci RA, Joyce GF, Wise M. Male urethral stricture disease. *J Urol.* 2007 May;177(5):1667-74. doi:10.1016/j.juro.2007.01.041.
- [4] McCallum RW, Colapinto V. *Urological Radiology of the Adult Male Lower Urinary Tract: Anatomy, Physiology, Pathology and Sequelae, Diagnosis and Management.* Springfield, Ill.: CC Thomas; 1976.
- [5] Davis HJ, Cian LG. Positive pressure urethrography: a new diagnostic method. *J Urol.* 1956 Apr;75(4):753-7. doi:10.1016/s0022-5347(17)66877-0
- [6] Shapeero LG, Friedland GW, Perkash I. Transrectal sonographic voiding cystourethrography: studies in neuromuscular bladder dysfunction. *AJR Am J Roentgenol.* 1983 Jul;141(1):83-90. doi:10.2214/ajr.141.1.83.
- [7] McAninch JW, Laing FC, Jeffrey RB Jr. Sonourethrography in the evaluation of urethral strictures: a preliminary report. *J Urol.* 1988 Feb;139(2):294-7. doi:10.1016/s0022-5347(17)42391-3.
- [8] Devine Jr CJ. Surgery of the urethra. In: Walsh PC, Gittes PC, Perlmutter AD, Stamey TA, editors. *Campbell's urology*, 5th ed. Philadelphia: WB Saunders; 1986. p. 2860-3.
- [9] Nash PA, McAninch JW, Bruce JE, Hanks DK. Sonourethrography in the evaluation of anterior urethral strictures. *J Urol.* 1995 Jul;154(1):72-6. doi:10.1016/S0022-5347(01)67231-8
- [10] Morehouse DD, Belitsky P, Mackinnon K. Rupture of the posterior urethra. *J Urol.* 1972 Feb;107(2):255-8. doi:10.1016/s0022-5347(17)60996-0.
- [11] Albers P, Fichtner J, Brühl P, Müller SC. Long-term results of internal urethrotomy. *J Urol.* 1996 Nov;156(5):1611-4 doi:10.1016/S0022-5347(01)65461-2
- [12] Gluck CD, Bundy AL, Fine C, Loughlin KR, Richie JP. Sonographic urethrogram: comparison to roentgenographic techniques in 22 patients. *J Urol.* 1988 Dec;140(6):1404-8. doi:10.1016/s0022-5347(17)42056-8.
- [13] Merkle W, Wagner W. Sonography of the distal male urethra—a new diagnostic procedure for urethral strictures: results of a retrospective study. *J Urol.* 1988 Dec;140(6):1409-11. doi:10.1016/s0022-5347(17)42057-x
- [14] Heidenreich A, Derschum W, Bonfig R, Wilbert DM. Ultrasound in the evaluation of urethral stricture disease: a prospective study in 175 patients. *Br J Urol.* 1994 Jul;74(1):93-8. doi:10.1111/j.1464-410x.1994.tb16553.x
- [15] Wagner M, Bayne A, Daneshmand S. Application of the Yang-Monti channel in adult continent cutaneous urinary diversion. *Urology.* 2008 Oct;72(4):828-31. doi:10.1016/j.urology.2008.06.015.
- [16] Albers P, Fichtner J, Brühl P, Müller SC. Long-term results of internal urethrotomy. *J Urol.* 1996 Nov;156(5):1611-4.
- [17] Gupta S, Majumdar B, Tiwari A, Gupta RK, Kumar A, Gujral RB. Sonourethrography in the evaluation of anterior urethral strictures: correlation with radiographic urethrography. *J Clin Ultrasound.* 1993 May;21(4):231-9. doi:10.1002/jcu.1870210404.
- [18] Morey AF, McAninch JW. Role of preoperative sonourethrography in bulbar urethral reconstruction. *J Urol.* 1997 Oct;158(4):1376-9
- [19] Webster GD, Koefoot RB, Sihelnik SA. Urethroplasty management in 100 cases of urethral stricture: a rationale for procedure selection. *J Urol.* 1985 Nov;134(5):892-8. doi:10.1016/s0022-5347(17)47512-4.
- [20] Morey AF, McAninch JW. Sonographic staging of anterior urethral strictures. *J Urol.* 2000 Apr;163(4):1070-5. doi:10.1016/S0022-5347(01)64219-8
- [21] McCammon KA, Zuckerman JM, Jordan GH. Surgery of the penis and urethra. Alan J wein, Louis R kavoussi, Alan W partin, Craig A peters, editors. *Campbell-Walsh Urology.* 11th ed. Philadelphia: Elsevier. 2016:907-45.
- [22] Klosterman PW, Laing FC, McAninch JW. Sonourethrography in the evaluation of urethral stricture disease. *Urol Clin North Am.* 1989 Nov;16(4):791-7. doi:10.1016/S0094-0143(21)01812-7
- [23] Mullin EM, Peterson LJ, Paulson DF. Retrograde urethrogram: diagnostic aid and hazard. *J Urol.* 1973 Oct;110(4):462-6. doi:10.1016/S0022-5347(17)60251-9



Original Article

An In Vitro Study of Histology of Nonfluorosed and Fluorosed Bone

Zahid Sarfaraz Khan^{1*}, Muhammad Ataullah², Syeda Gulrukh Saba Shah³, Nabiha Naeem⁴, Maryam Aslam⁴, Aqsa Khalid⁴, Ulfat Shehzadi⁴, Muhammad Akram⁴, Irfan Ullah⁴

¹Department of Anatomy, Khyber Girls Medical College, Peshawar, Pakistan

²Department of Anatomy, Pak International Medical College, Peshawar, Pakistan

³Anatomy Department, Kabir Medical College, Gandara University, Peshawar, Pakistan

⁴Department of Life Sciences, School of Science, University of Management and Technology, Lahore, Pakistan

ARTICLE INFO

Key Words:

Femur Bone, Fluorosis, Periodontitis, Periodontal therapy,

How to Cite:

Sarfaraz Khan, Z. ., Ataullah, M. ., Gulrukh Saba Shah, S., Naeem, N. ., Aslam, M. ., Khalid, A., Shehzadi, U. ., Akram, M. ., & Ullah, I. . (2022). An In Vitro Study of Histology of Nonfluorosed and Fluorosed Bone: Histology of Nonfluorosed and Fluorosed Bone. *Pakistan Biomedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.584>

*Corresponding Author:

Zahid Sarfaraz Khan
 Department of Anatomy, Khyber Girls Medical College, Peshawar, Pakistan
zahidsurfarazmc@gmail.com

Received Date: 22nd June, 2022

Acceptance Date: 27th June, 2022

Published Date: 30th June, 2022.

ABSTRACT

The study of the epidemiologic association between fluorosis and periodontitis, as well as the effects of fluorosis on periodontal tissues and the effects of periodontal therapy on teeth of non-fluorosed and fluorosed. There has been limited research into the effects of fluorosis on organic tissues for example bones. The biomechanical, histology and biochemical properties of fluorosed bones have still not been studied in alveolar bone, which, like extremities, is an important component of the periodontal tissue. **Objective:** The goal of this research was to compare the histology of fluorosed femur bones to that of non-fluorosed femur bones. **Method:** 40 non-fluorosed and fluorosed healthy bone (femoral) samples were tested using a microscope to compare and assess the histology of non-fluorosed with fluorosed bone. **Results:** When comparing the non-fluorosed group (11.835.21, 9.853.45) to the fluorosed group (7.724.42, 6.702.42), bone of cortical and cancellous cellularity was shown to be substantial in term of statistics. The non-fluorosed and fluorosed bone had the same trabecular density statistically not significant, p-value is equal to 0.726]. Nonfluorosed bone had thick trabeculae, while fluorosed bone had short and thin trabeculae. **Conclusion:** The identified histologic variations could affect the pathogenesis of periodontitis / the efficacy of periodontal therapy. In widespread fluorosed regions, dental fluoride could likely be identified as an important public health issue.

INTRODUCTION

Fluorine is indeed a key denominator in the crust of the earth and is required for bone and tooth calcification. Fluoride ions have played a key role in significantly lowering caries during the last forty years. Excess fluoride exposure can disrupt the homeostasis of bone, the development of enamel (enamel fluorosis), and calcification Fluorosis severity on periodontium soft and hard tissues is dosage dependent, as well as the exposure of fluoride time and period throughout growth [1]. While "fluorosis" is a national and global issue, few studies are examining the effect of fluoride on "periodontal tissues", which are likely known to be periodontitis due to changes including both soft and hard tissues of the periodontal tissues [2]. While

developing a successful treatment, it is necessary to consider the involvement of non-skeletal tissue in the disease process. Fluoride ions, among the most volatile components, have been detected such as fluoride in several tissues and organs other than the teeth and bones [3]. Before defluorination substances such as serpentine and magnesite can be used effectively, it is critical to study the of fluoride ions mechanism and the intensity of multiple numerous different tissues, particularly those that lack a buffering agent such as crystallites, which are used to neutralization of fluoride ions into the bones. In contrast to periodontal tissues, the research on the effect of fluoride on dental caries is thoroughly addressed. "Moreover, 15th

years of scientific research and a recent review have addressed not only an epidemiologic study linked between fluoride and disease of periodontal then it also the impact of structures of fluorosis in periodontal, as well as a comparison of the impact of treatment of periodontal on teeth which is fluorosed and non-fluorosed" There is a limited information that tells us the impact of fluorosis on human body tissues for example cementum and bone[4]. The histological components of fluorosed bone have received limited attention. "A clinical study [biopsied specimen] revealed that root surface of fluorotic is asymmetrical and have deposit a huge calcified masses at the apical portion of the teeth in the form of excessive amounts of fluorine as well as cementosis, osteosclerosis and roots of periapical resorption radiographically" [5]. According to the literature, the bone histology from an endemically fluorosed region has not been researched. "As a result, a new research area of fluorosis is to compare of fluorosed with nonfluorosed bone" The study's purpose is to evaluate differences in the histology of fluorosed and nonfluorosed bone.

METHODS

The orthopedic department of Lady Reading Hospital provided 20 healthy non-fluorosed and fluorosed bone (femoral) specimens. Participants of both genders aged 30-50 years were included. All participants provided written consent and ethical clearance. The bone specimens had to fulfill the basic inclusion criteria includes, Systemically healthy individuals' bone samples, "Following criteria for the selection of the Fluorosed subject was depend who survive in the water fluoride area for 5 to 10 years that consume the fluoride water above the levels 1.2 to 3 ppm and the levels of Peshawar water fluoride "0.2 mg/l to 2.41 mg/l" Participants having enamel with mottled appearance, that is, fluorosis stains on the teeth were evaluated using "Jackson's simplified fluorosis index scores C, D, E, and F". Bone samples were collected from participants who had surgical intervention after fractures due to trauma in which a portion of the bones (femur) was removed. The bone samples were chosen using the same criteria as the fluorosed teeth. Participants' metabolic bone problems "thyroidism, Paget's disease, hypophosphatasia, and infectious diseases" were excluded. Non-fluorosed and fluorosis good health bones were taken and placed in a jar containing 10 percent neutral buffer paraformaldehyde. paraffin-embedded blocks were prepared. The collected bone samples were decalcified using nitric acid (10%) at 25°C, with changes in solution at periodic times until the endpoint was achieved. For tissue preparation, decalcified bone was washed with water (24 h) before being processing routinely. Following that, the

prepared bone was embedded into the wax which is paraffin and masses of tissue were obtained. Segments were cut with a microtome and mounted to a slide. Tissue samples then deparaffinized with xylene about 28 minutes before being rehydrated in a decreasing ethanol sequence (100 percent for 25 minutes, 90 percent for 5 minutes, and 80 percent for 5 minutes) and rinsed in de-ionized- water for 25 minutes. "Section of the rehydrated and deparaffinized were immersed in Hematoxylin for 5 minutes before being it washed with the opened water for the removal of stain in excess mount for hematoxylin and eosin (H&E) staining" The stain section hematoxylin was dipped once in 1 percent alcohol before being immersed in bluing. They were then dipped in eosin for two min, rinsed with water to remove stain in excess amount, dehydrated alcohol sequence in an ascending orders (80%, 1 minute, 90%, 1 minute, and 100%, 1 minute), cleared in xylene, and prior to mounting with "DPX" for histological evaluation. The relevant parameters were analyzed: The density of cells in cortical and trabecular bones was measured at 40X power and averaged across 5 fields, Under 40X magnification, the occurrence or lack of latent and reversing appearances was also seen, The presence/absence of osteoclasts was related to the presence/absence of how ships lacunae, The density of Trabecular was graded as either sparse (+) or packed (++) , Bone marrow (fatty or red). The results from the histologic examination were recorded, assembled, and statistically analyzed using SPSS 20. The t-test and Mann – Whitney U were used for the contrast of the groups. The p-value of 0.05 was considered significant.

RESULTS

To examine and compare the histology of fluorosed by non-fluorosed bone, almost 20 healthy non-fluorosed and fluorosed bone (femur) samples were collected. Cellularity of cortical and cancellous bone is statistically significant in the non-fluorosed category (11.835.21, 9.853.45) compared to the fluorosed group (7.724.42, 6.702.42). as shown in Table 1. The density of Trabecular was the identical in non-fluorosed and fluorosed bone (p-value is equal to 0.726). On the other hand "Trabeculae which were thin and short in size present in fluorosed bone and thick in non-fluorosed bone. The lines of resting and reversing were more prominent in non-fluorosed bone than in fluorosed bone". Content of Fatty marrow were observed in equally groups, but in case of osteoclasts presence in all patients in which osteoclasts were found in non-fluorosed bones and few in fluorosed bone (Table 2).

Bone	fluorosed	Non- fluorosed	p-value	t-test
Cortex Cell	11.83 ± 5.21	7.72 ± 4.42	0.034 s	-3.57
Cell in cancellous	9.85 ± 3.45	6.70 ± 2.42	0.020 s	-3.99

Table 1: Density of cell in Fluorosed and non- Fluorosed bone of

Cancellous and Cortical calculation of p-value, t-test (s is significant)

2	2
1	1
2	2
1	1
2	2
2	2
2	2
1	1
2	2
2	2
2	2

Table 2: Compares the densities of bones of non-fluorosed and fluorosed Mann-Whitney U test = 52; p=0.726

DISCUSSION

A total of 40 human bone (femoral) specimens (fluorosed and non-fluorosed) were evaluated in our investigation. Many authors have carried out investigations on the femoral, tibial, fibula, calvaria, ribs, vertebrae, iliac crest, and mandible of bones of humans, rabbits, and mice, with sample sizes ranging from 2 to 5, 14, 69, 127. In 1997, study stated in a clinical investigation that there is a link between the bone density of the jaws and the carpal bones, forearms bones, vertebra, and femoral. As a result, the femur bone was chosen for the current research. Decalcification with 5 percent nitric was utilized in our investigation. The preservation of living hard tissues is important for knowing sub-cellular structure and function [5]. Mostly in cases of tissue like bone and teeth, cutting tiny amounts manually is difficult. These tissues should be processed to eliminate calcium phosphate through a process called "decalcification," which softens the tissues to be processed by a microtome machine. "Decalcification is accomplished through the use of chemicals, whether acid to make solvent salts or calcium/chelator mediators that adhere to ions of calcium. Decalcification of Microwave is a revolutionary approach that was shown to be faster than the manual procedure [9]. In this literature, there are no comparison studies on the valuation of non-fluorosed and fluorosed bone of cortical and cancellous histologically. The cell density of cortical bone and trabecular marrow, the occurrence or lack of resting lines and reversing lines, the existence/ deficiency of Osteoclasts, density of trabecular, and types of marrow were all evaluated in this study (red or yellow) [10]. Cell density in non-fluorosed & fluorosed cortical and cancellous bones Cellularity was substantially higher in non-fluorosed cortical and cancellous bones (11.835.21, 9.853.45; p-value is equal to 0.035, 0.021) than in fluorosed cortical and cancellous bones (6.613.31, 5.691.31), accordingly. Other histological criteria including rest and reverse lines, marrow contents, and osteoclast were examined in the present study. Non-fluorosed bone has more noticeable resting and reversing

lines than fluorosed bones. Both groups had high-fat content in their marrow. Non-fluorosed bone participants had osteoclast in abundance, but fluorosed bone patients had few to none. The cause for the preceding observation must be explained. Bone trabecular density these non-fluorosed and fluorosed bone had the identical trabecular density [statistically non-significant, p= [0.726]. Non-fluorosed bone had thick trabeculae, while fluorosed bone had short and thin trabeculae. The literature's clinical and experimental findings accept the concept of an important activity of fluoride [11] on the osteoblast and osteoclast cell populations. This influence is regularly observed, in the early stages of administration [12], and shows functional and morphological cell alterations that indicate greater activity in existent metabolic cells [13]. Fluoride's potential to enhance bone densification is of two types, according to an in vitro and in vivo experimental investigation employing sustained-release bone cement which is sodium fluoride. Biochemically, fluoride quickly binds to the hydroxyapatite mineral structure of bone, forming fluorapatite with enhanced the properties of mechanical and biochemical; and biologically, the ion of fluoride acts directly on osteoblasts, promoting differentiation and resulting in an osteoid wall of bone which is enlarged trabeculae as well as an improved the capacity of trabeculae. Such influence is regularly observed, in the initial steps of administration, and shows itself as functional and morphological cell alterations that indicate greater activity in existent metabolic cells. These benefits, if achieved properly by slow fluoride release from bone cement, might be highly helpful in preventing periprosthetic bone resorption [14,17]. The most notable histo-morphological changes were in the component of trabecular [18], which was replicated in a higher total volume of trabecular in both the portion of mineralized and non-mineralized. Clinical investigators still suspect an excessive amount of non-mineralized tissue, because of osteoid tissue in excess amount may obstruct treatment objectives or potentially raise the risk of long-bone cracks, mainly of the hips [19]. In clinical studies the other finding, appear to support Kanis and Meunier's hypothesis [19] that such changes of histomorphometry are nearly linked to the quantity of fluoride which varies depend on the dose which intake daily and secondly, the treatment time. Additional osteoid tissue is commonly detected in the early phases in oral treatment and at high doses [20]. There have been reports of histologic alterations in fluorosed bone. Bones become radiopaque on X-Ray because of accumulation of huge partially mineralized and less organized bone, which is not attributable to enhanced mineralization/resorption failure [20]. Various publications have also documented high mineralization of cortical bone in widespread and fluorosis

industrially [10]. This occurrence of elevated glycosaminoglycan concentrations could explain the mineralized collagen fibres detected in the resorbed areas. Sulfated glycosaminoglycans, which are powerful hindrance of mineralization, have been found in significant amounts in bone [1]. Mineralization of collagen fibers requires the removal of glycosaminoglycans. As a result, excessive glycosaminoglycan concentrations could be the cause of inadequately mineralized collagen fibrils [12]. Fluoride's role in raising GAG, Fluoride has been shown to raise GAG, or dermatan sulfate, levels in cortical bone, which limits development. There has also been evidence of elevated dermal tansulphate in human teeth in cases of dental fluorosis [7]. Fewer cross-link precursors of collagen & collagen synthesis could explain the alteration in the shape of fibers of collagen and the medium [16]. As a result, decreased collagen cross-links and synthesis, as well as a considerable rise in Glycosaminoglycan's might be the causes of uncultured alterations forms in fluoride bone. Fluoride accumulation in calcification and non-calcified tissue is associated with a variety of symptoms. This has been investigated in particular with regard to collagen fibers and non-collagenous components. The amount of hydroxyapatite higher in the cancellous bone rather than cortical bone. These results indicate that hydroxyproline contents are lowered in both osseous and non-osseous tissues during fluoride overdose. This could have an impact on the tissue's collagen content. This shows that collagen produced after fluoride consumption would be under oxidized and inter-linked inadequately, and is promptly assimilated. Collagen deposition in osseous and nonosseous tissues is irregular as a result of high fluoride consumption [15]. The nature of the cells in osteoid related to cartilage cells, chondrocytes and formation of osteoid resemble to the fibrocartilage and trabeculae is also present in chondrocytes due to the intoxication of Fluoride. The variation of the striking structural were observed in the cortical bone due to the ingestion of fluoride in huge amount (1) that why the thickness of cortical increased (2) and enhanced the diameter of Osteon [21]. In this study, the density of cellular cortical & cancellous bones was investigated. The study of the effects of fluoride on bone is an excellent source of information for studying biochemical reactions in fluorosed bones.

CONCLUSIONS

The studies that are similar to the goals of our current investigation aren't comparable because their participants, age, gender, water fluoride consumption, and technique differ from our study. The relevant studies date back to 1950, and there is limited research on a prominent aspect of human study currently. This may be due to the

chronic situation of fluoride-related disorders that shows up later in life as accumulative effect. As previously said that there is no treatment for this disease and no prevention, the government policies should be mandatory for the measurement of defluoridation, initially detection and treatment as the reversible changes in fluoride induced form.

REFERENCES

- [1] Lakhani N, Vandana KJWJPR. Mineral content of nonfluorosed and fluorosed bone-an in vitro study. 2018;15:422-33.
- [2] Lakhani N, Laxman KVJSJoRiDS. Microhardness of nonfluorosed and fluorosed dental cementum: An in vitro study. 2017;8(2):74. doi: 10.4103/srmjrds.srmjrds_81_16
- [3] Vandana K, Srishti Raj B, Desai RJBTER. Dental fluorosis and periodontium: an original research report of in vitro and in vivo institutional studies. 2021;199(10):3579-92. doi: 10.1007/s12011-020-02494-0.
- [4] Vandana KL, Girotra N, Jayashree NV, Bhat KJJotICDR0. Comparative assessment of fluorosed and nonfluorosed fibroblast attachment on fluorosed and nonfluorosed teeth after scaling and root planning and ethylenediaminetetraacetic acid root biomodification. 2014;6(1):29. doi: 10.4103/2231-0754.139090.
- [5] Girotra N, Vandana KJJolSoP. Fluorosed fibroblast attachment on fluorosed and nonfluorosed teeth after SRP and EDTA root biomodification. 2014;18(1):26. doi: 10.4103/0972-124X.128195.
- [6] Nazamlakhani and K. L. Vandana. Histology of Nonfluorosed and Fluorosed Dental Cementum-an Invitro Study. International Journal of Biomedical and Advance Research 2017; 8(03): 76-81. doi: <https://dx.doi.org/10.7439/ijbar>
- [7] Nakano Y, Besten PD. Fluoride effects on the dentin-pulp Complex. The Dental Pulp: Springer; 2014:191-9.
- [8] Laxman KV, Ghosh S, Dhingra K, Patil R. Effect of Er: YAG or Nd:YAG Laser Exposure on Fluorosed and Non-Fluorosed Root Surfaces: An In Vitro Study. Laser Ther. 2015 Mar 31;24(2):93-101. doi: 10.5978/islsm.15-OR-08.
- [9] Aswin PS, Vandana KLJJolSoP. A comparative assessment of clinical parameters, sialic acid, and glycosaminoglycans levels in periodontitis patients with and without dental fluorosis: A clinical and biochemical study. J Indian Soc Periodontol. 2020 May-Jun;24(3):237-243. doi: 10.4103/jisp.jisp_214_19.
- [10] Dalvi PJ, Ghosh S, Joshi VM, Bhat K, Prakash

- VHJJoPM, Education, Research. Fluorosis: Environmental Risk Factor for Periodontal Disease? 2017;51(4):157-61.
- [11] Vandana K, Sadanand K, M Cobb C, Desai RJTOCJ. Effects of tetracycline, EDTA and citric acid application on fluorosed dentin and cementum surfaces: an in vitro study. *Open Dent J*. 2016 Apr 8;10:109-16. doi: 10.2174/1874210601610010109.
- [12] Zipkin I, McClure F, Lee WJAoOB. Relation of the fluoride content of human bone to its chemical composition. 1960;2(3):190-5. doi: 10.1016/0003-9969(60)90022-4.
- [13] Jha Mohan, Susheela AK. Scanning electron microscopic and electron microprobe X-ray analysis of cortical bone of fluoride-treated rabbits. *Int J Tissue React*. 1984;6(3):255-61.
- [14] Neuman W, Neuman M, Main ER, O'leary J, Smith FJJoBC. The surface chemistry of bone: II. Fluoride deposition. 1950;187(2):655-61.
- [15] Call RA, Greenwood DA, Lecheminant WH, Shupe JL, Nielsen HM, Olson LE, Lamborn RE, Mangelson FL, Davis RV. Histological and chemical studies in man on effects of fluoride. *Public Health Rep (1896)*. 1965 Jun;80(6):529-38.
- [16] Wolff W, Kerr EJAJoMS. The composition of human bone in chronic fluoride poisoning. *Americal Journal of Medical Sciences*. 1938;195:493-7.
- [17] Zipkin I, McClure F, Leone N, Lee WJPHR. Fluoride deposition in human bones after prolonged ingestion of fluoride in drinking water. *Public Health Report (1896)*. 1958;73(8):732-740.
- [18] Susheela A, Jha MJIMS-B. Effect of Fluoride ingestion on cortical and cancellous bone-composition. 1981;9(11):1021-2.
- [19] DenBesten P, Li WJF, environment to. Chronic fluoride toxicity: dental fluorosis. 2011;22:81-96.
- [20] Abhinav A, Chandra SRS, Satyanarayana D, Jagadish RG, Rajababu PJIJoDA. Comparison of subgingival microbiota in fluorosed and non-fluorosed chronic periodontitis patients. *Indian Journal of Dental Advancements*. 2015;7(1):26-32.
- [21] Han J, Kiss L, Mei H, Remete AM, Ponikvar-Svet M, Sedgwick DM, et al. Chemical aspects of human and environmental overload with fluorine. 2021;121(8):4678-742. doi.org/10.1021/acs.chemrev.0c01263.



Original Article

High Risk of Cardiovascular Events in Patients, Biosynthesis of Aspirin-Resistant Thromboxane and the Risk of Stroke, Myocardial Infarction or Death

Erum Rehman¹, Syed Hasnain Ali Shah², Muhammad Nabi³, Zakia Subhan⁴, Shah Zaman^{1*}, Nabiha Naeem⁵, Dua-E-Jamila Khurram⁵ and Irfan Ullah⁵

¹Department of Pharmacology, Peshawar Medical and Dental College, Peshawar, Pakistan

²Department of Pharmacology, Kabir Medical College, Peshawar, Pakistan

³Institute of Pharmaceutical Sciences, Khyber Medical University, IPS-KMU, Pakistan

⁴Department of Pharmacology, KMU-IMS Kohat, Pakistan

⁵Department of Life Sciences, School of Science, University of Management and Technology, Lahore, Pakistan,

ARTICLE INFO

Key Words:

Cardiovascular, Aspirin, Thromboxane, Myocardial Infarction, Stroke.

How to Cite:

Rehman, E. ., Hasnain Ali Shah, S. ., Nabi, M. ., Subhan, Z. ., Zaman, S., Naeem, N. ., Khurram, D.-E.-J., & Ullah, I. . (2022). High Risk of Cardiovascular Events in Patients, Biosynthesis of Aspirin-Resistant Thromboxane And The Risk Of Stroke, Myocardial Infarction Or Death: Biosynthesis of Aspirin-Resistant Thromboxane & Risk of Stroke. Pakistan BioMedical Journal, 5(6).<https://doi.org/10.54393/pbmj.v5i6.583>

***Corresponding Author:**

Shah Zaman
 Department of Pharmacology, Peshawar Medical and Dental College, Peshawar, Pakistan
dr.shahzamanmankhan@gmail.com

Received Date: 22nd June, 2022

Acceptance Date: 27th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Objective: In a higher-risk group, we investigated if aspirin resistance, which is defined as inability to reduce production of thromboxane, enhanced the risk for cardiovascular disease.

Methods: The Cardiac Outcome Preventive Assessment Study collected baseline urine samples from 5000 patients. A level of urinary 11-dehydro-thromboxane B2 was measured, which is a marker of within vitro cell generation of thromboxane, in 400 cured patients with aspirin having a cardiovascular death, stroke and infarction, stroke during a 5-year follow-up and in 400 age- and matching sex control subjects, which did not have an event, using a nested case-control design. **Result:** After accounting for baseline differences, the risks of infarction, strokes, or cardiac mortality rose with every fourth of 11-dihydro-thromboxane B2, with individuals in the top fourth section having a 1.9-fold greater threat than those from the lower portion ("OR, 1.9; 95% CI, 1.3 to 2.8; $p=0.009$). The upper quartile showed a 2-fold increased myocardial infarction risk ("OR, 2.1; 95% CI, 1.3 to 3.5; $p=0.07$) and a 3.6-fold elevated risk of cardiac death ("OR, 3.6; 95% CI, 1.78 to 7.5; $p=0.01$) than the lower quartile. **Conclusions:** the 11-dehydro thromboxane B2 level in urine, better determine the risk of cardiovascular events or cardiovascular death in aspirin-treated patients. These findings also depicts that patients with elevated urine 11-dehydro thromboxane B2 concentrations are more impervious to aspirin, and could profit from greater antiplatelet medications or therapies that even more efficiently stop thromboxane generation in vivo or activities.

INTRODUCTION

In a broad population of therapeutic with arterial vascular disease, the threat events of cardiovascular are decreased by 25%, by using aspirin [1]. But, although 10 to 20% of patients who are suffering from venous thromboembolism are treated with repeated vascular episodes of aspirin, during long-term sequel, its effectiveness is limited [2]. Aspirin prevents thrombosis by irreversible acetylation of platelet cyclooxygenase-1 [3], which inhibits the thromboxane A2 production. Although it was also depicted that aspirin have other less defined functions which in result effects the platelet functionality, but their role to

aspirin's antithrombotic effect is unknown. The poor efficacy of aspirin could be due to several factors [4]. To begin with, it is widely known because platelets can be triggered by mechanisms that are unaffected by aspirin. Secondly, it has been proposed that in some cases, greater dosages of aspirin (75-325 mg/d) could be necessary to get the optimum antithrombotic benefit of aspirin [5]. On the other hand, aspirin which is present in low-dose, stop the activity of platelet cyclooxygenase-1 by 95% [6] and having proof that the antithrombotic efficacy of this medicine is depended upon dosage [6, 7]. Third, certain patients might

have the ability to produce thromboxane A2, in spite of receiving standard aspirin dosages and hence fail to improve from aspirin therapy [8]. This third mechanism's clinical significance is unknown. Aspirin resistance has been labeled as all three probable reasons for aspirin failure. The word used by us, in order to depict the third putative process in this investigation: insufficient thromboxane suppression of production with the typical aspirin dosage. The 11-dehydro thromboxane B2 metabolite, which is a stable thromboxane A2 metabolite, present in urine with different concentrations is also measured, which can be recycled further to calculate the amount of thromboxane A2 inhibition [9]. As a result, the levels of baseline urine 11-dehydro thromboxane B2 was evaluated in 800 participants that were treated with aspirin, from tertiary care who were at higher risk of cardiovascular events. To see if insufficient inhibition of thromboxane production is related with the higher chances of getting cardiac events or diseases in future.

METHODS

Participants were enrolled in a randomized, placebo-controlled, prospective study of ramipril plus vitamin E for subsequent cardiac preventing sickness. The institutional review committee approved the study at each participating center and gave informed consent in all subjects. Overall, 9652 patients, having a previous record of strokes, diabetes, coronary complications of heart and peripheral neuropathy, as well as at least one additional possible cardiac risk, were categorized randomly into 4 groups: Ramipril titrated to a maximum of 10 mg per day, 400 IU Vit E per day, both, or none. The trial began in 1993 and was prematurely ended in 1999, due to clear proof of ramipril's efficacy. Collection of Urine Samples at the time of randomization, each study participant was requested to produce a first-morning urine sample. The baseline urine samples were provided by 9393 patients (98%) out of a total of 9652 patients. The central laboratory at the city laboratory received 18 sample data (5638) from 139 study participants, which were held at 80°C until evaluation. Health Outcomes Monitoring and Assessment All participants were monitored for 30 days, 60 days, and 6 months till the trial was completed. Health consequences were documented and pharmaceutical use, particularly aspirin, was reported at each follow-up. Infarction, strokes, and mortality from CVD, as described earlier, were the primary outcomes. Cases & Control Subjects were chosen. Only patients who were taking aspirin at the start of the run-in phase (before randomization), at randomization (coinciding with the time of urine collection), and at each follow-up visit were included. Cases were classified such patients which are treated by aspirin who submitted a

sufficient baseline urine sample and after the randomization it also had a verified stroke, myocardial infarction, or mortality of cardiovascular. After randomization, Some subjects which are under-control were chosen at random from those patients who gave an urine sample as an acceptable baseline but had no infarction, strokes, / cardiovascular mortality. Analytical Procedures Urine was collected and held at baseline for each case and the control subject was thawed and tested for 11-dehydro-TXB2 concentrations by an available commercially enzyme immunoassay with intraassay & intra-assay coefficients of variation in coefficients of intra-assay is 12.1% and 10%, accordingly. Assessments were carried out by laboratory personnel who were unaware of whether the patient was a case or a control participant. Furthermore, the control specimens and case were tested in a random order, limiting the risk of biases. Statistical Analysis: For cases and controls, we estimated means or percentages for baseline demographic and threat variables. The Student's 2-tailed for means and McNemar 2 test were used to determine the statistical importance of any alterations between cases and controls. The median levels were also estimated, and Wilcoxon's rank-sum test was used to compare values in case and control groups. After splitting the data into sections established by the division of the entire unit, trend tests were conducted to see if there was any link between rising baseline urine 11-dehydro-TXB2 levels and chance of infarction, strokes / cardiac mortality. A separate multivariable regression model was used to investigate the relationship between urinary 11-dehydro-TXB2 concentrations and baseline patient characteristics such as age, gender, heart rate, blood pressure, Mass index, history of vascular disease, conventional vascular risk factors, lipid-lowering therapy, blockers, diuretics, and randomized treatment allocation (ramipril or vitamin E). The intervals of confidence were determined at the 95% level and all probabilities are two-sided.

RESULTS

The general characteristics of the groups of case and control shown in Table 1.

Variables	Case total 400	Case total 400	p-value
Age	68.4 ± 8.3	68.5 ± 8.3	0.89
Gender female %	78 (16.9)	78 (16.9)	.
Mass index	28.9 ± 5.2	27.8 ± 4.8	Less than 0.001
Heartbeat rate	67.3 ± 11.4	66.7 ± 11.8	0.5
DBP	77.7 ± 8.9	76.7 ± 8.5	0.09
SBP	148.2 ± 21.7	144.6 ± 19.1	0.03
Coronary history %			
Any other	478(97%)	475(96%)	0.65
Infraction	375(75.7)	310(64%)	Less than 0.01

Angina stable	366 (73.80)	347 (64.8)	0.19
Angina unstable	195 (38.8)	187 (37.2)	0.76
CABG	187 (37.2)	165 (32.7)	0.26
PCI	88 (18.9)	105 (22.4)	0.07
PVS %	250 (50.3)	174 (36.6)	Less than 0.01
HYPERTENSTION	120 (45.8)	155 (32.7)	Less than 0.01
Diabetic %	160 (33.7)	106 (22.6)	Less than 0.01
Total colterol level	280 (57.3)	311 (64.6)	0.49
Smoking habit	82 (17.7)	58 (12.8)	0.04
Medicine %			
Aspirin	400 (100)	400 (100)	.
Beta blocker	242 (50.5)	236 (49.3)	0.87
Lipid low agent	122 (25.9)	167 (35.1)	0.03
Diuretics	74 (16.0)	35 (8.1)	Less than
Calcium blocker	290 (60.3)	249 (49.9)	0.01
Ramipril	238 (47.6)	285 (57.2)	0.03
Vitamin E	257 (51.5)	263 (53.7)	0.85

Table 1: Study Participants' Baseline Characteristics

"Values are mean±SD or n (%). CABG indicates coronary artery bypass graft surgery; CV, cardiovascular; DBP, diastolic blood pressure; MI, myocardial infarction; PCI, percutaneous coronary intervention; SBP, systolic blood pressure; and TIA, transient ischemic attack" Patients who had cardiovascular death, stroke or myocardial infarction, stroke, had a mean BMI highly and baseline blood pressure and have a history of smoking, high blood pressure diabetes, infarction, or peripheral vascular disease than those who did not have these events. At the outset, cases were more likely to be given diuretic or blockers of calcium channel, and few likely to be given such drugs which were lipid-lowering or assigned to a therapy of ramipril. The gender and age of the patients and controls were similar as a result of the similarity. The result of myocardial infarction in patients who developed the composite, stroke, or mortality of cardiovascular had significantly greater median and mean of geometric urine quantity at baseline of 11-dehydro-TXB2 than those who did not experience these events, Table 2.

Concentration, 11-Dehydro Thromboxane B2 ng/mmol Creatinine			
Result	Case	Control	P- value
CV death, stroke MI or (n=488)			
Geometric mean	25.6	22.6	.02
Median	23.8	22.1	.01
MI (n=388)	25.6	21.8	.04
Geometric mean			
Median	23.9	21.4	.02
Stroke (n=80)	26.1	28.5	0.58
Geometric mean			
Median	22.4	26.8	.51
death in CV (n=255)			
Geometric mean	26.7	21.5	<.01
Median	25.1	18.8	<.01

Table 2: Concentrations of Urine (11 Dehydro Thromboxane B2) In Case Control Group Baseline Myocardial infarction is referred to as MI, while cardiovascular disease is referred to as CVD

Those who had an infarction (25.6 vs 21.8 ng/mmol creatinine, P=0.04) or died of a cardiac reason (26.7 vs 21.5 ng/mmol creatinine, P=0.02) exhibited the highest difference between cases and controls. In the urine of subjects, the quantities of 11-dehydro thromboxane B2 who went on to have a stroke and their comparison group (26.1 VS 28.5 mmol creatinine, P=0.58) were not substantially different. For each rising quartile of baseline urinary 11-dehydro thromboxane B2 concentrations (p for trend across quartiles, 0.02). The probable outcomes indicated that, the patients lies in the higher quartile have a greater probability of 1.8 folds of getting CV diseases, strokes and myocardial infarction and death as compared to the patients having lower quartile (p for trend across quartiles, 0.02). (1.9 95% of OR, CI, 1.3 to 2.8 P=0.09. Infarction (p-value= 0.005, for tendency across the quartiles) and cardiac mortality (p-value= 0.02, for trend across quartiles) showed a similar relationship, while stroke (value of p= 0.31, for tendency across quartiles) not in Table 3. Adjusting or non-adjusting for basis dissimilarities among the group of cases and controls, including traditional cointerventions, cardiovascular risk and randomized therapy allocation, the results were similar. Separate analyses was conducted on individuals that had an incident in one year of training enrollment and those who had an 12 months event later to see if elevated concentrations of baseline 11-dehydro-TXB2 were linked with initial CV events somewhat delay CV events. Using linear multivariable regression modeling, the adjusted odds for the composite outcome of myocardial infarction, stroke, or cardiovascular death that was associated with the highest quartile of urinary 11-dehydro-TXB2 as compared to the lowest quartile were 2.8 (95% CI, 0.8 to 9.2) for events occurring within the first 12 months and 1.8 (95% CI, 1.1 to 2.8) for events occurring after the first 12 months (p=0.05). These variables, however, were capable of predicting 5% of the difference in urine 11-dehydro-TXB2 levels when they were combined (R² .056), Table 3.

"11-Dehydro Thromboxane B2 Concentration Quartiles, ng/mmol Creatinine"					
Result/Outcome	<16.2	16-22.9	22.8-34.8	>34.9	P-value
MI/stroke/CV death (n 400)	1.1	1.4 (0.10T02.2)	1.5 (0.10T02.3)	1.9 (1.3T02.8)	0.02
P-value	1.1	.14	.010	0.010	
MI (n 389)		1.4 (0.09T02.2)	1.6 (0.11T02.6)	2.1 (1.3T02.4)	0.05
95 CI					
P	1.1	.27	.08	.07	0.30
stroke		2.6 (0.7T011.1)	0.7 (0.3T02.3)	0.7 (0.3T01.9)	
95 CI					
P	1.1	.19	.46	.35	0.01
CV death n 255		2.6 (1.1T03.8)	0.7 (0.3T02.3)	2.6 (1.8-7.5)	
95 CI					
P		0.07	.46	Less than 0.01	

Table 3: Adjusted Odds* of Future Cardiovascular Death, myocardial Infarction, and Stroke Based on 11-Dehydro Thromboxane B2 Urinary Concentrations at Baseline

DISCUSSION

This study shows a link between, aspirin resistance, which is defined as the inability to decrease thromboxane production, and cardiovascular events. Elevated baseline urine levels of 11-dehydro thromboxane B2 (11-dehydro-TXB2) were linked with a higher chance of cardiovascular events (CV), notably cardiovascular death and infarction that is exactly define as treated group of aspirin who were at great threat of cardiovascular. This link was graded, strong and unaffected by traditional vascular risk factors such as increased BMI, BP, hypertension, diabetic, smoking, and previous vascular disease history. Furthermore, changes in the majority of individuals having lipid-lowering/ antihypertensive treatment between cases and controls, as well as those randomized to vitamin E or Angiotensin-converting enzyme inhibitors, did not affect the strength of the connection. The inadequate inhibition of thromboxane production by aspirin can be explained by several processes [10]. To begin, polymorphisms/mutations in the "cyclooxygenase-1 genes" (COX-1) that enable it resistant to the effect of aspirin inhibition could give a biological basis for aspirin resistance. Secondly, Nucleated cells like monocytes and vascular endothelial cells can either supply prostaglandin Hydrogen gas to platelet to pass platelets COX-1 or use prostaglandin H2 to generate its "thromboxane A2" because they have a lot of it [11, 12]. COX-1 or -2 catalyzes the conversion of arachidonate to prostaglandin H2. Although low-dose aspirin kills COX-1 in platelets permanently and fully, Nucleated cells can renew the enzyme [13,14]. Whereas COX-1 is inhibited with the concentration of 90 to 400 mg of aspirin, a dose that is comparable to that used in the city laboratory. The suppression of COX-1 necessitates daily dosages of aspirin

above 500 mg [14,15]. Whereas, COX-1, which is stated continuously in nucleated cells, stimuli for inflammation increase the expression of COX-2 10 to 20-fold in nucleated cells. Because atherosclerosis is an inflammatory disease, increased COX-2 overexpression may lead to aspirin resistance in patients with ischemic heart disease [16]. Our result of an independent, albeit modest, the link between the disease history of peripheral vascular & urine 11-dehydro-TXB2 concentrations in the urine is reliable with previous research demonstrating that the intensity of atherosclerotic is a key predictor of production of thromboxane. Moreover, a very moderate dosages of aspirin effectively and irreversible block or stop platelet COX-1, changes in the degree or intensity of atherosclerotic are improbable to alter de novo platelet thromboxane generation in patients taking aspirin. Upregulation of COX-2 in atherosclerotic tissue 24 has been linked to increased prostaglandin H2 synthesis and transport to platelets, bypassing platelets COX-1 and resulting in these patients in aspirin-insensitive thromboxane manufacture. Since very modest dosages of aspirin effectively and irreversible block platelet COX-1, changes in the degree or intensity of atherosclerotic are unlikely to alter de novo generation of platelet thromboxane in patients taking aspirin. Up-regulation of COX-2 in atherosclerotic tissue24 has been linked to increased prostaglandin H2 synthesis and transport to Platelets, COX-1 platelet bypassing and resulting production of insensitive aspirin-thromboxane in the patients. The reason for the lack of an association between urinary 11-dehydro-TXB2 and risk of stroke is unclear. Increased concentrations of urine of 11-dehydro-TXB2 have been described to following aspirin failure, stroke in patients to decrease platelet reactivity or in response prevent platelet activation to different agonists of platelet has also been observed after stroke in these patients [17-19]. The mean 11-dehydro-TXB2 concentration of urine in stroke cases was comparable to that in all case scenarios (26.1 vs 25.6 ng /mmol, creatinine), but the relating matched concentration in urinary stroke was greater in control subjects than that in all subjects (28.5 vs 22.6 ng /mmol, creatinine). The figure of patients having stroke and matched control subjects, on the other hand, was small relatively (n80). Certain pure and ordered relationship among both urinary 11-dehydro-TXB2 concentration and also the complex results of stroke, infarction, or cardiac mortality, and also other discrete constituents of this outcome, the lack of a demonstrable relationship between stroke risk and urinary 11-dehydro-TXB2 concentration is most likely due to chance. There are various potential limitations to our research. First, there were important alterations between cases and controls in terms of

potentially critical confounders such as BMI, systolic, hypertensive, diabetes, smoking, and vascular disease history. Even after these differences were taken into account, a clear link was found between the concentration urine 11-dehydro-TXB2 and the threat of mortality, myocardial infarction, and stroke. The absence of a link among the concentrations urinary 11-dehydro-TXB2 and baseline patient characteristics adds to the evidence that confounding was not a factor in our findings. Secondly, a recently acute events of thrombotic like myocardial infarction or stroke, may have altered urine 11-dehydro-TXB2 concentrations, which are likely to be related to activation of platelet and increased the excretion of thromboxane metabolites in urinary. Patients that had an infarction or stroke during the past seven weeks were not included in the research, therefore this interpretation is less [20]. Thirdly, single baseline measurements of urine 11-dehydro-TXB2 levels may not adequately reflect the activation of platelet over time. However, the link between increased urine 11-dehydro-TXB2 levels at baseline with subsequent risk of cardiac events was visible both during the first 12 months following randomization and beyond that time, indicating a long-term relationship. Fourth, we could not use salicylate blood levels or urine to verify patient satisfaction with aspirin medication. Yet, at each follow-up visit, we particularly examined compliance with aspirin medication, and we only included patients who were using aspirin prior to randomization and at a six-month follow-up visit. At any point, patients who still taking aspirin throughout the research were excluded. Lastly, the variation magnitude in urine 11-dehydro-TXB2 levels is unidentified, which could restrict the use of this indicator in predicting the chance of potential CV cardiovascular events particularly in a patient.

CONCLUSIONS

It concludes that chronic thromboxane production, independently of certain other cardiovascular risk factors, expects the probability of composite results of aspirin-treated individuals in infarction, strokes, or death in cardiovascular at greater threat of cardiac events. These results suggest that higher urinary levels of 11-dehydro-TXB2 may be used to identify patients having resistance against a predictable dosage of aspirin antithrombotic and who might valuable from greater therapies or treatments of antiplatelet that more efficiently inhibit the activity or thromboxane generation.

REFERENCES

[1] Wang N, Vendrov KC, Simmons BP, Schuck RN, Stouffer GA, Lee CR. Urinary 11-dehydro-thromboxane B2 levels are associated with vascular inflammation and prognosis in atherosclerotic

cardiovascular disease. *Prostaglandins & other lipid mediators*. 2018 Jan; 134:24-31. doi: 10.1016/j.prostaglandins.2017.11.003.

- [2] Venketasubramanian N, Agustin SJ, Padilla JL, Yumul MP, Sum C, Lee SH et al. Comparison of Different Laboratory Tests to Identify "Aspirin Resistance" and Risk of Vascular Events among Ischaemic Stroke Patients: A Double-Blind Study *Journal of Cardiovascular Development and Disease*. 2022 May; 9(5):156. doi: 10.3390/jcdd9050156.
- [3] Sisodia P, Bhatia R. Aspirin resistance and stroke. *Journal of Stroke Medicine*. 2018 Jun; 1(1):19-27. doi:10.1177/2516608518777017
- [4] Chauhan S, Singh A, Karkala YR, Devasia T, Kareem H, Uppunda D et al. Gender-specific 11-dehydro-thromboxane B2 levels in acute coronary syndrome and its association with clinical outcomes. *Journal of Applied Pharmaceutical Science*. 2020 Nov; 10(11):010-7.
- [5] Ebrahimi P, Farhadi Z, Behzadifar M, Shabaninejad H, Abolghasem Gorji H, Taheri Mirghaed M et al. Prevalence rate of laboratory defined aspirin resistance in cardiovascular disease patients: A systematic review and meta-analysis. *Caspian Journal of Internal Medicine*. 2020; 11(2):124-134. doi: 10.22088/cjim.11.2.124..
- [6] Liu H, Xu Z, Sun C, Chen Q, Bao N, Chen W et al. Perioperative urinary thromboxane metabolites and outcome of coronary artery bypass grafting: a nested case-control study. *BMJ Open*. 2018 Aug; 8(8):e021219. doi: 10.1136/bmjopen-2017-021219
- [7] Block RC, Shearer GC, Holub A, Tu XM, Mousa S, Brenna JT et al. Aspirin and omega-3 fatty acid status interact in the prevention of cardiovascular diseases in Framingham Heart Study. *Prostaglandins, Leukotrienes and Essential Fatty Acids*. 2021 Jun; 169:102283. doi: 10.1016/j.plefa.2021.102283
- [8] Noor M, Nawaz U, Fazal I, Waheed A. Aspirin resistance: An emerging threat to cardiovascular disease patients and its association with age and gender. *Pakistan Heart Journal*. 2018; 51(2).
- [9] Furtado RHM, Giugliano RP, Dalcoquio TF, Arantes FBB, Barbosa CJDG, Genestreti PRR et al. Increased bodyweight and inadequate response to aspirin in individuals with coronary artery disease. *Journal of Thrombosis and Thrombolysis*. 2019 Aug; 48(2):217-224. doi: 10.1007/s11239-019-01830-z
- [10] Wang IE, Yi S, Block RC, Mousa SA. Aspirin and omega-3 polyunsaturated fatty acid use and their interaction in cardiovascular diseases and colorectal adenomas. *Nutrition Research Reviews*. 2021 Jul:1-13. doi: 10.1017/S0954422421000238.

[11]

- [11] Behera KG, Samal S, Swain J, Mohanty JN. Aspirin Resistance in Patients with Ischemic Stroke: Study at a Tertiary Care Teaching Hospital. *Annals of the Romanian Society for Cell Biology*. 2021 May; 14:486-94.
- [12] McCarthy NS, Vangjeli C, Surendran P, Treumann A, Rooney C, Ho E, et al. Genetic variants in PPARGC1B and CNTN4 are associated with thromboxane A2 formation and with cardiovascular event free survival in the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT). *Atherosclerosis*. 2018 Feb; 269:42-49. doi: 10.1016/j.atherosclerosis.2017.12.013.
- [13] Lim ST, Thijs V, Murphy SJX, Fernandez-Cadenas I, Montaner J, Offiah C, et al. Platelet function/reactivity testing and prediction of risk of recurrent vascular events and outcomes after TIA or ischaemic stroke: systematic review and meta-analysis. *Journal of Neurology*. 2020 Oct; 267(10):3021-3037. doi: 10.1007/s00415-020-09932-y.
- [14] De Stefano V, Rocca B, Tosetto A, Soldati D, Petrucci G, Beggiato E, et al. The Aspirin Regimens in Essential Thrombocythemia (ARES) phase II randomized trial design: Implementation of the serum thromboxane B2 assay as an evaluation tool of different aspirin dosing regimens in the clinical setting. *Blood Cancer Journal*. 2018 Jun 1;8(6):49. doi: 10.1038/s41408-018-0078-3.
- [15] Alegbeleye BJ, Akpoveso OO, Mohammed RK, Asare BY. Pharmacology, pharmaceuticals and clinical use of aspirin: a narrative review. *Journal of Drug Delivery and Therapeutics*. 2020 Oct; 10(5-s):236-53. /doi.10.22270/jddt.v10i5-s.4351
- [16] Rezabakhsh A, Soleimanpour HJFiCDR-A-AAV. Aspirin Desensitization/Challenge in Patients with Cardiovascular Diseases: Current Trends and Advances. 2022; 5:147. doi.10.2174/9 789815040 616122050007
- [17] Gurbel PA, Bliden KP, Zhu J, Troullos E, Centofanti R, Jarvis S, et al. Thromboxane inhibition during concurrent therapy with low-dose aspirin and over-the-counter naproxen sodium. *Journal of Thrombosis and Thrombolysis*. 2018 Jan; 45(1):18-26. doi: 10.1007/s11239-017-1593-y.
- [18] Horyniecki M, Łączka-Gaździk B, Niewiadomska E, Mazur B, Śnit M, Łabuz-Roszak B. Prevalence of high on-treatment platelet reactivity in patients with chronic kidney disease treated with acetylsalicylic acid for stroke prevention. *Pol Arch Intern Med*. 2018 Nov; 128(11):667-676. doi: 10.20452/pamw.4349.
- [19] Patrono C. Aspirin. In *Platelets*. Academic Press. 2019 Jan: 921-936. doi.10.1016/B978-0-12-813456-6.00050-3
- [20] Abu Subeih H. Aspirin for Optimising Pregnancy Outcome in Pregestational Diabetes The Ireland Study (Investigating the Role of Early Low-dose Aspirin in pre-existing Diabetes) (Doctoral dissertation, Royal College of Surgeons in Ireland). 2021 Jan.



Original Article

Rate and Factors Associated with Dentine Hypersensitivity among Pakistani Patients: A Cross Sectional Study

 Neelofar Nausheen¹, Mahirah Iqbal², Muhammad Ifham Khan Jadoon³, Pashmina Nisar¹, Ambereen Humayun⁴, Aqsa Khalid⁵ and Dua-E-Jamila Khurram⁵
¹Department of Oral Biology, Sardar Begum Dental College, Gandhara University, Peshawar, Pakistan

²Department of Periodontology, Peshawar Dental College and Teaching Hospital, Pakistan

³Department of Periodontology, Ayub Dental Section Ayub Medical College Abbottabad, Pakistan

⁴Department of Anatomy, Peshawar Dental College, Pakistan

⁵Department of Life Sciences, School of Science, University of Management and Technology, Lahore, Pakistan

ARTICLE INFO

Key Words:

Dentine Hypersensitivity, seriousness, demographics,

How to Cite:

 Nausheen, N. ., Iqbal, M. ., Ifham Khan Jadoon, M. ., Nisar, P. ., Humayun, A. ., Khalid, A. ., & Khurram, D.-E.-J. (2022). Rate and Factors Associated with Dentine Hypersensitivity Among Pakistani Patients: A Cross Sectional Study : Incidence of Dentine Hypersensitivity Among Pakistani Patients. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.586>

*Corresponding Author:

 Neelofar Nausheen
 Department of Oral Biology, Sardar Begum Dental College, Gandhara University, Peshawar, Pakistan
 Neelofarnaushen@hotmail.com

Received Date: 18th June, 2022

Acceptance Date: 25h June, 2022

Published Date: 30th June, 2022

ABSTRACT

As far as our knowledge is, on the pervasiveness of the sensitive teeth in the adults of Pakistani population, there is not much data published. The data is collected from dental clinical examination and some self-governed questionnaires. **Objective:** To find out how common Dentine Hypersensitivity is in Pakistani people and to search out the causative elements/factors **Methods:** At the Dental College in Peshawar, Out-Patient Department (OPD) examined 1605 people. The questionnaire was distributed among the patients suffering from dentine hypersensitivity. Dental history, demographics, DH symptoms data dietary habits as well as the factors linked to DH, were collected in order to acquire the following information. In total 732 questionnaires were completed. Oral examinations were used to assess DH in people who had DH in at least one tooth. The participants also used a ten-digit visual analog scale to rate the seriousness of DH. A quick, acute pain emanating from uncovered dentine in rejoinder to an explorer probe and triple syringe wind squall of the tooth surface confirmed the diagnosis of DH. **Results:** The self-reported prevalence of Dentine Hypersensitivity was 13%, while the clinically diagnosed percentage of DH was 8.2%. Females were evaluated in greater numbers than males. The highest percentage of DH was observed in the patients of age group 30-39 years. The first molars and mandibular central incisors were the teeth that were considerably damaged. The main reason for the dentine hypersensitivity observed was the cold (89.4%). Those with moderate sensitivity for more than six months relied on natural remedies such as brushing with a pain-reducing paste rather than visiting their dentist. However, out of the total just 41 (8.8%) participants stated that they had visited a dental office. **Conclusions:** According to the findings, DH is a usual and widespread dental ailment in Pakistan. Despite the fact that the illness seems to cause some discomfort, majority of the patients prefer to either disregard it or simply endure it. As a result, the ailment is unlikely to have a substantial impact on the patients complaining of both the problem's quality of life and lifestyle.

INTRODUCTION

Dentine hypersensitivity (DH) is a common occurrence in medical practice and a difficult condition to treat [1, 2]. Acute, temporary pain from an uncovered dentin area in reaction to stimulus which cannot be linked to any other disorder or disease characterizes DH. Thermal, tactile, chemical, osmotic, or even evaporation-related stimuli are common [3]. The symptoms of Dentine Hypersensitivity

can be similar to other severe oral disorders, thus the identification is dependent on looking for risk factors, identifying wear lesions, and ruling out other dental diseases such cavities or periodontitis. DH can have a negative impact on one's life. It has the power to effect when as well as how the subject gets to eat and drink, to prevent dental cleaning, to have serious emotional effects,

and to change lives [4, 5]. DH prevalence has been reported to range from 4-74% depending upon that sample investigated in various data compilations [6]. There could be various reasons for these differences. Some studies asked respondents about sensitive teeth (ST) and gums using self-governed questionnaires, whereas others identified DH following a professional clinical assessment. People who claim to have ST may have DH as well as other oral disorders such as cavities or periodontitis, which would support the increased prevalence. Even if investigations are classified into two parts focused on clinical versus self-data, the estimate range remains wide (13-57% versus 4-74%, correspondingly). Other explanations, such as characteristics of the sample, have been developed to describe these disparities (study location, ethnic origin, dental care regime, periodontal status, socio-economic status, oral hygiene habits). The information given for determining the existence or non-existence of DH might be based on one of two approaches: a receptive approach that relies on the subject's assertion of pain, or an actively strategy that involves the application of various thermo-mechanical stimulations [7, 8]. Another aggravating element is the condition's episodic character, which can either elicit or suppress painful feelings [9]. Furthermore, there are only a few researches that have sought to 1) quantify the problem and 2) study factors linked to DH in the Pakistani community. Thus, the focus of this research was to identify the frequency of DH in a Pakistani community and to examine the factors linked to it. In Pakistan, there is limited information about the general public's awareness of dentine hypersensitivity. As a result, the primary goal of our research was to determine the incidence of dentine hypersensitivity and to investigate the many characteristics related with it within patients who visited the dentistry outpatient clinics of the Institute of Dentistry Peshawar.

METHODS

The current study was a survey and clinical extensive research study that carried out at the Dental College in the Out-Patient Department (OPD) in Peshawar from December of 2021 to April 2022. Examined and assessed adult subjects aged 20 years or above in the current study. Only 732 patients were selected to complete a form from a total of 1605 patients evaluated in the general OPD. The study excluded those teeth that have been carious, broken, or cracked. Patients who had trouble in communicating and/or were on analgesics or sedatives were also ruled out of the trial. For data collection, a relevant clinical data sheet was created. The DH responsiveness was measured using a visual analogue scale (VAS). The purpose of the study was communicated to the evaluating dentists as well as the

criteria of DH occurrence. A demonstration of the process for DH intra-oral examinations was given to the evaluating dentists. Followed by a short description of how and why the perceived pain will be reported on the visual analog, patients assessed the ensuing sensation of pain on the visual analogue sheet. The evaluators were validated by evaluating 15 participants over the course of a week until they achieved 95% inter- and intra-examiner concordance. During the visit to the Dental Clinic, interviews were performed. The presence of discomfort in the participants' teeth was investigated. The first section of the survey was intended to extract descriptive information from the participants, such as their name, gender, age and profession. The second section consisted of questions aimed at eliciting reasons for Dentine Hypersensitivity, which included systemic illnesses such as stomach troubles, indigestion, and vomiting (e.g., inherent erosional components); oral hygiene standards including such as brushing teeth and teeth whitening practice, including the use of some toothpaste for whitening purpose or both, are all essential. The periodontium general health of each respondent, including latest scaling antiquity over the last 3 months' initial interview and orthodontic appliances within the last 3 months; individual routine background of liquids consumption and period of DH. Participants too were questioned about their whereabouts of numbing toothpaste in the past and any expert therapy for Dentine Hypersensitivity they had received from their dentists. Participants who had been officially diagnosed with DH were encouraged to share the factors that triggered their DH reaction. Water, drinks, hot food, tooth brushing and cold were the stimuli which were triggering the response.

Intraoral Test Procedures: Individuals who said they had DH were evaluated clinically to see if they had it. A quick, intense pain emanating from uncovered teeth in reaction to osmotic and sensory stimuli mostly on the uncovered dentine of the tooth was used to diagnose Dentine Hypersensitivity. A 1 sec air shock wave was supplied by using orthodontic unit triple hypodermic needle, trying to blow a short shock (45 PSI force) of room temp air (19-23°C), held right angles and 2.5 cm away out from the tooth surface, while the neighboring teeth were shielded with palms or cotton wraps to produce evaporative triggers. A dental probe was passed horizontally to the surface of the tooth with distal sweeps to evaluate sensory stimulation, and the force was risen steadily until the patients responded. Cracked tooth syndrome/Chipped teeth/Dental caries/fractured restorations/Gingival inflammation/Marginal leakage/Pulpitis Post-restorative sensitivity and sensitivity to both surgical and non-surgical treatments were all ruled out during the examination.

Dentine Hypersensitivity Measurement on Visual Analogue Scale (VAS):

The participants were given a Visual analogue rating sheet to gauge their reaction to DH. The Visual analogue sheet consisted of a 10-centimeter line graph with ten digits (0-10). Patients with Dentine Hypersensitivity in one of the teeth was asked to mark a vertical line on the Visual Analogue Score to assess their impression of the discomfort magnitude of its most hypersensitive tooth. The marks between the numbers would be as follows: 0-1 meant minimal pain, >1- 4 meant minor discomfort, >4- 7 meant mild pain, and >7-10 meant extreme pain.

RESULTS

Out of total 732 respondents, 398 (54.4%) were females and 334 (45.6%) were males. Among total, 286 (39%) were reported dentine hypersensitive in their teeth (Table 1). Twenty-one percent (21 %) of male participants and 18 % of female participants tended to eat from one part of their mouth, while 13.5% of females and males avoided particular meals to avoid discomfort. Cold food and drinks were indicated by the population of individuals (n=226/286, 79%) as a major cause in dental sensitivity. The percentage of hot food and drinks causing hypersensitivity was 21%. Brushing teeth vigorously was reported as a major factor in 23 % of males, whereas brushing for longer periods of time, i.e. 2-3 minutes, was identified as a major component in females (35%). The maxillary back teeth were the most commonly reported as sensitive in both men and women, following the maxillary central incisors. When the participants were asked to nominate the parts of mouth in which they are having dentine hypersensitivity, among total 286, 65 (22.7%) of the participants were experiencing pain in the lower posterior portion, about 50 (17.5%) of the participants were having pain in the lower part of the left region. About 57 (19.9%) of the participants showed that they were having pain on the inner palatal and inner lingual surfaces of the teeth, however 90 (31.5%) of the participants showed that they were having pain on the outside surfaces such as facial, labial, buccal of the teeth. About 24 (8.4%) of the participants did not answer the questions. When the participants were questioned about the scaling and polishing of the teeth, out of the total only 105 (36.7%) of the participants claimed that they had recently cleaned their teeth. Based on a 0-10 (VAS), 73 (25.5%) of the participants reported that they had no pain as from the scaling treatments, whereas 213 (74.5%) stated that they had some pain. About 10 (3.5%) of the respondents said their dentist had performed any periodontist surgery, and they said they were in pain for up to two weeks afterward. When the participants were investigated of the discomfort and other factors, 65

(22.7%) reported periodontal disease which is known as gingivitis, about 152 (53.2%) were having tooth brushing, 27 (9.5%) were having restorative materials, about 13 (4.5%) were having professional cleaning, about 11 (3.8%) of the participants were having orthodontic treatment, 10 (3.5%) were having bleaching, and the participant 8 (2.8%) were having vomiting.

Dentine Hypersensitive	Females (%)	Males (%)
Present	176 (44.2)	110 (32.9)
Absent	166 (41.7)	140 (41.9)
Occasionally	53 (13.3)	67 (20.1)
Rare	3 (0.8)	17 (5.1)
Total	398 (54.4)	334 (45.6)

Table 1: Incidence of Dentine hypersensitive among patients (n=732)

DISCUSSION

In a study 39% of people had dentine hypersensitivity, which is consistent with a study done in China [10]. Furthermore, investigations conducted in India and Nigeria found greater rates of Dentine Hypersensitivity, with rates of 52.5% and 55%, correspondingly [11, 12]. This disparity can indeed be attributable to differing approaches for detecting DH, such as utilizing a survey alone and in conjunction with a clinical assessment, as well as a shortage of patients understanding and a tendency to associate pain from other sources with DH. According to some previous studies, dentine hypersensitivity is more common in females [13, 14]. Similarly, in the another study, a numerically significant correlation was found between groups, the females being more vulnerable than men. This could be because women are more mindful of tooth brushing and visiting the dentist more regularly [15]. Cold items and carbonated beverages are well-known contributors to tooth sensitivity. In our study, 79% of the participants were sensitive to cold items; these findings are similar to those of Olak et al, Bamise et al., and Gillam et al., [16-18]. The most of male and female participants preferred to chew with one half of their mouth; these changes that occur enabled them overcome their discomfort. These results were similar to those of a Kielbassa survey, which found that around three-quarters of people avoided utilizing the damaged side of their mouth [19]. Sensitivity and periodontal abrasion in teeth are caused by the use of a stiff bristled brush and poor brushing techniques [20, 21]. Brushing period and manner have been found as causal factors for gingival inflammation in studies undertaken by Kassab and Cohen, Drisko C [22, 23]. In the current study, the proportion of male respondents washed their teeth vigorously, whereas female respondents cleaned their teeth for lengthier periods of time, resulting

in DH. These findings are in accordance with those of Levitch et al, researchers found that people who cleaned their mouths for extended periods of time and used much more aggressive cleaning methods were much more likely to develop DH [24]. The molars and maxillary premolars and were the teeth particularly likely to be affected by Dentine Hypersensitivity, following the maxillary teeth. These results are consistent with Ye et al., and Deogade et al., surveys [25, 26]. Moreover, our results differed from those of Awartani and Taani who found tooth structure to be the most usually damaged. When it came to treating DH, the majority of participants chose to use desensitization toothpaste [27]. This is in line with a study conducted by Rao et al., who found that desensitizing drugs play a significant role in preventing sensitivity by occluding the dentine through mineralization process [28]. The study's sample size was low by the fact that it relies on a specific center. Second, it was a survey study that relied primarily on patients' opinions of the identification of this ailment and was conducted with no clinical tests. As a result, it's not uncommon for patients to associate pain from other origins with DH.

CONCLUSION

According to the recent study 39% of the patients were suffering from dentine hypersensitivity, which is in accordance to the studies conducted before. The percentage of females having DH was more than the percentage of males having DH. The major cause of the dentine hypersensitivity was cold food as it triggers the sensitivity. The more affected teeth by the sensitivity was the molars and premolars.

REFERENCES

- [1] Wang Y, Que K, Lin L, Hu D, Li X. The prevalence of dentine hypersensitivity in the general population in China. *J Oral Rehabil.* 2012 Nov;39(11):812-20. doi: 10.1111/j.1365-2842.2012.02334.x
- [2] Addy M, West NX. The role of toothpaste in the aetiology and treatment of dentine hypersensitivity. *Monogr Oral Sci.* 2013;23:75-87. doi: 10.1159/000350477
- [3] Canadian Advisory Board on Dentin Hypersensitivity. Consensus-based recommendations for the diagnosis and management of dentin hypersensitivity. *J Can Dent Assoc.* 2003 Apr;69(4): 221-6
- [4] Addy M. Tooth brushing, tooth wear and dentine hypersensitivity—are they associated? *Int Dent J.* 2005;55(4 Suppl 1):261-7. doi: 10.1111/j.1875-595x.2005.tb00063.x.
- [5] Addy M. Dentine hypersensitivity: New perspectives on an old problem. *International Dental Journal.* 2002 Oct;52(S5P2):367-75. doi:10.1002/j.1875-595X.2002.tb00936.x
- [6] Rees JS, Addy M. A cross-sectional study of buccal cervical sensitivity in UK general dental practice and a summary review of prevalence studies. *Int J Dent Hyg.* 2004 May;2(2):64-9. doi: 10.1111/j.1601-5029.2004.00068.x
- [7] Bamise CT, Kolawole KA, Oloyede EO, Esan TA. Tooth sensitivity experience among residential university students. *Int J Dent Hyg.* 2010 May;8(2):95-100. doi: 10.1111/j.1601-5037.2009.00385.x
- [8] Gangarosa LP Sr. Current strategies for dentist-applied treatment in the management of hypersensitive dentine. *Arch Oral Biol.* 1994;39 Suppl: 101S-106S. doi: 10.1016/0003-9969(94)90195-
- [9] West NX. Dentine hypersensitivity: preventive and therapeutic approaches to treatment. *Periodontol* 2000. 2008;48:31-41. doi: 10.1111/j.1600-0757.2008.00262.x
- [10] Wang Y, Que K, Lin L, Hu D, Li X. The prevalence of dentine hypersensitivity in the general population in China. *J Oral Rehabil.* 2012 Nov;39(11):812-20. doi: 10.1111/j.1365-2842.2012.02334.x.
- [11] Udoye CI. Pattern and distribution of cervical dentine hypersensitivity in a Nigerian tertiary hospital. *Odontostomatol Trop.* 2006 Dec;29(116):19-22.
- [12] Vijaya V, Sanjay V, Varghese RK, Ravuri R, Agarwal A. Association of dentine hypersensitivity with different risk factors – a cross sectional study. *J Int Oral Health.* 2013 Dec;5(6):88-92. Epub 2013 Dec 26
- [13] Dababneh RH, Khouri AT, Addy M. Dentine hypersensitivity - an enigma? A review of terminology, mechanisms, aetiology and management. *Br Dent J.* 1999 Dec 11;187(11):606-11; discussion 603. doi: 10.1038/sj.bdj.4800345.
- [14] Afo; abi, AO, Olojede, AC, Aregbesola, SB & Ogunipe OK. Prevalence and perception of self reported dentine hypersensitivity among dentate populations in South-Western Nigeria. *Tanzania Dental Journal.* 2010 May 1;16(1):29-34. doi/10.4314/tdj.v16i1.62037
- [15] Chrysanthakopoulos NA. Prevalence of dentine hypersensitivity in a general dental practice in Greece. doi/10.4317/jced.3.e445
- [16] Colak H, Aylikci BU, Hamidi MM, Uzgur R. Prevalence of dentine hypersensitivity among university students in Turkey. *Nigerian journal of clinical practice.* 2012;15(4):415-9. doi 10.4103/1119-3077.104514
- [17] Bamise CT, Kolawole KA, Oloyede EO, Esan TA. Tooth sensitivity experience among residential university students. *International journal of dental hygiene.* 2010 May;8(2):95-100. doi 10.1111/j.1601-

- 5037.2009.00385.x
- [18] Gillam DG, Seo HS, Newman HN, Bulman JS. Comparison of dentine hypersensitivity in selected occidental and oriental populations. *J Oral Rehabil.* 2001 Jan;28(1):20-5. doi: 10.1046/j.1365-2842.2001.00631.x
- [19] Kielbassa AM. Dentine hypersensitivity: Simple steps for everyday diagnosis and management. *International dental journal.* 2002 Oct;52(S5P2):394-6.doi10.1002/j.1875-595X.2002.tb00939.x
- [20] Bamise CT, Olusile AO, Oginni AO. An analysis of the etiological and predisposing factors related to dentin hypersensitivity. *J Contemp Dent Pract.* 2008 Jul 1;9(5):52-9.
- [21] Haneet RK, Vandana LK. Prevalence of dentinal hypersensitivity and study of associated factors: a cross-sectional study based on the general dental population of Davangere, Karnataka, India. *International Dental Journal.* 2016 Feb 1;66(1):49-57 doi./10.1111/idj.12206
- [22] Drisko C. Oral hygiene and periodontal considerations in preventing and managing dentine hypersensitivity. *International Dental Journal.* 2007 Dec;57(S6):399-410.doi 10.1111/j.1875-595X.2007.tb00167.x
- [23] Moawia M. The etiology and prevalence of gingival recession/Moawia M. Kassab And Robert E. Cohen. *J. Of the American Dental Association.* 2003(134):220-5.
- [24] Levitch LC, Bader JD, Shugars DA, Heymann HO. Non-carious cervical lesions. *Journal of dentistry.* 1994 Aug 1;22(4):195-207.doi10.1016/0300-5712(94)90107-4
- [25] Deogade SC, Suresan V, Rathod JR, Naitam D. Prevalence and Impact of Dentine Hypersensitivity among Undergraduates in a University Campus of Central India. *Annals of Medical and Health Sciences Research.* 2017;7(3).
- [26] Ye W, Feng XP, Li R. The prevalence of dentine hypersensitivity in Chinese adults. *Journal of oral rehabilitation.* 2012 Mar;39(3):182-7.doi/10.1111/j.1365-2842.2011.02248.x
- [27] Taani DQ, Awartani F. Prevalence and distribution of dentin hypersensitivity and plaque in a dental hospital population. *Quintessence International.* 2001 May1;32(5).
- [28] Vandermaas-Peeler M, Nelson J, Bumpass C, Sassine B. Numeracy-related exchanges in joint storybook reading and play. *International Journal of Early Years Education.* 2009 Mar 1;17(1):67-84.doi/10.4103/1658-5984.127980



Original Article

Prevalence and Factors Leading to Hallux Valgus in Adults

Arooj Iftikhar¹, Saira Aslam¹, Faiza Amjad¹, Saima Jabbar¹, Ayesha Alam¹¹Afro Asian Institute, Khayaban-e-kareem, Ferozpur Road, Lahore

ARTICLE INFO

Key Words:

Hallux Valgus, Big Toe Pain, Lahore Population, Bunion.

How to Cite:

Iftikhar, A., Aslam, S., Amjad, F., Jabbar, S., & Alam, A. (2022). Prevalence and Factors Leading to Hallux Valgus in Adults: Leading to Hallux Valgus in Adults. *Pakistan BioMedical Journal*, 5(6), 224–228. <https://doi.org/10.54393/pbmj.v5i6.564>

*Corresponding Author:

Arooj Iftikhar
Lecturer at Afro Asian Institute, Khayaban-E-Kareem, Ferozpur Road, Lahore
Aroojmughal473@gmail.com

Received Date: 21st June, 2022

Acceptance Date: 26th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Hallux valgus deformity is an abnormal aberration of the main metatarsal and parallel aberration of the Hallux (Big Toe), which is mistakenly interpreted as an augmentation of bone or tissue surrounding the Big Toe joint. **Objective:** The goal of this cross-sectional study was to determine the prevalence of hallux valgus in adults and the variables that cause it. **Methods:** A sample of 160 young adults (both genders aging b/w 18 to 55 years) was evaluated for hallux valgus using the non-probability purposive sampling technique in Lahore Pakistan. The data were collected through a standardized Bunion Questionnaire and Manchester scale. It took six months to complete, whereas, the data was analyzed using SPSS version 21. **Results:** For data analysis means, standard deviations were used along with chi-square testing. Adults had a 37.5 percent prevalence of hallux valgus, and the current study indicated that the primary risk variables were growing age, with females suffering more than males. The usage of heels on a regular basis was one of the key risk factors for patients with hallux valgus. **Conclusion:** The outcomes of the research might lead to improved biomechanical therapies to eliminate needless foot posture loads and the usage of non-ergonomic shoes.

INTRODUCTION

Foot and ankle issues are linked to mobility and stability impairment, incapacity, falls, and fractures in the elderly [1]. Bunion or hallux valgus deformity is a typical deviation of the main metatarsal and Hallux (Big Toe) parallel deviation that is mistakenly perceived as bone or tissue enlargement surrounding the Big Toe joint. Hallux valgus was assumed to be a protrusion of additional tissue, the first metatarsal head, or both, caused by ill-fitting footwear in the eighteenth century [2]. Commonly hallux valgus is associated with foot discomfort and substantial functional disability [3]. Hallux valgus is seen to be more common in females than males and in Caucasians and African Americans. Additionally, older age and body mass index

variations are also responsible for hallux valgus [4]. Other associated factors with HV are ligamentous laxity, race, flat foot, the shape of the first metatarsal head, knee pain, osteoarthritis [5]. In this typical condition, hallux valgus pain and inactivity are significant factors. In older individuals, hallux valgus can be a cause of disability and increases the risk of falling [6]. In older individuals; osteoarthritis is a condition that can cause many other conditions described by Kellgren and Moore. Radiographic findings reveal that osteoarthritis in the first metatarsophalangeal joint can be related to the presence of osteoarthritis in the knee joint and joint of hands [7]. Whereas, theories revealed osteoarthritis of the first

metatarsophalangeal joint is responsible for the occurrence of hallux valgus [8]. Positive family history can be a cause of hallux valgus, in ~90% of individuals. Other contributing factors are uncomfortable shoes like shoes with high heels, tight front parts, and other secondary factors like a large first metatarsophalangeal joint, round first metatarsophalangeal joint, large inter-metatarsal edge, and prolonged pronated foot. In older individuals' chance of occurrence is ranging b/w 21-65% (including 4,249 individuals age >30 years) reported with a prevalence of 28%. Ratio for the chance of occurrence in both genders is 9:1 for females and males respectively and obviously related with increasing age. A huge number of medical procedures around the lower leg and foot are used to cure this condition [9]. Hallux valgus is a main cause of orthopedic foot and lower leg medical procedures every year, because of its huge connection with foot pain and handicap, disability, and high risk of falls in older age individuals. Hallux valgus is most likely to be in African Americans than white, whereas, an increase in weight in different affects differently. Pes planus and hallux valgus can also be related because of the disarrangement of the foot [4]. In a general observation rheumatoid joint inflammation forefoot distortion can be a major cause of hallux valgus [10]. Radiographs are used to examine hallux valgus angle measurements in order to determine the severity and incidence of hallux valgus. A hallux valgus angle greater than 15° explains the existence of HV [5]. The sagittal plane is particularly essential for evaluating the range of motion in the metatarsophalangeal joint since here is where the typical range is assessed, which is around 45° of plantar flexion to around 90° of dorsiflexion [1]. While mobility during weight bearing generally requires only a few degrees of plantar flexion to less than 70 degrees of dorsiflexion, a small amount of adduction and abduction can occur in the inclined plane at the metatarsophalangeal joint of the big toe during weight bearing and non-weight bearing. On radiography, hallux valgus is produced by a 15-degree prominence rise in the edge shape longitudinal bisections of the first metatarsal and proximal phalanx [11]. Sheree Nix et al. undertook a fundamental inquiry into the prevalence of Hallux Valgus in the general population, as well as a meta-analysis, revealing a high frequency of Hallux Valgus in the general population and highlighting the broad variance in commonness ratings among exams. Our data also back up idea that Hallux Valgus affects more women and the elderly. This paper identifies the difficulties that make it difficult to present an accurate picture of HV prevalence in general public, as well as recommendations for further research [12]. Artful dancing movement produces hallux valgus, according to a research done by Hildur Einarsdottir et al. among artists. In comparison to

non-artists [13], radiographs of 63 active and 38 resigned artists of both genders indicated no differences in the valgus angulations of the hallux [14]. Hylton B. Menz et.al Finally, regardless of age, sex, weight file (BMI), or discomfort in various regions, there is a dynamic decline in foot specific HRQOL with increasing severity of hallux valgus deformation [15]. These findings show that hallux valgus is a severe and incapacitating musculoskeletal disorder, and they imply that acting to repair or slow the development of the deformity might have considerable advantages beyond pain reduction [16]. K. Matsubura his investigation demonstrates that feeble TGS corresponds with hallux valgus in 10-12 year- old young ladies. Frail TGS may add to hallux valgus in the potential or beginning times. In this way, fortifying TGS is important for keeping the beginning of hallux valgus and growing great foot act [17]. Pedro v. Munuera et.al Another study found that in feet with partite sesamoids, the bulge and length of the primary metatarsal are more pronounced than in feet without this disease. In contrast to normal feet, feet with hallux valgus had a much greater frequency of bipartite average sesamoid [18]. R.Raymakers and W. Waugh et.al The researchers found that arthrodesis of the first metatarsophalangeal joint, along with excision of the lesser arch of the foot with stabilized subluxation and painful callosities, is a good therapy or treatment for painful hallux valgus. According to research, this pooling procedure was conducted on thirty feet in twenty-five individuals [19]. A.H.N.Robinson et.al concluded that Medical procedure for hallux valgus, while in fact requesting, has a high rate of accomplishment in fittingly chosen patients. Nonetheless, few patients have poor results following the task. Randomized controlled preliminaries are expected to elucidate the elements which finish up a decent result [20]. There are many reasons behind the occurrence of hallux valgus, current cross-sectional study will help find the prevalence of hallux valgus among adults along with of risk factors responsible for the development of hallux valgus. The current study will manifest the occurrence of hallux valgus in an Asian country Pakistan, various factors can be a result of this discomforting condition The study will raise awareness about the factors that cause hallux valgus, as well as how to prevent it from progressing to disability or functional limitations.

METHODS

The current cross-sectional study was taken to find the prevalence of hallux valgus and its causative factors in adults. A sample of 160 young adults was evaluated for hallux valgus using the non-probability purposive sampling technique in Lahore Pakistan. The data were obtained

using a standardized Bunion Questionnaire and Manchester scale after the individuals signed an informed consent form. A self-evaluation of hallux valgus is the Manchester Scale. It has four different levels of severity: 0 for no deformity, 1 for mild deformity, 2 for moderate deformity, and 3 for severe deformity (hallux valgus). The baseline survey asked about personal information such as name, age, and gender, as well as questions about risk factors for hallux valgus. E.g. BMI, flat foot, foot discomfort, osteoarthritis, and rheumatoid arthritis are all factors to consider. It took six months to complete, and SPSS version 21.0 was used to analyse the data. For data analysis means, standard deviations were used along with chi-square testing to find the association of hallux valgus with risk factors. Inclusion Criteria was Adults (both genders, ages 18 to 55 yrs) with discomfort in the first metatarsophalangeal joints, with flat feet, obese people, with osteoarthritis and rheumatoid Arthritis. While exclusion criteria were adolescents, children, people with bone Tumors, neuroma and with metatarsal hairline fractures

RESULTS

Table 1 reveals that the average age of persons in my study sample is 27.9, and the majority of those who took part in the study were b/w 20 to 30 years of age.

Total (N)	160
Mean+SD	27.59+10.1
Minimum	18.00
Maximum	55.00

Table 1: Expressive statistics for age

Table 2 shows that 86.9% of people in current study sample wear open shoes, 80.6% of participants were not having complain of hallux valgus preventing them from doing daily activities, and 19.4% of participant activities of daily living were prevented due to hallux valgus. 14.4% of patients had mild deformity, 8.1 percent had moderate deformity, and 15.0 percent had severe deformity, according to the results.

Characteristics	Frequency	Percent
Usage of Open or Flat Shoes	No	21
	Yes	139
	Total	160
Avoid participating in daily living activities	No	129
	Yes	31
	Total	160
Deformity	No deformity	100
	mild deformity	23
	Moderate deformity	13
	Severe deformity	24

Table 2: Different characteristics among participants

The p-value (p-value=0.01) indicates that there is a substantial link between hallux valgus or bunions, which make walking difficult, and wearing heels, Table 3.

Uncomfortable to walk because of hallux valgus or bunions	Use of heels		Total	P-value
	No	yes		
No	87	36	123	0.01
Yes	18	19	37	
Total	105	55	160	

Table 3: Association between use of heels and uncomfortably to walk because of your hallux valgus or bunions

There is a strong link (p=0.01) between diagnosed hallux valgus and hallux valgus or bunions that cause foot or back discomfort, Table 4.

Knowledge of hallux valgus	Bunions or hallux valgus are the source of your foot or back pain		Total	P-value
	No	yes		
No	108	9	117	0.01
Yes	20	23	43	
Total	128	32	160	

Table 4: Association between bunions or hallux valgus as a source of your foot or back pain

The p-value indicates that there is substantial relation between diagnosed hallux valgus and gender (p-value=0.01), Table 5.

Gender	Diagnosed with hallux valgus		Total	P-value
	No	yes		
Male	58	12	70	0.01
Female	59	31	90	
Total	117	43	160	

Table 5: Cross tabulation b/w gender and hallux valgus

The p-value for the substantial connection between Manchester scales for measuring hallux valgus and gender is significant (P-value=0.02), Table 6.

Manchester Scale for evaluating hallux valgus (provided for better understanding)	Gender		Total	P-value
	M	F		
No deformity	Frequency	53	47	0.02
	Percentage	75.7%	52.2%	
Mild deformity	Frequency	7	16	
	Percentage	10.0%	17.8%	
Moderate deformity	Frequency	3	10	
	Percentage	4.3%	11.1%	
Severe deformity	Frequency	7	17	
	Percentage	10.0%	18.9%	
Total	Frequency	70	90	
	Percentage	100.0%	100.0%	

Table 6: Cross tabulation b/w gender and Manchester Scale for evaluating hallux valgus

DISCUSSION

According to a recent research, hallux valgus is a prevalent condition that has all the earmarks of being inextricably related to age and female sex. It has been associated to nodal osteoarthritis, knee pain, big toe pain, self-revealed osteoarthritis, and self-detailed rheumatoid joint +pain and inflammation [21]. A recent study found a connection between hallux valgus and age and gender [22]. When Mafart conducted the greatest epidemiologic study of hallux valgus, he observed that males had a higher incidence of the condition than females. Hallux valgus is a

frequent condition that appears to be inextricably tied to ageing and female sex. In this study, females had a higher prevalence of Hallux Valgus than males. This assertion is supported by previous studies [23, 24]. Current study indicated a strong relationship (20%) between hallux valgus and foot and back discomfort. In Australia, the prior research is the most thorough population-based assessment of foot discomfort. According to the data, one out of every five persons has foot pain, discomfort, or hardness, with females, those aged 50 and over, and those classed as overweight having a higher frequency [25]. Nonetheless, even in those under the age of 45, at least 10% of patients suffer from substantial foot discomfort. The total prevalence rate recorded in this research is higher than that found in the United Kingdom's Cheshire Foot Pain and Disability Survey (10 percent) [26]. According to this study, 19.4% of adults prevent participation in daily living activities for those who had Hallux Valgus, and 80.6% of adults had not prevented in daily living activities for those who had Hallux Valgus. Current study 31.3% of participants changed in normal foot movement due to hallux valgus and 68.8% of participants does not change in normal foot movement due to hallux valgus. 17.5% of participants had laterally deviated foot while walking. According to recent prevalence data from the Framingham Study, 19 percent of men and 29 percent of women reported foot pain on most long days of the month, with a predominance of anguish in specific foot regions ranging from 7 percent to 13 percent of those who refrain from walking due to foot pain [27]. Results shows Hallux valgus was also caused by the form of the shoes. J.E.Dunn and colleagues Finally, studies in the United States that included clinical assessments of more particular groups showed outcomes that were identical to ours. Bunions, corns, and calluses are more frequent among women, according to some. Women's shoes are commonly considered as a contributing element. Increased heel stature distributes pinnacle weight to the hallux and increases forefoot top weight. Prior to the advent of Western footwear styles, bunions were considered to be uncommon in Japan [28]. According to this study, the Hallux Valgus angle, which is generally measured clinically using radiographs, is utilised to detect hallux valgus. The severity of Hallux Valgus is typically measured using criteria such as the Manchester scale on photographs or diagrams of the foot, or by measuring the Hallux Valgus angle in the tracing's outlines [29]. The Manchester scale was used to measure the severity of hallux valgus, with some participants having no deformity (62.5%), mild deformity (14.4%), moderate deformity (8.1%), and severe deformity (15.0%). According to H. B. Menz and S. E. Munteanu, the Manchester scale is a feasible test for

assessing hallux valgus angle using radiograph data [28].

CONCLUSION

Hallux valgus affects 37.5 percent of adults, and the primary risk variables, according to the present study, were rising age and females suffering from hallux valgus more than males. The everyday use of heels was one of the most significant risk factors for patients suffering with hallux valgus. Bunions or hallux valgus are more common in people who wear heels, making walking difficult and causing back pain, reducing their quality of life. The incidence of hallux valgus is also associated with work-related stress.

REFERENCES

- [1] Dunn JE, Link CL, Felson DT, Crincoli MG, Keysor JJ, McKinlay JB. Prevalence of foot and ankle conditions in a multiethnic community sample of older adults. *American journal of epidemiology*. 2004 Mar; 159(5):491-8. doi.org/10.1093/aje/kwh071
- [2] Ekwere EO, Usman YM, Danladi A. Prevalence of hallux valgus among medical students of the University of Jos. *Annals of Bioanthropology*. 2016 Jan; 4(1):30. DOI: 10.4103/2315-7992.190457
- [3] Nix S, Smith M, Vicenzino B. Prevalence of hallux valgus in the general population: a systematic review and meta-analysis. *Journal of foot and ankle research*. 2010 Dec; 3(1):1-9.
- [4] Golightly YM, Hannan MT, Dufour AB, Renner JB, Jordan JM. Factors associated with hallux valgus in a community-based cross-sectional study of adults with and without osteoarthritis. *Arthritis care & research*. 2015 May; 67(6):791-8. doi.org/10.1002/acr.22517
- [5] Okuda H, Juman S, Ueda A, Miki T, Shima M. Factors related to prevalence of hallux valgus in female university students: a cross-sectional study. *Journal of epidemiology*. 2014 May; 24(3):200-8. doi.org/10.2188/jea.JE20130110
- [6] Cho NH, Kim S, Kwon DJ, Kim HA. The prevalence of hallux valgus and its association with foot pain and function in a rural Korean community. *The Journal of Bone and Joint Surgery. British volume*. 2009 Apr; 91(4):494-8. doi.org/10.1302/0301-620X.91B4.21925
- [7] Shereff MJ. Pathophysiology, anatomy, and biomechanics of hallux valgus. *Orthopedics*. 1990 Sep 1; 13(9):939-45. doi.org/10.3928/0147-7447-19900901-06
- [8] Roddy E, Zhang W, Doherty M. Prevalence and associations of hallux valgus in a primary care population. *Arthritis Care & Research: Official Journal of the American College of Rheumatology*.

- 2008 Jun; 59(6):857-62. doi.org/10.1002/art.23709
- [9] Menz HB, Roddy E, Thomas E, Croft PR. Impact of hallux valgus severity on general and foot-specific health-related quality of life. *Arthritis care & research*. 2011 Mar; 63(3):396-404. doi.org/10.1002/acr.20396
- [10] Budiman-Mak E, Conrad KJ, Roach KE, Moore JW, Lertratanakul Y, Koch AE, et al. Can foot orthoses prevent hallux valgus deformity in rheumatoid arthritis? A randomized clinical trial. *Journal of Clinical Rheumatology: Practical Reports on Rheumatic & Musculoskeletal Diseases*. 1995 Dec; 1(6):313-22. DOI: [10.1097/00124743-199512000-00001](https://doi.org/10.1097/00124743-199512000-00001)
- [11] Menz HB, Munteanu SE. Radiographic validation of the Manchester scale for the classification of hallux valgus deformity. *Rheumatology*. 2005 Aug; 44(8):1061-6. doi.org/10.1093/rheumatology/keh687
- [12] D'Arcangelo PR, Landorf KB, Munteanu SE, Zammit GV, Menz HB. Radiographic correlates of hallux valgus severity in older people. *Journal of foot and ankle research*. 2010 Dec; 3(1):1-9.
- [13] Einarsdottir H, Troell S, Wykman A. Hallux valgus in ballet dancers: a myth?. *Foot & ankle international*. 1995 Feb; 16(2):92-4. doi.org/10.1177/107110079501600208
- [14] Polastri M. Postoperative rehabilitation after hallux valgus surgery: a literature review. *Foot Ankle Online Journal*. 2011 Jun 4(6): 1-8. doi: 10.3827/faoj.2011.0406.0004
- [15] Teodoro EC, Tomazini JE, Nascimento LF. Hallux valgus and flat feet: are plantar forces equal?. *Brazilian Orthopedic Act*. 2007; 15:242-5. doi.org/10.1590/S1413-78522007000500001
- [16] Nix SE, Vicenzino BT, Smith MD. Foot pain and functional limitation in healthy adults with hallux valgus: a cross-sectional study. *BMC musculoskeletal disorders*. 2012 Dec; 13(1):1-0.
- [17] Hurn SE, Vicenzino BT, Smith MD. Correlates of foot pain severity in adults with hallux valgus: a cross-sectional study. *Journal of foot and ankle research*. 2014 Dec; 7(1):1-0.
- [18] Hurn SE, Vicenzino BT, Smith MD. Non-surgical treatment of hallux valgus: a current practice survey of Australian podiatrists. *Journal of foot and ankle research*. 2016 Dec; 9(1):1-9. DOI 10.1186/s13047-016-0146-5
- [19] Matsubara K, Tasaka S, Fukumoto T, Nishiguchi S, Fukutani N, Tashiro Y, et al. Weak TGS correlates with hallux valgus in 10-12 year old girls: A cross-sectional study. *Clin Res Foot Ankle*. 2016 Jun; 4(189):2. DOI: 10.4172/2329-910X.1000189
- [20] Portaluri M. Hallux valgus correction by the method of Bösch: a clinical evaluation. *Foot and Ankle Clinics*. 2000 Sep; 5(3):499-511.
- [21] Thordarson DB, Leventen EO. Hallux valgus correction with proximal metatarsal osteotomy: two-year follow-up. *Foot & ankle*. 1992 Jul; 13(6):321-6. doi.org/10.1177/107110079201300605
- [22] Munuera PV, Domínguez G, Reina M, Trujillo P. Bipartite hallucal sesamoid bones: relationship with hallux valgus and metatarsal index. *Skeletal radiology*. 2007 Nov; 36(11):1043-50. DOI 10.1007/s00256-007-0359-6
- [23] Ross FD. The relationship of abnormal foot pronation to hallux abducto valgus—a pilot study. *Prosthetics and Orthotics International*. 1986 Aug; 10(2):72-8. doi.org/10.3109/03093648609164503
- [24] Borton DC, Stephens MM. Basal metatarsal osteotomy for hallux valgus. *The Journal of Bone and Joint Surgery. British volume*. 1994 Mar; 76(2):204-9. doi.org/10.1302/0301-620X.76B2.8113277
- [25] Raymakers R, Waugh W. The treatment of metatarsalgia with hallux valgus. *The Journal of Bone and Joint Surgery. British volume*. 1971 Nov; 53(4):684-7. doi.org/10.1302/0301-620X.53B4.684
- [26] Robinson AH, Limbers JP. Modern concepts in the treatment of hallux valgus. *The Journal of bone and joint surgery. British volume*. 2005 Aug; 87(8):1038-45. doi.org/10.1302/0301-620X.87B8.16467
- [27] Leveille SG, Guralnik JM, Ferrucci L, Hirsch R, Simonsick E, Hochberg MC. Foot pain and disability in older women. *American journal of epidemiology*. 1998 Oct; 148(7):657-65. doi.org/10.1093/aje/148.7.657
- [28] Garrow AP, Silman AJ, Macfarlane GJ. The Cheshire Foot Pain and Disability Survey: a population survey assessing prevalence and associations. *Pain*. 2004 Jul; 110(1-2):378-84. doi.org/10.1016/j.pain.2004.04.019
- [29] Menz HB, Morris ME. Determinants of disabling foot pain in retirement village residents. *Journal of the American Podiatric Medical Association*. 2005 Nov 1; 95(6):573-9. doi.org/10.7547/0950573



Original Article

Oral Hygiene Awareness Among Transgenders in Twin Cities of Pakistan

 Muhammad Muhammad¹, Arfa Sabir¹, Marium Sanaullah¹, Saqlain Bin Syed Gilani¹, Mansoor Khan², Rana Mohammad Ahmad³
¹Riphah International University, Islamabad, Pakistan²Foundation University College of Dentistry, Islamabad³University of Lahore

ARTICLE INFO

Key Words:

Transgender Persons, Oral Health Awareness, Oral Hygiene

How to Cite:

 Muhammad, M. ., Sabir Hussain, A. ., Sanaullah, M. ., Bin Syed Gilani, S., Khan, M. ., & Mohammad Ahmad, R. . (2022). Oral Hygiene Awareness Among Transgenders in Twin Cities of Pakistan: Oral hygiene awareness among transgenders. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.594>

*Corresponding Author:

 Muhammad Muhammad
 Riphah International University, Islamabad, Pakistan
 dr.muhammad@riphah.edu.pk

Received Date: 19th June, 2022

Acceptance Date: 24th June, 2022

Published Date: 30th June, 2022

ABSTRACT

An Individual's oral health condition is related to awareness of the practices that can enhance oral hygiene. The transgender community is less privileged in society. As a result, they may be more vulnerable to oral diseases due to limited access to healthcare and adverse living conditions. The aim of this study was to assess the oral hygiene awareness among the transgenders residing in Rawalpindi and Islamabad (Twin cities). **Material and methods:** A questionnaire-based descriptive cross-sectional was conducted on the transgender community residing in the twin cities. The study questionnaire was translated in Urdu language and distributed among trans-genders in person. The convenience sampling technique was used to recruit the participants. Data analysis was conducted by utilizing SPSS version 26. **Results:** A total of 73 individuals (Rawalpindi=60.3%, Islamabad=39.7%) participated in the study out of the 100 that were approached. Most of the participants (52%) were from the 25-34 years age group. The relationship between oral hygiene awareness and age/city was found to be statistically insignificant. Only 26% transgenders used toothpaste for teeth cleaning and 70% did not use any adjunctive aid for teeth cleaning. Moreover, 98.7% of the participants noted that they are using either betel nut, pan, or tobacco. **Conclusion:** The study participants were aware of the basic oral hygiene requirements; however, their oral hygiene practices were to be well below the established standards. It is recommended that public and private sector welfare organizations should fund and organize oral health promotion programs among the transgender communities. Moreover, healthcare professionals should be encouraged and trained to deal with the transgender community with empathy and care.

INTRODUCTION

Pakistan has a total population of 216.6 million according to the 2017 census, with a total transgender population of 21,744 [1]. In 2009, the Supreme Court of Pakistan finally granted legal rights to transgenders or more commonly known as 'Khwaja siras' in Pakistan. Khwaja siras are one of the most marginalized individuals not only in Pakistani society but all over the world [2-4]. They are seen with skepticism not only because of their ambiguous physical attributes but also due to the belief that they possess special powers to bless and curse [5]. Most transgenders leave their homes at an early age after being socially

ridiculed or isolated by their friends and family and seeking refuge in the marginalized transgender communities [6]. Lack of family support and acceptance of their identity in society results in very little formal education and consequently fewer job opportunities. Consequently, many transgenders end up as beggars, street performers, sex workers, and drug addicts, making them prone to sexually transmitted diseases. Lack of acceptance in society, inferior social status, living in secluded transgender communities, unhealthy lifestyle, and limited access to health care services makes them vulnerable to many

medical and dental problems [7-10]. Oral health condition is strongly related to the knowledge and awareness of oral hygiene practices [11, 12]. The social stigma attached to the transgender communities and lack of formal education are barriers to attaining awareness about their oral health. Oral health status and oral hygiene awareness of the transgender community have not been given due importance [13]. Studies on the awareness of oral health in transgenders are very scarce, henceforth, this research was conducted in the twin cities of Islamabad and Rawalpindi to assess the oral hygiene awareness among the transgenders.

METHODS

A cross-sectional study was conducted to assess oral hygiene awareness of transgenders in twin cities of Pakistan using a self-administered questionnaire on oral hygiene awareness. The questionnaire was translated into Urdu, the national language of Pakistan. The study was conducted from December 2021 to February 2022. Ethical approval was obtained from the Ethical Review Board at Riphah International University. A sample size of 73 transgenders was calculated using OpenEpi (version 3.01) with a total population size of 21,744 at a 90% confidence interval and 10% absolute precision. A convenient sampling technique was used and only those individuals were included who gave consent to be part of the research. Out of 100 transgenders who were approached from the main hubs of the transgender community, 73 consented to fill out the questionnaire. Participation in the survey was voluntary and the responder's identities were kept anonymous. The questionnaires were distributed in the hard copy and responses were collected in person. The data collected were analyzed using IBM SPSS (version 26.0).

RESULTS

Seventy-three individuals who identified themselves as transgenders filled the forms which were given to them by hand. 60.3% were from Rawalpindi and 39.7% were from Islamabad. Most of the transgender people (52%) were from the 25-34 years age group while the least (8%) were from the 45-54 years age group as shown in Figure 1

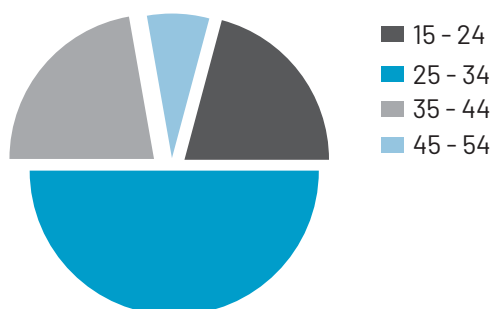


Figure 1: Different age groups of the participants.

Regarding the use of toothbrushes, only 26% transgenders in this study use toothbrushes for cleaning their teeth while most of them use their fingers alone or in combination with dental powder or toothpaste as shown in Table 1. 70% transgenders in this study clean their teeth once daily, while 28.7% twice daily and only 1.3% after every meal as shown in Table 1. 49% transgenders do not clean their tongue as part of their oral hygiene maintenance and 70% transgenders in this study do not use any adjunctive dental cleaning aid such as dental floss and mouthwashes as shown in Table 1.

Question Statement	Frequency (%)			
	How do you clean your teeth	I use my finger 15 (20.5%)	I use dental powder with finger 10 (13.5%)	I use tooth paste with finger 29 (40%)
Which additional dental aids do you use?	Mouth-wash 18 (24.7%)	Interdental Brush 1 (1.3%)	None 51 (70%)	Did not answer 3 (4%)
	How frequently do you clean your teeth	Once Daily 18 (24.7%)	Twice Daily 1 (1.3%)	After Every Meal 51 (70%)

Table 1: Responses to questions related to methods and frequency of tooth cleaning

All the respondents except 1 (98.7%) use either betelnut, pan or tobacco (cigarette and chewable and most of them (88%) use tea, coffee, or other carbonated drinks as shown in Figure 2 & 3. Almost half of them (49%) never visited a dentist in their lifetime.

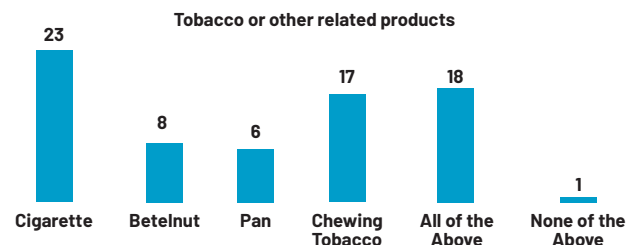


Figure 2: Use of tobacco and related products among participants

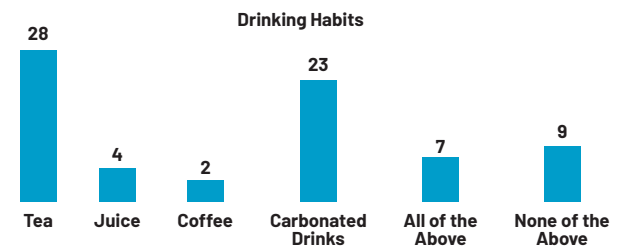


Figure 3: Drinking habits of transgenders in twin cities

DISCUSSION

In a developing country like Pakistan where people face a lot of problems like hunger, poverty, health, education, and economy; challenges of minor communities like

transgenders are not brought into light. The education and health of these communities are largely ignored by the Government. The current study was conducted with the aim to assess the oral hygiene awareness among the transgender community of the twin cities. Reaching out to the transgender community was a challenge in itself because of the ongoing pandemic situation and the general lack of mistrust of the targeted community towards survey teams and health professionals [14]. This study reported that 26% transgenders use toothbrushes as a method of maintaining regular dental hygiene. Few studies have been carried out to assess the oral hygiene awareness of transgenders in India which reported the use of toothbrushes as a method of dental cleaning ranging from 57-93% [15-17]. Less frequent use of toothbrushes in the twin cities draws attention to the dire conditions of oral hygiene prevailing in the transgender community as compared to India. This study identified that 70% transgenders of the twin cities clean their teeth once daily which is close to what is reported by the school children and their teachers in some of the schools of the peri-urban locality of Islamabad [18]. But we must keep in mind that in our study most transgenders use their fingers in place of the toothbrush as their primary device for cleaning their teeth. Regarding the cleaning of the tongue, 51% transgenders in our study responded with yes which corresponds to the findings of one of the studies in Japan [19]. Tobacco or other related products such as betel nut and pan are reportedly used by 98.6% of the transgenders in this study; mostly in the form of tobacco smoking as compared to 57% in Pune City, India [17]. This again shows that the prevailing adverse practices in our transgender communities are detrimental to their general and oral health. The current study inquired about their visits to a dentist and 49% transgenders in this study never visited a dentist which is comparable to the findings of the study on transgenders in Chennai, India, which reported that over 60% of the transgender population never visited a dentist in their lifetime [20]. This could be due to the mistrust of the transgender community on the healthcare professionals and may also be related to their economic and financial woes. Socioeconomic status has been shown to be strongly related with oral health awareness and prevention of oral diseases. As most of the participants in this study belonged to the low socioeconomic strata, this study did not address the impact of socioeconomic status on the awareness and practice of oral hygiene measures exclusively in the transgender community. This may be considered as the limitation of this study. The study furthered our understanding of the oral hygiene practices prevailing in transgender communities. Future studies should also target the clinical assessments of the oral

hygiene indices in the transgender communities in different cities of Pakistan. The goal should be to educate everyone, especially the marginalized communities such as transgender on their general and oral health needs.

CONCLUSION

The study highlighted the oral health awareness among the transgender community in the twin cities. Although the transgender community was aware of the basic oral hygiene needs, their oral hygiene practices were not up to the mark. Furthermore, the government and non-governmental organizations should fund transgenders' dental assessments and take steps to shift the mindset of our society toward the transgender community by sensitizing the health professionals to properly communicate and handle such patients with equal care.

REFERENCES

- [1] Final Results (Census-2017) | Pakistan Bureau of Statistics [Internet]. [cited on 2022 Jun 22]. Available from: <https://www.pbs.gov.pk/content/final-results-census-2017>
- [2] Saddique KA, Mirbehar S, Batool H, Ahmad I, Gang C. Transgender issues in Pakistani community. *European Academic Research*. 2017;4(10):9048-57.
- [3] Zwickl S, Wong AF, Dowers E, Leemaqz SY, Bretherton I, Cook T, et al. Factors associated with suicide attempts among Australian transgender adults. *BMC psychiatry*. 2021 Dec; 21(1):1-9.
- [4] Vincent BW. Studying trans: recommendations for ethical recruitment and collaboration with transgender participants in academic research. *Psychology & Sexuality*. 2018 Apr; 9(2):102-16. doi/abs/10.1080/19419899.2018.1434558
- [5] Rath AK. Transgender studies in india: Locating folklore and autobiographies as transgressive sites. *In Women's and Gender Studies in India 2019 Apr*: 225-34. Routledge India.
- [6] Koken JA, Bimbi DS, Parsons JT. Experiences of familial acceptance-rejection among transwomen of color. *Journal of Family Psychology*. 2009 Dec; 23(6):853. doi.org/10.1037/a0017198
- [7] Fuller KA, Riggs DW. Family support and discrimination and their relationship to psychological distress and resilience amongst transgender people. *International Journal of Transgenderism*. 2018 Oct; 19(4):379-88. doi.org/10.1080/15532739.2018.1500966
- [8] Operario D, Soma T, Underhill K. Sex work and HIV status among transgender women: systematic review and meta-analysis. *JAIDS Journal of Acquired Immune Deficiency Syndromes*. 2008 May; 48(1):97-

103. doi: 10.1097/QAI.0b013e31816e3971
- [9] Riggs DW, Bartholomaeus C. Transgender young people's narratives of intimacy and sexual health: implications for sexuality education. *Sex Education*. 2018 Jul; 18(4):376–90. doi.org/10.1080/14681811.2017.1355299
- [10] Romanelli M, Lindsey MA. Patterns of Healthcare Discrimination Among Transgender Help-Seekers. *American journal of preventive medicine*. 2020 Apr; 58(4):e123–31. doi.org/10.1016/j.amepre.2019.11.002
- [11] Tadin A, Poljak Guberina R, Domazet J, Gavic L. Oral hygiene practices and oral health knowledge among students in Split, Croatia. *InHealthcare* 2022 Feb; 10(2): 406. MDPI.
- [12] Kumar G, Sethi AK, Tripathi RM, Barman D. Assessment of knowledge, attitude, and practice of dental and medical interns toward toothbrush maintenance and replacement in Bhubaneswar city, Odisha, India. *Journal of pharmacy & bioallied sciences*. 2018 Apr; 10(2):77.
- [13] Kumar G, Sethi AK, Bagchi A, Rai S, Tamilselvan P. Knowledge, attitudes and behaviour towards oral hygiene of transgenders in Bhubaneswar during COVID-19. *Journal of Family Medicine and Primary Care*. 2021 Mar; 10(3):1353.
- [14] D'Avanzo PA, Bass SB, Brajuha J, Gutierrez-Mock L, Ventriglia N, Wellington C, Sevelius J. Medical mistrust and PrEP perceptions among transgender women: a cluster analysis. *Behavioral Medicine*. 2019 Apr 3; 45(2):143–52. doi/abs/10.1080/08964289.2019.1585325
- [15] Saravanan N, Thiruneervannan R, Christopher P. A Study to Assess the Periodontal Status of Transgender in Chennai City. *Biosciences Biotechnology Research ASIA*. 2014; 11(3):1673–8. doi.org/10.13005/bbra/1567
- [16] Knowledge, attitude, and practice on brushing habits among transgenders residing in Chennai City: Cross-sectional questionnaire Study [Internet]. [cited on 2022 Jun 22]. Available from: <http://scopeindex.org/handle/sc/1402>
- [17] Kumbhalwar A, Shetiya SH, Kakodkar P, Mehta V. Oral Health Status and Treatment Needs of Transgender in Pune City, Maharashtra, India: A Pilot Survey. *International Journal of Current Research and Review*. 2021; 13(19):159–63. doi.org/10.31782/IJCRR.2021.131914
- [18] Oral hygiene practices in primary school children and their teachers in a peri-urban locality of Islamabad | Pakistan Oral & Dental Journal [Internet]. [cited 2022 Jun 22]. Available from: <http://podj.com.pk/index.php/podj/article/view/139>
- [19] Matsuda S, Saito T, Yoshida H, Yoshimura H, Sano K. Prevalence of Tongue Cleaning Using a Toothbrush: A Questionnaire Survey in Fukui Prefecture, Japan. *BioMed Research International*. 2019; 2019. doi.org/10.1155/2019/6320261
- [20] Bharath Marlecha R, Mary AV, Kesavan R, Christopher P, Nagavalli KB, Salam H. Oral health status, dental awareness, and dental services utilization barriers among transgender population in Chennai. *Drug Invent Today*. 14:2020



Original Article

Association of Obesity with Food Choices among Children Between Age Group of 5 To 12 Years in Different Areas of Lahore.

 Hafsa Tahir¹, Sania Maqbool¹, Shafaq Shahid¹, Riffat Shabbir¹, Hafiz Muhammad Uzair Asghar², Fizza Masood¹, Amna Naeem¹ and Fizah Irfan¹
¹University of Management Sciences & Technology Lahore, Pakistan²Lahore Medical & Dental College, Lahore, Pakistan

ARTICLE INFO

Key Words:

Socioeconomic status (SES), parent's education, food choices, nutritional habits, body mass index (BMI), food frequency questionnaire

How to Cite:

Tahir, H., Maqbool, S., Shahid, S., Shabbir, R., Uzair Asghar, H. M., Masood, F., Naeem, A., & Irfan, F. (2022). Association of Obesity with Food Choices among Children Between Age Group of 5 To 12 Years in Different Areas of Lahore: Obesity & Food Choices in Children of Lahore. Pakistan Biomedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.547>

*Corresponding Author:

Sania Maqbool,
 University of Management Sciences and Technology,
 Lahore, Pakistan
Saniamaqbool28@gmail.com

Received Date: 12th June, 2022Acceptance Date: 27th June, 2022Published Date: 30th June, 2022

ABSTRACT

The relationship between the socioeconomic status (SES) of parents and the effect of socioeconomic status on the food intake pattern of their children was examined in this study. Children of low SES generally have poorer diets than children of high SES. **Objective:** To observe the association of child obesity with food choices in different areas of Lahore **Methods:** Data were collected from 38 participants, from different areas of Lahore, Pakistan. From which 20 were female and 18 were male children. Their parents were requested to solve a questionnaire which comprised of different questions related to child age, height, weight, eating habits and parent's socioeconomic status and their education. **Results:** Study showed that children growing up in families with a lower SES had a higher body mass index (BMI), lower quality of life, less healthy nutrition, and less physical activity as compared to children growing up in families with a higher SES. The food frequency questionnaire showed that children belonging to lower SES consumed 17% grains, 18% dairy sources, 16% vegetables, 12% pluses and lentils, 0% meat, 11% fruits, and 13% tea and coffee in a day. While children belonging to higher SES consumed 17% grains, 29% dairy sources, 6% vegetables, 2% pulses and lentils, 13% meat, 13% fruits, and 7% tea and coffee daily. **Conclusions:** SES has an exquisite impact at the food alternatives and food intake among college-going youngsters. Lower SES children devour greater veggies, less meat, and dairy products at the same time as better SES kids devour fewer vegetables and extra meat and dairy products. Children from DHA were more obese and they were consuming more protein based diet and practicing sedentary life style.

INTRODUCTION

Nutrition occupies a very important place in every one's life. Good or bad health of any individual is related to a dietary pattern. Nutritional status is compromised in both developing and under developing countries [1]. Malnutrition can be described as when there is no balance in supply of nutrients and calories. Malnutrition can be categorized in both under nutrition and over-nutrition. As stated by UNICEF 40% children of the all over world are under nourished of India and Pakistan [2,3]. Malnutrition can adversely affect the child's cognitive function, poor performance in activities, ceased growth, more susceptible to diseases which further lead to adult life with

various health issue like hypertension, diabetes, and various psychological concerns. Malnutrition can develop due to many reasons especially when there is low SES and uneducated mother both are influencing factors [4]. Starvation could be a fundamental open wellbeing danger in Pakistan and in South Asian state with more than 130 million individuals [5]. Obesity is the increased body weight than normal body weight. when body mass index (BMI) is 25-29.9kg/m² it considers as overweight and when BMI is ≥ 30 it will fall in obese category. Physiologically and psychologically impairment are prominent concern in obesity. Chronic disorders related to heart attack, kidney

disorders, hypertension, prostate cancer, breast cancer are common in adulthood [6]. Assessment of nutritional status of children is required through anthropometry measurements, body habitus, food recall and vital history. Anthropometry is the parameter to evaluate the human body that gives useful information about a child growth pattern and present nutritional status when compared with regular findings. Anthropometric measurements include the weight, height/length, head circumference etc. [7]. Eating behavior starts from infancy as parent play a more influencing role to adopting this behavior. A child weight is directly linked to eating pattern and parent attention towards the children. There are many public health interventions that designed to make improvements in child eating behavior and reduce the obesity and malnutrition during childhood. A study was conducted in Australia which demonstrated that appropriate knowledge, positive attitude and a decent feeding practice is 54%, 99%, 92% accordingly [8]. Childhood weight problems has spread in a wide variety amongst advanced and developing international locations. Both are the cause for the development of obesity inside the later life. They in addition have an expanded risk of growing continual illnesses like diabetes, CVD at a younger age. the exact mechanism for weight problems improvement continues to be now not honestly diagnosed however it is thought to be consider that this will be due to multiple factors which include cultural and environmental issue and way of life changes and so on. all these have a better chance of developing obesity at some stage [9]. The health complications regarding obesity are increase in developing countries due to inappropriate fast-food consumption with massive quantity. Dense calories with high sugar contained soft drinks are the major contributing factors of high obesity prevalence. Fast foods are energy dense, poor nutrition or poor micronutrient, high glycemic load, large in portion size and poor in fiber. In case BMI is < 18.5kg/m², it is considered as underweight, when 18.5-24.9kg/m² it is ordinary, when 25-29.9kg/m² it is overweight and when ≥ 30kg/m² will drop in hefty category. In children BMI percentile could be a solid pointer of overweight or beneath nourishment [10]. Expanded systolic and diastolic blood weight has been experienced in undernourished children and in those who recuperated from ailing health. This may be a critical hazard figure for expanded BP afterward in life. Wholesome wellbeing chance are typically to be connected with more than one third of worldwide child passing's concurring to WHO, UNICEF, World Bank [11]. It changed into found from the beyond research that obesity is very epidemic among the kids worldwide. Co morbidities associated with weight problems and obese aren't most effective seen in kids but additionally seen in adult population. moreover, high blood

pressure, type 2 diabetes, dyslipidemia, and others also are seen in to be more often seem co morbidities related to overweight and obesity a number of the pediatric population [12]. The present study was commenced to study the nutritional status of school going children of different areas of Lahore including model town, Defense housing society, township and another city Rahim Yar Khan through food frequency questionnaires tool, anthropometric measurements and to know the fitness status of these children and their relationship with dietary habits. Recent study based on fast food consumption and how it will affect the health of children by consume in large amount.

METHODS

Our study was designed to check the intake of food of different variety that children of age 5 to 12 years are consuming. For this purpose, a questionnaire was designed and provided to students to check how frequent they are consuming food i.e per day, weekly or monthly etc. The eating behavior of children were recorded by such a study that was a quantitative type research. The research basically included school going children with age 5-12 years. The data was collected in different schools of Lahore city including DHA, Johar Town and Model Town areas. The main purpose was to check the reliability of food intake with increasing weight in this specified age group. All children of this age group were specifically focused in our research. The sample size for our study was 100. As children couldn't response well to the questions so their parents and teachers helped in answering those questions. We surveyed different schools and gathered information related to eating patterns of children. Data was in a hard form questionnaire which was then compiled by software's on computer. For this, graphs and charts were designed on excel sheet and then final result was collected by using SPSS version 21.

RESULTS

Table 1 shows the descriptive characteristics of total 100 participants. Males were 40% while female participants were 60%. BMI for the DHA, Model town and Johar Town participants was categorized as obese, underweight, normal and some were overweight. Table 2 signifies the mean values of Diet Constituents especially proteins (beef, chicken burger, nuggets and eggs) in different Areas of Lahore city. Table 3 depicts the mean value for plant based diet such as vegetables, fruits, rice, grains and snacks.

Gender	40% (M) 60% (F)
BMI (DHA)	14%(Ob) 38% (Over W) 40%(N) 8% (Under W)
BMI (MD)	9%(Ob) 38% (Over W) 36%(N) 18% (Under W)
BMI (TS)	9%(Ob) 38% (Over W) 36%(N) 18% (Under W)

Table 1: Descriptive statistical analysis (N=100)

M=Male,F=Female,BMI=Body mass Index, DHA(Defence Housing society), MD(Model town),TS(Township), Ob(Obese),Over W(over weight),N(Normal),Under W(Under weight)

Diet Constituents (PROTEINS)	Area of data collection		
	DHA (n=24)	Model Town (n=23)	Johar Town (n=29)
Beef	1.96 ±0.806	2.48 ±0.947	2.24± 0.872
Chicken burger	2.63± 0.770	2.43± 0.72	2.41 ±0.780
Nuggets	2.67± 0.868	82.65± 1.027	2.31 ±0.930
Eggs	1.13± 0.338	1.43± 0.662	1.21±0.491

Table 2: Mean values of dairy products in different areas of Lahore city

Diet Constituents (Dairy Products)	Area of data collection		
	DHA (n=24)	Model Town (n=23)	Johar Town (n=29)
Dairy milk	1.21 ±0.658	1.13 ±0.344	1.17±0.468
Yogurt	1.50± 0.780	1.57± 0.843	1.21±0.491
Custard	2.54± 0.833	2.96± 0.706	2.38±0.622
Chesse	2.33± 1.090	2.61± 0.988	2.34 ±0.76
Ice cream	2.42±0.830	2.31±0.783	2.21±0.559

Table 3: Mean values of other diet constituents in different areas of Lahore city

Diet Constituents (Dairy Products)	Area of data collection		
	DHA (n=24)	Model Town (n=23)	Johar Town (n=29)
Vegetables	1.58 ±0.776	1.61 ±0.656	1.69±0.761
Fruits	1.29± 0.550	1.43± 0.590	1.24±0.511
Rice	1.88± 0.448	1.43± 0.590	1.59±0.501
Grains	1.33± 0.702	1.17± 0.388	1.28 ±0.528
Snacks	2.42± 0.776	2.57±0.843	2.24 ±0.689

Table 4: Mean values of plant based diet in different areas of Lahore city

DISCUSSION

Obesity, that is commonly wide spreading factor almost in every part around the globe. It's prevalence among children is a current rising and hard issue to be encounter by health professionals. Not only an unhealthy eating behaviors are responsible for this obesity epidemic but rather irregular lifestyles and disturbed eating routines that are now so common in practice among children of growing age. The age between 5 to 12 years is critical period for them to grow on health outcomes that will ultimately help them through their rest of lives by enhancing immune system and excellent body and mental health as well. But now a day it seems as a hard and fast rule to eat in balance and healthy. Children are being indulging themselves in sedentary activities and they do rare focus on physical activity. They happily prefer to eat fast foods, cold drinks, sodas, vendor items, bakery eatables and various out door foods as their nerve instincts find these foods delicious and highly acceptable to their taste buds instead of homemade healthy and clean diet. The most recent country wide

vitamins Survey that performed by means of the rural studies service is persevering with Survey of meals Intakes by way of individuals (CSFII). This survey includes countrywide based totally pattern of people of virtually all age organizations. It presents a detailed statistics of nutrient consumption for both fashionable and occasional-profits population. This statistics also allows to discover the association between poverty and meals inadequacy. For this reason, meals inadequacy popularity changed into mentioned in 2 income families; high and coffee [13]. Among youth, obesity has grown to be a plague amongst developed countries. It's far noted that obese and weight problems are developed via the high intake of candy gadgets, excessive consumption of calories and fat, taking elevated element size with reduced hobby. So, both weight loss program that consumed in extra and bodily inaction are concerned in weight problem [14]. In Seventies, the costs of overweight have come to be expanded in most of the youngsters and adolescent of North. adolescence obesity has been increased daily. For this, prevention and treatment packages have been made to reverse the action of obesity. But, evidence for this effective action isn't finished but, in particular for the formative years weight problems[15]. In order to analyze the prevalence of obesity among children of various areas of Lahore, we have conducted a study of sample size 100 with age groups between 5 to 12 years. Areas we have covered Model Town, Town Ship and DHA in Lahore. Overall analysis suggests that children do their eating practice according to their area and opportunities provided as well as their socio economic status also matters. Moreover, they select food items according to their like based choices which majorly consist of those less healthy diet that gradually lead them towards obesity and overweight. Further, their sedentary habits and lifestyles tend to prevent them from needed physical activity that ultimately affects metabolism and digestion.

CONCLUSIONS

If we see the statistics of all participants, we can see that children overall consume all food groups in their diet, so we studied the factors that affect food consumption in school-going children, one of the factors that we majorly studied and statistics show that socioeconomic have a great effect on the food choices and food consumption among the school-going children. Socioeconomic status greatly affects meat, dairy, and fruit consumption among children. Low socioeconomic status children consume more vegetables, less meat, dairy on the other hand children with high socioeconomic status consume fewer vegetables, more meat, and dairy.

REFERENCES

- [1] Mkhize M, Sibanda M. A Review of Selected Studies on the Factors Associated with the Nutrition Status of Children Under the Age of Five Years in South Africa. *Int J Environ Res Public Health*. 2020 Oct 30;17(21):7973. doi: 10.3390/ijerph17217973.
- [2] Arif I, Batool M, Schenk PM. Plant Microbiome Engineering: Expected Benefits for Improved Crop Growth and Resilience. *Trends Biotechnol*. 2020 Dec;38(12):1385-1396. doi: 10.1016/j.tibtech.2020.04.015.
- [3] Chan AML, Ng AMH, Mohd Yunus MH, Idrus RBH, Law JX, Yazid MD, Chin KY, Shamsuddin SA, Lokanathan Y. Recent Developments in Rodent Models of High-Fructose Diet-Induced Metabolic Syndrome: A Systematic Review. *Nutrients*. 2021 Jul 22;13(8):2497. doi: 10.3390/nu13082497.
- [4] Ahmad D, Afzal M, Imtiaz A. Effect of socioeconomic factors on malnutrition among children in Pakistan. *Future Business Journal*. 2020 Dec;6(1):1-11. doi:10.1186/s43093-020-00032-x
- [5] Pålsson H, Pettersson F, Hiselius LW. Energy consumption in e-commerce versus conventional trade channels-Insights into packaging, the last mile, unsold products and product returns. *Journal of cleaner production*. 2017 Oct 15;164:765-78. doi:10.1016/j.jclepro.2018.09.138
- [6] Zeraatkar D, Bhasin A, Morassut RE, Churchill I, Gupta A, Lawson DO, Miroshnychenko A, Sirotych E, Aryal K, Mikhail D, Khan TA, Ha V, Sievenpiper JL, Hanna SE, Beyene J, de Souza RJ. Characteristics and quality of systematic reviews and meta-analyses of observational nutritional epidemiology: a cross-sectional study. *Am J Clin Nutr*. 2021 Jun 1;113(6):1578-1592. doi:10.1093/ajcn/nqab002..
- [7] NCD Risk Factor Collaboration (NCD-RisC). Height and body-mass index trajectories of school-aged children and adolescents from 1985 to 2019 in 200 countries and territories: a pooled analysis of 2181 population-based studies with 65 million participants. *Lancet*. 2020 Nov 7;396(10261):1511-1524. doi: 10.1016/S0140-6736(20)31859-6.
- [8] Burton Murray H, Riddle M, Rao F, McCann B, Staller K, Heitkemper M, Zia J. Eating disorder symptoms, including avoidant/restrictive food intake disorder, in patients with disorders of gut-brain interaction. *Neurogastroenterol Motil*. 2021 Oct 24:e14258. doi: 10.1111/nmo.14258.
- [9] Sserwanja O, Mutisya LM, Olal E, Musaba MW, Mukunya D. Factors associated with childhood overweight and obesity in Uganda: a national survey. *BMC Public Health*. 2021 Aug 3;21(1):1494. doi: 10.1186/s12889-021-11567-1.
- [10] Chowdhury MAB, Adnan MM, Hassan MZ. Trends, prevalence and risk factors of overweight and obesity among women of reproductive age in Bangladesh: a pooled analysis of five national cross-sectional surveys. *BMJ Open*. 2018 Jul 19;8(7):e018468. doi: 10.1136/bmjopen-2017-018468
- [11] Ghimire U, Aryal BK, Gupta AK, Sapkota S. Severe acute malnutrition and its associated factors among children under-five years: a facility-based cross-sectional study. *BMC Pediatr*. 2020 May 26;20(1):249. doi: 10.1186/s12887-020-02154-1
- [12] Deckelbaum RJ, Williams CL. Childhood obesity: the health issue. *Obes Res*. 2001 Nov;9 Suppl 4:239S-243S. doi: 10.1038/oby.2001.125.
- [13] Casey RE, Taylor MD, Klaine SJ. Mechanisms of nutrient attenuation in a subsurface flow riparian wetland. *J Environ Qual*. 2001 Sep-Oct;30(5):1732-7. doi: 10.2134/jeq2001.3051732x
- [14] Dehghan M, Akhtar-Danesh N, Merchant AT. Childhood obesity, prevalence and prevention. *Nutr J*. 2005 Sep 2;4:24. doi: 10.1186/1475-2891-4-24.
- [15] Birch LL, Ventura AK. Preventing childhood obesity: what works? *Int J Obes (Lond)*. 2009 Apr;33 Suppl 1:S74-81. doi: 10.1038/ijo.2009.22.
- [16] Visser J, McLachlan MH, Maayan N, Garner P. Community-based supplementary feeding for food insecure, vulnerable and malnourished populations - an overview of systematic reviews. *Cochrane Database Syst Rev*. 2018 Nov 9;11(11):CD010578. doi:10.1002/14651858.CD010578.
- [17] Hashan MR, Das Gupta R, Day B, Al Kibria GM. Differences in prevalence and associated factors of underweight and overweight/obesity according to rural-urban residence strata among women of reproductive age in Bangladesh: evidence from a cross-sectional national survey. *BMJ Open*. 2020 Feb 4;10(2):e034321. doi:10.1136/bmjopen-2019-034321.
- [18] Were JM, Stranges S, Creed IF. Fertility is a key predictor of the double burden of malnutrition among women of child-bearing age in sub-Saharan Africa. *J Glob Health*. 2020 Dec;10(2):020423. doi: 10.7189/jogh.10.020423.
- [19] Birch LL, Fisher JO. Development of eating behaviors among children and adolescents. *Pediatrics*. 1998 Mar;101(3 Pt 2):539-49.
- [20] Whitaker RC, Deeks CM, Bauchcum AE, Specker BL. The relationship of childhood adiposity to parent body mass index and eating behavior. *Obes Res*. 2000 May;8(3):234-40. doi: 10.1038/oby.2000.27.



Original Article

Comparison of Choroidal Filling and Optic Nerve Head Perfusion Pattern in Glaucoma Patients with Healthy Controls

Fatima Ansari¹, Syed Raza Ali Shah², Ayeza Nadeem Butt³, Syed Muhammad Aun Ali Shah⁴, Zaeema Ussama³, Muhammad Hassaan Ali⁵

¹Consultant Ophthalmologist, DHQ Hospital Jhang, Pakistan

²Associate Professor of Ophthalmology, Allama Iqbal Medical College, Jinnah Hospital, Lahore, Pakistan

³House Officer, Services Institute of Medical Sciences, Services Hospital, Lahore, Pakistan

⁴House Officer, CMH Institute of Medical Sciences, CMH, Lahore, Pakistan

⁵Senior Registrar Ophthalmology, Allama Iqbal Medical College, Jinnah Hospital, Lahore, Pakistan

ARTICLE INFO

Key Words:

glaucoma, choroidal filling, optic nerve head perfusion, hypofluorescence.

How to Cite:

Ansari, F., Shah, S. R. A., Butt, A. N., Shah, S. M. A. A., Usama, Z., & Ali, M. H. (2022). Comparison Of Choroidal Filling and Optic Nerve Head Perfusion Pattern in Glaucoma Patients with Healthy Controls: Comparison of Glaucoma patients and normal individuals. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.598>

***Corresponding Author:**

Muhammad Hassaan Ali
 Department of Ophthalmology, Allama Iqbal Medical College, Jinnah Hospital, Lahore, Pakistan
mhassaanali@hotmail.com

Received Date: 14th June, 2022

Acceptance Date: 21st June, 2022

Published Date: 30th June, 2022

ABSTRACT

Glaucoma is a primary cause of irreversible blindness worldwide, it kills the vision silently, having a financial burden on society regarding therapy expenses and loss of valuable hours of the day.

Objective: To compare the choroidal filling time and grade the status and pattern of optic nerve head (ONH) perfusion by fundus fluorescein angiography (FFA) in glaucoma patients **Methods:** Patients with various types of glaucoma were enrolled and compared them with healthy volunteers with no history and findings of glaucoma. Perfusion status using FFA was studied and analyzed corresponding visual fields (VF) and optical coherence tomography (OCT) findings **Results:** There were 70 participants in the study, including 48 glaucoma patients and 22 healthy controls. Choroidal filling time (CFT) was 9-12, 13-17, 15-22, and 20-33 seconds in healthy individuals and patients with ocular hypertension (OH), primary open-angle glaucoma (POAG), and normal-tension glaucoma (NTG), respectively. In OH, inferonasal and inferotemporal hypofluorescence pattern of ONH perfusion was noted, whereas POAG showed an inferonasal, patchy, and undefined pattern of hypofluorescence. In contrast with the healthy volunteers that showed uniform fluorescence, patients with NTG showed inferonasal hypofluorescence. CFT was significantly delayed in NTG patients ($p < 0.05$). We found a strong correlation between findings of FFA, OCT, and corresponding VF defects in glaucoma patients **Conclusions:** The choroidal filling time is prolonged in patients with various types of glaucoma, especially in cases of normal-tension glaucoma. FFA reveals perfusion defects in the form of areas of hypofluorescence and multiple characteristic optic nerve head perfusion patterns in cases of POAG, NTG, and OH.

INTRODUCTION

Glaucoma is an optic neuropathy that worsens over time and is associated with optic disc cupping and peripheral and central visual field defects, and increased loss of ganglion cells. In the study conducted in 2010, the number of individuals suffering from glaucoma was found to be 60.5 million [1]. The global figure for glaucoma prevalence in 2010 was 1.96% for open-angle glaucoma and 0.69% for angle-closure glaucoma [2]. A national survey of blindness 2002-2004 indicated that 113600 (7.1% of total blind) were blind due to glaucoma. Glaucoma is the fourth foremost cause of vision loss in our country [3]. Intraocular pressure

(IOP) is the only modifiable risk factor in successfully managing glaucoma [4]. Vascular or hematological disorders also play a vital part in glaucomatous optic nerve damage. There is a marked reduction in blood flow volume and velocity parameters in patients with glaucomatous optic neuropathy [5]. In patients with primary open-angle glaucoma (POAG) and ocular hypertension (OH), it was reported that choroidal blood flow was lower as compared to normal [6]. Alterations in the choroidal blood have also been seen in patients with central serous retinopathy, diabetic retinopathy, age-related macular degeneration,

glaucoma, and as well as in smokers [7]. Several methods have been developed to evaluate blood flow in the retina and choroid of the eye, such as radioactively labeled microspheres, laser speckle phenomenon, and color doppler imaging of various large vessels showing blood flow velocity in these vessels [8]. A study showed marked localized narrowing of retinal arterioles in glaucoma patients compared to normal [9]. Angiography is another fundamental method for assessing blood flow by which choroidal circulation has been studied, giving great information about the blood flow in normal individuals, glaucoma patients, and patients with other retinal disorders. Different dyes have been used for angiography, like sodium fluorescein and indocyanine green (ICG) [10]. ICG is an equally good but expensive dye compared to sodium fluorescein dye and is not routinely used in Pakistan. A study showed noticeable optic disc hypoperfusion in patients with ocular hypertension and glaucoma, assessed using fundus fluorescein angiography (FFA) [11]. Glaucoma damages the optic nerve progressively, so if any abrupt change in chorio-retinal blood flow occurs during a follow-up visit, it can be picked easily and the treatment modality adjusted [12]. Choroidal filling and optic nerve head perfusion patterns correlate with visual field defects and optical coherence tomography (OCT) defects. This study was conducted to compare the choroidal filling time and grade the pattern and status of optic nerve head perfusion in patients with normal-tension glaucoma (NTG), OH, and POAG patients and compare the findings with those of healthy individuals. The secondary objective was to correlate the FFA findings with corresponding visual field (VF) and optical coherence tomography(OCT)defects.

METHODS

It was a case-control study in which choroidal filling time and optic nerve head perfusion pattern in the eyes of glaucoma patients were compared with normal individuals. The study was conducted at King Edward Medical University and Allama Iqbal Medical College, Lahore, Pakistan, following principles laid down in the declaration of Helsinki. The patients belonging to either gender and above 40 years of age were recruited following non-probability purposive sampling following the below-mentioned selection criteria. Inclusion criteria was open angle glaucoma, Glaucomatous cupping of disc, visual field defects, Retinal nerve fiber layer (RNFL) defects on Optical coherence tomography (OCT), Intraocular pressure (IOP)> 21mmHg, normal-tension glaucoma was diagnosed on the same criteria as for primary open-angle except IOP<21mmHg. Ocular hypertension was considered when there was no glaucomatous cupping, no RNFL defects on

OCT, no visual field defect and IOP> 21mmHg. Exclusion criteria was media opacities (cataract, corneal opacities, vitreous hemorrhage, etc., History of diabetes mellitus, History of ischemic heart disease, Any past glaucoma surgery, History of other variants of glaucoma such as secondary open-angle glaucoma, congenital glaucoma, and primary and secondary angle-closure glaucoma and Individuals having any other ocular pathologies. Fundus angiograms of normal healthy volunteers were taken as controls. These healthy subjects had IOP < 21mmHg and normal findings of anterior and posterior segments on slit-lamp biomicroscopy, visual fields, and OCT of the optic nerve head. Seventy patients were taken out of which 22 were normal healthy individuals, and 48 suffered from ocular hypertension (OH) or glaucoma. The visual fields, OCT of optic nerve head, and gonioscopy were done before FFA. The choroidal and optic nerve head areas were divided into six quadrants so that defects found in VF, OCT, and FFA could be compared anatomically. From OCT retinal nerve fiber layer (RNFL) was taken for comparison. These analyzed quadrants were drawn as follows:

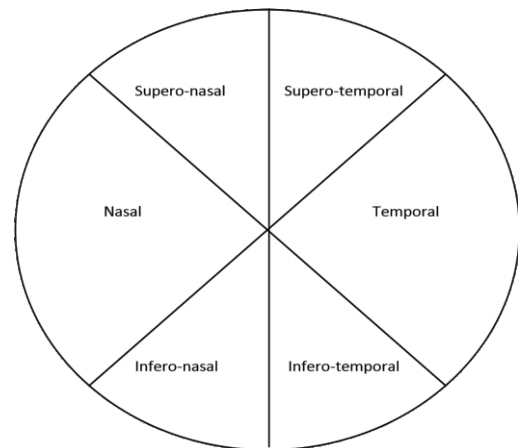


Figure 1: Six Quadrants of Optic Nerve Head for Evaluation

Informed written consent was obtained from all the participants. FFA was performed using the Topcon TRC-50DX FFA machine. As choroidal vessels were filled in seconds, the examination of the fellow eye was missed and was not included in the study. A single eye from each individual was included in the study. Before giving an injection of 25% sodium fluorescein 3ml with a dosage of 250mg/ml into the antecubital vein, baseline colored, and black & white red-free fundus images were taken. A series of black & white images of the chorio-retinal circulation every second for 30-40 seconds and delayed images after 10 and 15 minutes were taken. Pathological changes were recognized by hyper- or hypo-fluorescence of the optic nerve head that exhibited different fluorescence patterns. The collected data was entered and analyzed using statistical software SPSS version 23.0. Quantitative data

are presented as mean ± SD, whereas qualitative variables are presented in frequencies and percentages. Choroidal filling time (CFT) in cases and normal individuals was compared using an independent sample t-test. Choroidal filling patterns and optic nerve head perfusion patterns in cases and normal individuals were compared using a Chi-square test, taking a p-value ≤ 0.05 as statistically significant.

RESULTS

This study included 22(31%) normal individuals and 48(69%) diseased patients. Out of 48 affected individuals, 24 (50.0%) had POAG, 14(29.2%) had NTG, and the rest 10 (20.8%) patients suffered from OH. The age distribution of the study population is shown below (Table 1):

Age Range (years)	Number (%)
40-50	30(43%)
51-60	30(43%)
61-70	8(11%)
71-80	2(3%)

Table 1: Distribution of Patients in Various Age Groups

There were 49% male and 51% female patients in the study. The RNFL loss and the corresponding visual field defects in POAG and NTG patients are presented in Table 3. Most patients (41.7%) showed RNFL loss in the inferonasal quadrant with related VF defects in the supero-temporal quadrant. No patient showed any RNFL loss and visual field defect in the normal healthy population and patients with OH.

Quadrants	RNFL Loss (n %)		Visual Field Defect (n %)	
	POAG, (N=24)	NTG, (N=14)	POAG, (N=24)	NTG, (N=14)
Inferonasal	10 (41.7)	6 (42.9)	3 (12.5)	0 (0.0)
Inferotemporal	6 (25.0)	4 (28.6)	3 (12.5)	2 (14.3)
Superonasal	3 (12.5)	2 (14.3)	5 (20.8)	4 (28.6)
Nasal	2 (8.3)	1 (7.1)	1 (4.2)	1 (7.1)
Superotemporal	2 (8.3)	0 (0.0)	10 (41.7)	6 (42.9)
Temporal	1 (4.2)	1 (7.1)	2 (8.2)	1 (7.1)

POAG: Primary open angle glaucoma
NTG: Normal tension glaucoma

Table 2: RNFL Loss and Corresponding Visual Field Defect in Various Types of Glaucoma

We performed FFA in our patients and studied choroidal filling time and optic nerve head perfusion pattern (ONHPP). The results of choroidal filling time in various conditions are listed below (Table 3):

Diagnosis	Choroidal Filling Time (seconds)
Ocular hypertension (OH)	13 to 17
Primary Open Angle Glaucoma (POAG)	15 to 22
Normal-Tension Glaucoma	20 to 33
Normal Individuals	09 to 12

Table 3: Choroidal Filling Time in Ocular Hypertension, Primary Open Angle Glaucoma, Normal-Tension Glaucoma, and Normal

Individuals

Analysis of the ONH perfusion pattern showed that in patients with ocular hypertension, 2 (20.0%) showed inferonasal, 1 (10.0%) each showed inferotemporal, extensive, patchy hypofluorescence, and 4(40.0%) showed normal fluorescence. In POAG, 6(25.0%) showed extensive, 5 (20.8%) patchy, 4 (16.7%) inferonasal, 4 (16.7%) inferotemporal, 3 (12.5%) normal, 1 (4.3%) each nasal, superonasal and superotemporal. In NTG, 4 (28.6%) individuals showed inferonasal hypofluorescence, 3 (21.4%) patchy hypofluorescence, 2 (14.3%) each superonasal, inferotemporal, extensive, and 1 (7.1%) showed nasal hypofluorescence. Normal Individuals showed normal fluorescence in all quadrants.

DISCUSSION

The study's primary objectives to compare the choroidal filling time and optic nerve head perfusion patterns in glaucoma patients with healthy individuals were successfully met. In OH, FFA showed vascular disturbance, but no defects were present in VFs and OCT, which implied that the areas highlighted in FFA could become the actual defects, and these cases could become glaucomatous in old ages. The choroidal filling time was delayed in both NTG and POAG, showing that this parameter could potentially indicate optic nerve head perfusion in glaucoma patients. Characteristically, glaucomatous damage causes RNFL and retinal ganglion cell loss that occurs focally and diffusely. OCT, a non-contact, non-invasive technology, yields high-resolution cross-sectional in vivo imaging of retinal layers. While structural abnormalities might pave the way for functional anomalies, it may be expected that an OCT abnormality would be observed clearly when no glaucomatous VF loss is present. We observed corresponding areas of visual field defect in glaucoma patients, which correlated with the areas of OCT structural damage. In a study by Weinreb and Robert et al., blood flow was measured in peripapillary choroidal tissue and optic nerve head area using indocyanine green (ICG) dye. It was found that choroidal filling time was significantly delayed in glaucoma patients. Hypofluorescence of ONH was also noted [13]. Similar results were seen in the current study using fluorescein as the study dye. Our findings authenticate the effectiveness of sodium fluorescein in diagnosing different abnormalities in glaucoma patients. The study participants' responses showed that sodium fluorescein was easy to apply, less expensive, and had tolerable side effects. Clinically, the primary purpose of FFA is to examine blood circulation within chorioretinal tissue to understand glaucoma better [14]. A systematic understanding of the circulation appearance and phases of the dye in an individual with a normal eye is necessary for

developing a better understanding of these abnormalities [15]. To correlate the FFA findings with defects in VFs & OCT anatomically, we divided the peri-papillary choroidal area and ONH into six quadrants/sections (nasal, temporal, superonasal, superotemporal, inferonasal, and inferotemporal). We observed a strong correlation between these three parameters, with defects in VFs and OCT corresponding with each other. Numerous studies have reported that the prevalence of glaucomatous changes in patients with OH without defects in the visual field or ONH changes with age over 40 years varies between 4 - 10% [16]. The OH patients that progress to overt glaucoma in untreated individuals is about 2% per year, and about 1% per year in individuals on anti-glaucoma treatment [17]. In our study, patients with OH showed that 61.1% of individuals had an abnormality in the choroidal filling and ONH perfusion pattern in the absence of visual fields and RNFL loss. It showed that these individuals are at risk of developing open-angle glaucoma later in their lives. The current study showed that 44% of individuals of POAG had defects in corresponding regions of FFA, VFs, and RNFL, and 48% showed patchy and undefined generalized filling defects along with quadrant/sectoral defects. Another study reported that the raised IOP in POAG caused generalized compression on choroidal vasculature and ONH, resulting in a generalized type of defects compared to specific defects in a particular quadrant [18]. In NTG, 71% of individuals showed defects in the corresponding RNFL quadrant with reciprocal VF changes. We propose that raised IOP was well documented in POAG, which caused a generalized effect on all the choroidal and ONH vasculature resulting in generalized filling defects. However, patients with NTG showed quadrant-wise defects as a specific quadrant was primarily involved in these patients [19-23].

CONCLUSIONS

The choroidal filling time is delayed in patients with various types of glaucoma. FFA revealed perfusion defects in the form of hypofluorescence and multiple patterns of optic nerve head perfusion in cases POAG, NTG, and OH. FFA revealed corresponding vascular flow disturbances in the quadrants that showed changes in RNFL loss with reciprocal VF changes in POAG and NTG patients. In the case of OH, FFA would help individuals be screened before defects are detected on VFs and OCT.

REFERENCES

- [1] Butt NH, Ayub MH, Ali MH. Challenges in the management of glaucoma in developing countries. *Taiwan journal of ophthalmology*. 2016 Sep 1;6(3):119-22. doi: 10.1016/j.tjo.2016.01.004.
- [2] Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. *Br J Ophthalmol*. 2006;90(3):262-7. dx.doi.org/10.1136/bjo.2005.081224
- [3] Dineen B, Bourne RR, Jadoon Z, Shah SP, Khan MA, Foster A, et al. Causes of blindness and visual impairment in Pakistan. The Pakistan national blindness and visual impairment survey. *Br J Ophthalmol*. 2007;91(8):1005-10. doi: 10.1136/bjo.2006.108035.
- [4] Mamikonian VR, Galoian NS, Sheremet NL, Kazarian EE, Kharlap SI, Shmeleva-Demir OA et al. Peculiarities of ocular blood flow in ischemic optic neuropathy and normal tension glaucoma. *Vestnik Oftalmologii*. 2013 Jul 1;129(4):3-8.
- [5] Javaid U, Ali MH, Jamal S, Butt NH. Pathophysiology, diagnosis, and management of glaucoma associated with Sturge-Weber syndrome. *International Ophthalmology*. 2018 Feb;38(1):409-16. doi: 10.1007/s10792-016-0412-3.
- [6] Portmann N, Gugleta K, Kochkorov A, Polunina A, Flammer J, Orgul S. Choroidal blood flow response to isometric exercise in glaucoma patients and patients with ocular hypertension. *Invest Ophthalmol Vis Sci*. 2011;52(10):7068-73. doi: 10.1167/iovs.11-7758.
- [7] Duijm HF, van den Berg TJ, Greve EL. Choroidal haemodynamics in glaucoma. *Br J Ophthalmol*. 1997;81(9):735-42. doi: 10.1136/bjo.81.9.735.
- [8] Aquino MV. Suggested Formula for Setting Target Intraocular Pressure. *Asian J Ophthalmol*. 2004;6(1):2-6
- [9] Zhong Y, Wang J, Luo X. Integrins in trabecular meshwork and optic nerve head: possible association with the pathogenesis of glaucoma. *BioMed Research International*. 2013 Jan 1;2013. doi: 10.1155/2013/202905.
- [10] Harris A, Kagemann L, Chung HS, Ciulla TA. The use of dye dilution curve analysis in the quantification of Indocyanine green angiograms of the human choroid. *Ophthalmol Clin. North Am*. 1998;11(3):331-337. doi.org/10.1016/S0896-1549(05)70060-2.
- [11] Schmidl D, Boltz A, Kaya S, Werkmeister R, Dragostinoff N, Lasta M, et al. Comparison of choroidal and optic nerve head blood flow regulation during changes in ocular perfusion pressure. *Invest Ophthalmol Vis Sci*. 2012;53(8):4337-46. doi: 10.1167/iovs.11-9055.
- [12] Yoneya S. A new approach for studying the retinal and choroidal circulation. *Nippon Ganka Gakkai Zasshi*. 2004 Dec 1;108(12):836-61.
- [13] Weinreb RN, Bartsch DU, Freeman WR. Angiography of the glaucomatous optic nerve head. *J Glaucoma*. 1994 Jul 1;3:S55-60.
- [14] Yasuzumi K, Ohno-Matsui K, Yoshida T, Kojima A,

- Shimada N, Futagami S, Tokoro T, Mochizuki M. Peripapillary crescent enlargement in highly myopic eyes evaluated by fluorescein and indocyanine green angiography. *Br J Ophthalmol*. 2003 Sep 1;87(9):1088-90. doi: 10.1136/bjo.87.9.1088.
- [15] Zakir R, Iqbal K, Tarar AA, Azhar Z, Ali MH, Hashmani N, Zakir M. The role of ocular coherence tomography angiography in the diagnosis of diabetic retinopathy and a comparison with the current gold standard fundus fluorescein angiography. *Journal of Fatima Jinnah Medical University*. 2021;15(4):184-8. doi.org/10.37018/100X6573
- [16] Akagi T, Zangwill LM, Shoji T, Suh MH, Saunders LJ, Yarmohammadi A, Manalastas PI, Penteadó RC, Weinreb RN. Optic disc microvasculature dropout in primary open-angle glaucoma measured with optical coherence tomography angiography. *PLoS One*. 2018 Aug 7;13(8):e0201729. doi: 10.1371/journal.pone.0201729.
- [17] Ali MH, Shah SR, Butt AN, Jamal S, Hamza U, Butt NH. Efficacy And Surgical Outcome of Trabeculectomy with Mitomycin-C In Congenital Glaucoma with Hazy Cornea: Outcome of Trabeculectomy with Mitomycon-C in Congenital Glaucoma. *Pakistan BioMedical Journal*. 2022 May 31:272-5. doi.org/10.54393/pbmj.v5i5.458
- [18] Hitching RA, Spaeth GL. Fluorescein angiography in chronic simple and low tension glaucoma. *Br J Ophthalmol*. 1977; 61: 126-32. doi: 10.1136/bjo.61.2.126.
- [19] Usman M, Iqbal K, Ali MH, Nafees K. Features and diagnostic accuracy of optical coherence tomography angiography in neovascular age-related macular degeneration. *Cureus*. 2019 Dec 28;11(12):e6485. doi:10.7759/cureus.6485.
- [20] Ayub A, Akhtar FM, Saleem N, Ali MH, Ayub MH, Butt NH. Frequency and risk factors of dry eye disease in Pakistani population, a hospital based study. *Pakistan Journal of Ophthalmology*. 2017 Dec 1;33(4). doi.org/10.36351/pjo.v33i4.26
- [21] Jamal S, Ali MH, Ayub MH, Butt NH. Frequency and grading of diabetic retinopathy in diabetic end stage renal disease patients. *Pakistan Journal of Ophthalmology*. 2016 Jun 30; 32(2). doi.org/10.36351/pjo.v32i2.100.
- [22] Ali MH, Javaid M, Jamal S, Butt NH. Femtosecond laser assisted cataract surgery, beginning of a new era in cataract surgery. *Oman journal of ophthalmology*. 2015 Sep;8(3):141. doi: 10.4103/0974-620X.169892.
- [23] Zakir R, Iqbal K, Ali MH, Mirza UT, Mahmood K, Riaz S, Hashmani N. The outcomes and usefulness of Intraoperative Optical Coherence Tomography in vitreoretinal surgery and its impact on surgical decision making. *Romanian Journal of Ophthalmology*. 2022 Jan;66(1):55-60. doi: 10.22336/rjo.2022.12.



Original Article

Role of Ultrasound in First Trimester Vaginal Bleeding: An Observational Study at a Tertiary Care Hospital in Mardan, Pakistan

Zubair Janan Orakzai¹, Nuzhat Malik Awan², Nadia Khattak^{3*}, Bakht Rokhan⁴, Fauzia Rashid⁵ and Ayesha Kamran⁶

¹Department of Diagnostic Radiology, Bacha Khan Medical College/ Mardan Medical Complex, Mardan, Pakistan

²Department of Gynaecology and Obstetrics, Amna Inayat Medical College, Lahore, Pakistan

³Department of Diagnostic Radiology, Peshawar Institute of Cardiology, Peshawar, Pakistan

⁴Department of Radiology, Saidu Medical College/ Saidu Teaching Hospital, Saidu Sharif, Swat, Pakistan

⁵Department of Radiology, HBS General Hospital, Islamabad, Pakistan

⁶Department of Radiology, Sargodha Medical College, DHQ Hospital, Sargodha, Pakistan

ARTICLE INFO

Key Words:

First trimester bleeding, Ultrasonography, vaginal bleeding, Ectopic abortion, Inevitable Abortion

How to Cite:

Janan Orakzai, Z. ., Malik Awan, N. ., Khattak, N. ., Rokhan, B., Rashid, F. ., & Kamran, A. .(2022). Role Of Ultrasound in First Trimester Vaginal Bleeding Observational Study at Tertiary Care Hospital: Role of Ultrasound in First Trimester Vaginal Bleeding. *Pakistan Biomedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.550>

***Corresponding Author:**

Nadia Khattak
 Department of Diagnostic Radiology, Peshawar Institute of Cardiology, Peshawar, Pakistan
nadiaishfaq.7@gmail.com

Received Date: 13th June, 2022

Acceptance Date: 24th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Vaginal bleeding in first trimester is most common complication of pregnant women. The ratio of vaginal bleeding in pregnant women is 20-25%. About 50% of pregnant women experiencing vaginal bleeding in first trimester have viable pregnancy. 50% cases of abortion are reported in first trimester vaginal bleeding. Therefore, it is necessary to evaluate the significance of ultrasonography in diagnosis of first trimester vaginal bleeding. **Objective:** Objective of the study is to elaborate the fundamental role of ultrasonography in first trimester vaginal bleeding. The ratio of misdiagnosis in putatively nonviable pregnancy will be reduced by complete understanding of ultrasonography significant. In this way the premature interventions can be avoided that ultimately leads to mismanagement. **Study Design:** It was an observational study with statistical approaches, conducted in BKMC / MMC, Mardan for the duration of six months from December 2020 to May 2021. **Methods:** All the antenatal women having complaint of first trimester vaginal bleeding visited the hospital was included in this prospective observational study. Those who met the inclusion and exclusion criteria set by the Gynecology department of Hospital were followed for further analysis study. **Results:** Out of the 90 patients included in the study, 51% cases were of threatened abortion among viable pregnancies and 6% cases of normal pregnancy were reported. Various types of abortion were reported in the patients, out of which 11% cases were of missed abortion, 1% of complete abortion, and 11% of incomplete abortion, 5% of ectopic pregnancy and 10% of blighted ovum. The inevitable abortion cases were 3% and 1.1 % cases of hydatidiform mole. **Conclusion:** After developing better understanding of correlation between ultrasonography and first trimester vaginal bleeding, sonologist can elaborately explain the cause of vaginal bleeding. For the diagnosis of first trimester vaginal bleeding ultrasonography is the non-invasive imaging technology.

INTRODUCTION

Vaginal bleeding is the most common symptom during first trimester. First trimester can also be called as phase of rapid changes that includes fertilization, blastocyst formation, zygote implantation leading to gastrulation and neurulation [1,2]. Vaginal bleeding is the frequent obstetric emergency during first trimester. The previous studies indicated that 16% of all the pregnant women experience the vaginal bleeding. The first trimester vaginal bleeding can result in spontaneous abortion to life-threatening

blood loss [2,3]. The ratio of abortion is about 10-20%. Ultrasonography in first trimester of pregnancy play significant role in assessment of the cause of bleeding per vagina [3,4]. This assessment facilitates to develop better understanding of viability and location of pregnancy either intrauterine or extrauterine [5]. The color Doppler imaging combined with high-resolution transvaginal sonography can be used for assessment of uteroplacental vascularization volumes that provide prognostic values by

measuring the uteroplacental blood flow [6,7]. So, with the advent of growing technology now we can detect the intra-decidual gestational sacs within 35 days of pregnancy [8,9]. In about 50% cases of first trimester vaginal bleeding the women suffered from miscarriages. In order to reduce the ratio of maternal mortality the early diagnosis of first trimester bleeding is required and the advancing ultrasonography paving ways to diagnose such complications[10].

METHODS

It was an observational study with statistical approaches, conducted in Bacha Khan Medical College/ Mardan Medical Complex, Mardan for the duration of six months from December 2020 to May 2021. The ninety pregnant women with the 12 week or less than 12 weeks gestation periods and vaginal bleeding complaint were included in this observational study. Ethical committee of the hospital approved the study. All the antenatal women with the first trimester bleeding visited hospitals from September-March were included in the study. The non-pregnant women with the vaginal bleeding were excluded from the study. Clinicians performed the provisional diagnosis of all the patients. After the clinical evaluation of the patients, ultrasonography was suggested for further analysis. By using 3.5 MHz frequency transducer, Trans abdominal ultrasonography was conducted. Trans abdominal ultrasonography of few patients depicted the inconclusive results, they were referred with transvaginal ultrasonography with the 5-7 MHZ frequency transducer. Ectopic pregnancy was diagnosed in 6 cases, while in 8 out of eighty cases were diagnosed with the abnormal intrauterine gestation. The correlation between clinical finding and imaging finding was evaluated. Statistical Package for Social Sciences (SPSS version 21.0, IBM Corporation, USA) was used for statistical analysis of data. N (% of cases) represented the data of categorical variables, while the Mean and Standard deviations represent the data of continuous variables. For the clinical diagnosis the in-depth statistical analysis was carried out. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy values were calculated.

RESULTS

The patients were divided into groups on the basis of age. The standard deviation of each age group was calculated. Out of 90 cases studies, 51% of threatened abortion, 11% of missed abortion and incomplete abortion. Normal pregnancy was observed in 6% of cases. 1% cases of complete abortion, and 3% cases of inevitable abortion were reported. The mainstay in diagnosis of first trimester

vaginal bleeding is ultrasonography. The 5% cases of ectopic pregnancy, 10% cases of blighted ovum and 1% cases of hydatidiform mole was observed. The table showed that the major number of cases of first trimester vaginal bleeding are more common in the age group ranging from 23-27 years. While the patients having age between 18-22 years share only 20% cases. The vaginal bleeding is also common in women of age ranging between 28-32 years(Tabole 1).

Age Groups (years)	No. of cases (%)
18-22	18 (20)
23-27	45 (50)
28-32	15 (16.6)
33-37	12(13.3)
Total	90(100)

Table 1: Clinical diagnosed cases distribution according to ultrasonography diagnosed

Below table 2 showed the percentage of abortions and pregnancies. Out of 90 cases studies, 51% of threatened abortion, 11% of missed abortion and incomplete abortion. Normal pregnancy was observed in 6% of cases. 1% cases of complete abortion, and 3% cases of inevitable abortion were reported. The mainstay in diagnosis of first trimester vaginal bleeding is ultrasonography. The 5% cases of ectopic pregnancy, 10% cases of blighted ovum and 1% cases of hydatidiform mole was observed.

Variables	Threatened Abortion		Incomplete Abortion		Missed Abortion		Complete Abortion		Normal pregnancy		Ectopic pregnancy		H mole		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
USG diagnosis	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Threatened Abortion	39	60.9	2	22.2	3	37.5	0	0	2	66.6	0	0	0	0	46	51.1
Missed Abortion	7.5	12	1	11.1	2	25	0	0	0	0	0	0	0	10	11.6	
Incomplete Abortion	4	6.2	3	33.3	1	12.5	2	50	0	0	0	0	0	10	11.1	
Normal Pregnancy	5	7.8	0	0	0	0	0	0	1	33.3	0	0	0	6	6	
Complete Abortion	0	0	1	11.1	0	0	0	0	0	0	0	0	0	1	1.1	
Inevitable Abortion	1	1.5	0	0	1	12.5	1	25	0	0	0	0	0	3	3	
Ectopic Pregnancy	1.5	2.3	2	22.2	0	0	0	0	0	0	1	100	0	4	5	
Blighted Ovum	6	9.3	0	0	1	12.5	1	25	0	0	0	0	1	9	10	
H mole	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1.1	
Total	64	100	9	100	8	100	4	100	3	100	1	100	1	90	100	

Table 2: the percentage of abortions and pregnancies

DISCUSSION

Our study indicated that the women of age ranging between 23-27 years are more prone to suffer from first trimester vaginal bleeding [11,12]. Shivanagappa et al., conducted the similar study to find the correlation between first trimester vaginal bleeding and age, their results showed that women of the age group 21-25 years are more prone to vaginal bleeding in first trimester. In the present study, out of 90 cases, 51% were of threatened abortion, 11% of missed abortion and 11% of incomplete abortion. Normal pregnancy was observed in 6% of cases. 1% cases of complete abortion, and 3% cases of inevitable abortion were reported [13]. The study conducted by Khatod et al on the 107 patients, and their results showed 76.64% cases of threatened abortion, 4.67% cases of complete abortion, 6.54% as incomplete abortion, 3.74% as inevitable abortion, 3.74% as missed abortion, 4.67% as ectopic pregnancy [14,15]. By clinical examination of 165 patients Shivanagappa et al., concluded that 57% cases were of threatened abortion, 31% of incomplete abortion, 4% of missed abortion, 6 % ectopic pregnancy and 1.2% hydatidiform mole and 0.8 % complete abortion [16]. In our study, 51% cases of threatened abortion was diagnosed by ultrasound. A study showed 46 out of 94 cases of threatened abortion. They observed 15 cases of missed abortion, 7 cases of ectopic abortion, and 3 cases of molar pregnancy [17,18]. The clinical findings of our study and their comparison to the clinical findings of Deepti Kurmi shows that it not only removes the ambiguities of the clinical diagnosis but also pave way towards most accurate diagnosis. This indicates that the first trimester vaginal bleeding is more commonly seen in the women with the age group of 23-27 years with the highest ratio of 50%. The women of the age group 18-22 years attained second slot with the ratio of 20% [17]. In our study the number of cases of incomplete abortion were 6.2% while the results of other study were close enough to 4.65%. The 60.9% cases of threatened abortion were reported in our study, in case of

other study 58.13% cases of threatened abortion were reported [19]. A study reported the viable pregnancy in 64% cases while in present study indicated the viable pregnancy in 60.9% cases. The ratio of non-viable pregnancy in our study is 39.24%, while in other study clinical examination it is 46% [20].

CONCLUSIONS

To differentiate the various conditions and phases of first trimester bleeding in pregnant women, the ultrasonography is most accurate and non-invasive diagnostic tool. Early diagnosis of gestational-related problems with the help of ultrasonography, pave the new ways towards prompt treatment of patients and reduce mortality rates. Advancement in field of ultrasonography, will not only assure the safety of pregnant-women and children, but also will alleviate the anxiety among the couples.

REFERENCES

- [1] Shah K. Role of ultrasonography in cases of first trimester vaginal bleeding and its correlation with clinical findings: A prospective observational study. *International Journal of Clinical Obstetrics and Gynaecology*, 2019,3(5):96-100.doi.org/10. 33545/ gynae.2019.v3.i5b.336
- [2] Al-Memar M, Kirk E, Bourne T. The role of ultrasonography in the diagnosis and management of early pregnancy complications. *The Obstetrician & Gynaecologist*. 2015 Jul;17(3):173-81.
- [3] Jaffe R, Dorgan A, Abramowicz JS. Color Doppler imaging of the uteroplacental circulation in the first trimester: value in predicting pregnancy failure or complication. *AJR. American journal of roentgenology*. 1995 May 1;164(5):1255-8. doi: 10.2214/ajr.164.5.7717242.
- [4] Kaplan BC, Dart RG, Moskos M, Kuligowska E, Chun B,

- Hamid MA, Northern K, Schmidt J, Kharwadkar A. Ectopic pregnancy: prospective study with improved diagnostic accuracy. *Annals of emergency medicine*. 1996 Jul 1;28(1):10-7. doi: 10.1016/s0196-0644(96)70131
- [5] Eduwem Dianabasi U, Uduma Felix U, Okere Philip C, Edmund E. Obstetric Sonography in First Trimester Vaginal Bleeding (A Single Institution Study). *Merit Research Journal of Medicine and Medical Sciences* 4(7):356-362
- [6] Tezuka N, Sato S, Kanasugi H, Hiroi M. Embryonic heart rates: development in early first trimester and clinical evaluation. *Gynecologic and obstetric investigation*. 1991;32(4):210-2. doi: 10.1159/000293033.
- [7] Hasan R, Baird DD, Herring AH, Olshan AF, Funk ML, Hartmann KE. Association between first-trimester vaginal bleeding and miscarriage. *Obstetrics and gynecology*. 2009 Oct;114(4):860-867. doi: 10.1097/AOG.0b013e3181b79796.
- [8] Noblett D, Sekhon S, Corwin MT, Lamba R, McGahan JP. Retained Morbidly Adherent Placenta Presenting as a Myometrial Mass in Patients With Vaginal Bleeding: A Case Series and Review of Current Literature. *Ultrasound Quarterly*. 2022 Apr 15:10-97. doi: 10.1097/RUQ.0000000000000612.
- [9] Bakhtawar K, John A, Ali A, Mubbarka MM. Ultrasound Diagnosis and Risk Factors of 1st Trimester Complications in Pregnancy: Ultrasound Diagnosis and Risk Factors of 1st Trimester. *Pakistan BioMedical Journal*. 2022 Apr 30:41-5. doi.org/10.54393/pbmj.v5i4.293
- [10] Wladimiroff JW, Eik-Nes S, editors. *Ultrasound in obstetrics and gynaecology*. Elsevier Health Sciences; 2009.
- [11] Kalyani S. Assessment of first trimester vaginal bleeding using ultrasound sonography. *Asian J. of Biomed and Pharm. Sci*. 2016; 6:54-56.
- [12] Panes J, Bouzas R, Chaparro M, García-Sánchez V, Gisbert JP, Martínez de Guereñu B, et al. Systematic review: the use of ultrasonography, computed tomography and magnetic resonance imaging for the diagnosis, assessment of activity and abdominal complications of Crohn's disease. *Alimentary pharmacology & therapeutics*. 2011 Jul;34(2):125-45. doi: 10.1111/j.1365-2036.2011.04710.x.
- [13] Shivanagappa M, Sagar SG, Manoli N. Ultrasound evaluation of vaginal bleeding in first trimester of pregnancy: a comparative study with clinical examination. *International journal of scientific study*. 2015;3(7):202-6. doi: 10.17354/ijss/2015/477
- [14] Sofat R. Ultrasound evaluation of bleeding in early pregnancy. *J Obstet Gynaecol India*. 1987;31:344-7.
- [15] Tahmina S, Daniel M, Solomon P. Clinical analysis of ectopic pregnancies in a tertiary care centre in Southern India: a six-year retrospective study. *Journal of clinical and diagnostic research: JCDR*. 2016 Oct;10(10):QC13. doi: 10.7860/JCDR/2016 /21925.8718.
- [16] Aronu ME, Okafor CO, Mbachu II, Iloraah US, Ikeako L, Okafor CI. A review of the correlation between clinical diagnosis and ultrasound diagnosis in first trimester vaginal bleeding. *Annals of Medical and Health Sciences Research*. 2018;8(2).
- [17] Kurmi D, Jadhav VR, Misri A, Mishra N, Prabhu S, Savani G. Role of pelvic sonography in first trimester bleeding. *Journal of Evolution of Medical and Dental Sciences*. 2015 Jun 18;4(49):8516-26. dx.doi.org/10.14260/jemds/2015/1234
- [18] Stabile I, Campbell S, Grudzinskas JG. Ultrasonic assessment of complications during first trimester of pregnancy. *The lancet*. 1987 Nov 28;330(8570):1237-40. doi: 10.1016/s0140-6736(87)91853-8.
- [19] Mantoni M. Ultrasound signs in threatened abortion and their prognostic significance. *Obstetrics and gynecology*. 1985 Apr 1;65(4):471-5.
- [20] Harville EW, Wilcox AJ, Baird DD, Weinberg CR. Vaginal bleeding in very early pregnancy. *Human Reproduction*. 2003 Sep 1;18(9):1944-7. doi.org/10.1093/humrep/deg379



Original Article

Efficacy of Phloroglucinol vs Drotaverine Hydrochloride in Shortening the Active Phase of the First Stage of Labor in Primigravidae

Maryam Shahid^{1*}, Nida Arif¹, Iffat Hamid², Sohaib Arif¹ and Ayesha Naeem³¹ Department of Gynecology, The Indus Hospital QF-NST Campus Lahore, Pakistan² Department of Gynecology, Sharif Medical City Lahore, Pakistan³ Department of Gynecology, Khawaja Muhammad Safdar Medical College, Allama Iqbal Memorial Teaching Hospital, Sialkot, Pakistan

ARTICLE INFO

Key Words:

labour duration, phloroglucinol, drotaverine, first stage of labour

How to Cite:

Shahid, M. ., Arif, N. ., Hamid, I. ., Arif, S. ., & Naeem, A. . (2022). Efficacy of Phloroglucinol vs Drotaverine Hydrochloride in Shortening in Primigravidae at Term the Active Phase of the First Stage of Labor: Phloroglucinol vs Drotaverine Hydrochloride in Shortening the First Stage of Labor. *Pakistan BioMedical Journal*, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.571>

*Corresponding Author:

Maryam Shahid
 Department of Gynecology, The Indus hospital QF-NST Campus Lahore, Pakistan
dr.maryam.shahid@gmail.com

Received Date: 19th June, 2022

Acceptance Date: 26th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Primigravida women are those who conceive for the first time and are at high risk group for complications during childbirth. **Objective:** To compare the effectiveness of phloroglucinol i/v and drotaverine hydrochloride by measurement of the 1st stage of labor in primigravidae. **Methods:** This randomized controlled trial was held in the Obstetrics and Gynecology Department of Allama Iqbal Memorial Teaching Hospital Sialkot and The Indus hospital QF-NST Campus Lahore for six-months duration from July to December 2021. Several factors were used to determine the inclusion of primigravida females, including age range of 20- 35 years, 38-42 weeks of gestational age at LMP with single pregnancy, Uterine contractions up to 3 cm if they occur at 3-4, 10 minutes before both drugs are given, ROM, no signs of fetal and maternal distress, patient in the first stage of labour. All of the cases were divided into two groups: A and B. Group 'A' received phloroglucinol 40mg (4ml) i/v at 4 cm dilation, and the dosage was repetitive at 8 cm dilation. At 4cm dilation, Group 'B' received drotaverine 40mg i/v. The essential signs including uterine contractions and fetal heart rate were monitored every half an hour. **Results:** 80 patients were included, with 56.3% of cases in Group-A group B has 43.7% cases being between the ages of 20-35 years. There was a significant improvement in the first stage of active labour 'mean duration in Groups A and B is 160.21±4.29 minutes and 203.77±8.21 minutes, respectively. **Conclusion:** The mean active length of the 1st stage of labour in the group of phloroglucinol was substantially shorter than in the drotaverine group.

INTRODUCTION

The fetus, umbilical cord, placenta and membrane are excreted from the uterus as part of the physiologic process of conception [1,2]. It is performed by alterations in biochemical connective tissues as well as gradual dilatations and effacement of the uterine cervix as a consequence of proper frequency, duration, and intensity of uterine contractions [3,4]. Both obstetricians and active labour patients want to deliver the baby in the shortest time without jeopardizing the mother's and fetus's safety [5,6]. Following the onset of the active phase, uterine contractions increase in frequency, strength, and pace of cervix dilatation. The initial stage of the active phase of

labour is also known as the 'dilatation phase' [7,8]. Because hospitalization for childbirth is almost ubiquitous, practically all females will endure the 1st stage active period of labour in the hospital's obstetric unit [9,10]. As a result, the manner in which care is provided during this time period may impact the course of the labour and its final results. The causes of prolonged labor's first stage are multifaceted, and cervical dilation is the end result of these variables [11]. For numerous years, experts have recognized the dangers and risks of prolonged labour for both the mother and the fetus. Fetuses are at high risk for infection, including ketosis and obstructed labor, while

mothers suffer from high infection risks, including ketosis and oxygen deprivation [11]. The anti-spastic medication of choice is phloroglucinol. It is often used in obstetrics. It may decrease cervical edema and spasms, as well as lessen cervical muscular tension. As a consequence, it can be utilized to promote labour improvement and cervical dilatation progression. Drotaverine has also been shown to reduce all stages of labor [12]. In one study, the mean duration of the first phase of active delivery in patients receiving phloroglucinol was 227.74 ± 13.34 . No comparable studies have been conducted at the regional level. As a result, the purpose of this study was to compare in primigravidae at term, drotaverine vs phloroglucinol' efficacy in reducing the active period of the first stage of labour

METHODS

With the approval of the ethics committee, this randomized controlled trial was conducted in the Department of Gynecology, Allama Iqbal Memorial Teaching Hospital Sialkot and The Indus hospital QF-NST Campus Lahore for six months, from July to December 2021. In all cases, written informed permission was obtained. All women with obstetric morbidity such as gestational diabetes mellitus, polyhydramnios, pre-eclampsia, Antepartum hemorrhage (APH), medical abnormalities like renal, thyroid and heart diseases, intrauterine device (IUD) and cervical trauma were omitted from the research. All of the cases were divided into two groups: A and B. Group 'A' received phloroglucinol 40mg (4ml) i/v at 4 cm dilation, and the dosage was repetitive at 8 cm dilation. At 4cm dilation, Group 'B' received drotaverine 40mg i/v. The essential signs including uterine contractions, and fetal heart rate have been monitored every half hour. The progression of labour was charted on a partogram. On a pre-designed proforma, the primary result, which was the mean length of the first stage of active labour in both groups, was documented. SPSS version 21.0 was used to analyse the data. For both groups A and B, the mean time length of the active period of the 1st stage of labour was computed, and the *t* test was applied and $p \leq 0.05$ was regarded as significant.

RESULTS

80 patients were included, with 56.3% of cases in Group-A while 43.7% cases in Group-B, patients were in the age range of 20-35. Both groups had the same mean age of 23.85 ± 4.01 and 24.70 ± 3.11 (Table 1.)

Age	Group-A, (Phloroglucinol n=45)	Group-B, (Drotaverine n=35)	p-value
	Number of Patients (%)	Number of Patients (%)	
20-25 years	24(53.3%)	14(40.0%)	0.55
26-30 years	18(40.0%)	17(48.6%)	
31-35 years	03(6.7%)	4(11.4%)	
Total	45(100.0%)	35(100.0%)	
Mean and SD	23.85+4.01	24.70+3.11	

Table 1: The patient's distribution according to Age (n=80)

Between the gestation age 38-40 weeks, 62.2% of females in Group A and 65.7% of women were in Group B were, whereas between the gestation age 41-42 weeks, 37.8% of females in A Group and 34.3% of females were in B Group (Table 2). The first stage of active labour 'mean duration in Groups A and B is 160.21 ± 4.29 minutes and 203.77 ± 8.21 minutes, respectively (table 3).

Gestational age (in weeks)	Group-A, (Phloroglucinol n=45)	Group-B, (Drotaverine n=35)	p-value
	Number of Patients (%)	Number of Patients (%)	
38-40	28(62.2%)	23(65.7%)	0.300
41-42	17(37.8%)	12(34.3%)	
Total	45(100.0%)	35(100.0%)	

Table 2: Females division conferring to gestational age (n=80)

Mean duration	Group-A, (Phloroglucinol n=45)	Group-B, (Drotaverine n=35)	p-value
	Values in SD and mean (mints)	Values in SD and mean (mints)	
	160.21 ± 4.29	203.77 ± 8.21	0.002

Table 3: Mean duration of active phase of 1st stage of labour (n=80)

According to age groups, no significant difference was identified in either group, with p-values of 0.37 and 0.24, respectively. Between 20 and 25 years, patients were divided into three groups: (Table 4).

Age	Group-A, (Phloroglucinol n=45)	Group-B, (Drotaverine n=35)
	Values in SD and mean (mints)	Values in SD and mean (mints)
20-25	159.20 ± 2.98	201.01 ± 3.01
26-30	162.80 ± 2.70	199.14 ± 3.10
31-35	160.12 ± 3.41	202.54 ± 2.99
p-values	0.37	0.24

Table 4: Active Phase of 1st Stage of Labour Mean Duration Conferring to Age (n=80)

DISCUSSION

Prolonged labour is more common in primipara women than in multiparous women. Prolonged labour contributes considerably to maternal and foetal morbidity and death in poor countries such as Pakistan and India [13]. Ruptured uterus and prolonged labour are thought to be responsible for 70 percent of all maternal deaths and 7-15 percent of

foetal deaths [14]. In underdeveloped nations, vesicovaginal fistula, a serious consequence of prolonged labour, develops at a rate of 60-85 per one million live births. Dublin 'Driscoll, who spoke at NMH, introduced the notion of active labour management, which persuaded obstetricians to change their thoughts about the first stage of labour management. The low rate of C-sections and prolonged labour are connected to active treatment of it [15]. The Phloroglucinol chemical family includes semi-synthetic & synthetic moieties, with approximately 700 naturally occurring molecules. It is the most prevalent type of natural product that contains the fundamental component 1,3,5-trihydroxy benzene [16,17]. These chemicals have been demonstrated to have anticancer, antimicrobial, anti-inflammatory, antiallergic, neuro-regenerative, enzyme inhibitor, and anti-oxidant properties. Spasmolytic phloroglucinol (Spasfon). The goal of this study was to do comparability of the duration of the active phase of labour when phloroglucinol was administered intravenously vs drotaverine hydrochloride [18,19]. The 1st stage active phase of labour in A Group lasted 162.54+5.35 minutes and in Group-B lasted 205.64+7.35 mints, with 0.002 p-value indicating a significant variance between the two groups. The findings of the research contrast with those of Tabassum S et al, who found that the active 1st stage of labour lasted only 117.02 minutes in participants taking phloroglucinol [20,21]. Likewise, Ara B et al showed significantly shorter stages of labour length in the phloroglucinol group as 203.069±21 minutes compared to 311.12±10.89 minutes in the group of control, with 0.004 p-value. In the first stage of labour, Naqvi SB and contemporaries examined the effectiveness and safety of Phloroglucinol and drotaverine [22]. The length of the 1st stage of labour was 145.30 ±29.80 minutes in the Phloroglucinol group and 191.25 ±76.89 minutes in the drotaverine group, with a statistically significant difference ($p \leq 0.05$). These conclusions are consistent with the verdicts of this study [23]. Anjum N et al., concluded that Phloroglucinol has a positive effect on reducing the length of the 1st stage of labour, in the medicine group being 182 mins versus 315 mins in the placebo group, and that the cases given phloroglucinol had significantly shorter first and alternate stages of labour [24]. Although Singh et al found that uterine atony caused 18% of post-partum hemorrhage when spasmolytics were employed, they utilized Drotaverine hydrochloride rather than phloroglucinol. The use of Drotaverine in labour is restricted due to its statistically significant frequency [25].

CONCLUSION

Both medicines are effective for accelerating labour, however the mean active phase in the Phloroglucinol group

was much shorter than in the Drotaverine group. Additional local studies are needed to confirm these promising results.

REFERENCES

- [1] Janjua M, Waheed K, Iqbal T, Ejaz S. Efficacy of phloroglucinol in comparison to drotaverine hydrochloride in reducing duration of active phase of 1st stage of labour in primigravidae at term. *Journal of The Society of Obstetricians and Gynaecologists of Pakistan*. 2018 Apr 17;8(1):36-40.
- [2] Sinhasane H, Nishty GM. A comparative study on the efficacy of drotaverine and valethamate on cervical dilatation during labour. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2017 Feb 1;6(2):423-7. doi.10.18203/2320-1770.ijrcog20170017.
- [3] Soni M, Gupta D, Godara S. Drotaverine hydrochloride versus valethamate bromide for cervical dilatation in labour: a comparative study. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2020 May 1;9(5):1986-92. doi.10.18203/2320-1770.ijrcog20201793
- [4] Janjua M, Wajid R, Shaukat S, Sarwar A. Efficacy of Hyoscine Butyl Bromide Versus Drotaverine Hydrochloride Among Primiparous Women, in Term of Mean Duration of Active Phase of First Stage Labor. *Journal of The Society of Obstetricians and Gynaecologists of Pakistan*. 2019 Apr 21;9(1):46-50.
- [5] Khan SM, Khan H, Khan N, Qadir M, Gul H, Jadoon S. Phloroglucinol and drotaverine in accelerating the first stage of labour; a comparative study. *Journal of The Society of Obstetricians and Gynaecologists of Pakistan*. 2019 Dec 11;9(3):121-4.
- [6] Mandal AK, Molla N. Comparison of efficacy of Drotaverine hydrochloride and Valethamate bromide in the augmentation of labour: a hospital based randomized trial. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2018 Apr 1;7(4):157986. doi.10.18203/2320-1770.ijrcog20181359.
- [7] Riemma G, La Verde M, Schiattarella A, Cobellis L, De Franciscis P, Colacurci N, Morlando M. Efficacy of hyoscine butyl-bromide in shortening the active phase of labor: Systematic review and meta-analysis of randomized trials. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2020 Sep 1;252:218-24. doi.10.1016/j.ejogrb.2020.06.042
- [8] Kausar U, Siddiqui N. To compare the efficacy of Drotaverine Hydrochloride with Hyoscine Butyl bromide for increasing the rate of cervical dilatation. *International Journal of Reproduction,*

- Contraception, Obstetrics and Gynecology. 2017 Apr 1;6(4):1615.
- [9] Mukhopadhyay G, Das A. The effect of drotaverine on cervical dilatation—a comparative study with hyoscine in first stage of labour. *Journal of Evolution of Medical and Dental Sciences*. 2018 Jul 23;7(30):3369-73. doi./10.14260/jemds/2018/760
- [10] Withers PJ, van Dijk KC, Neset TS, Nesme T, Oenema O, Rubæk GH, Schoumans OF, Smit B, Pellerin S. Stewardship to tackle global phosphorus inefficiency: The case of Europe. *Ambio*. 2015 Mar;44(2):193-206. doi.o10.1007/s13224-020-01343-3
- [11] Tchente CN, Nana TN, Tolefac PN, Abanda MH, Angong FT, Tamambang RF, Kenfack GU, Mangala GN, Muhammad S, Doualla MS, Belley EP. Effects of phloroglucinol on the active phase of labour (EPAL trial): a single blinded randomised controlled trial in a tertiary hospital in sub-Saharan Africa. *Pan African Medical Journal*. 2018 May 9;30(1).doi.10.11604/pamj.2018.30.17.14728
- [12] Gebiril MM, Farhan AM, Arfat AM. Role of Intravenous Hyoscine Butylbromide Injection on The Duration and Progress of First Stage of Labour in Primigavidae. *Egyptian Journal of Hospital Medicine*. 2017 Oct 6;69(3).doi.10.12816/0041058
- [13] Chavan SK. Determination of rate and analysis of reasons for discarding blood and blood components in a blood bank of tertiary care hospital: a retrospective study. *Int J Res Med Sci*. 2017 Mar;5(3):11115.doi.10.18203/23201770.ijrcog20185291
- [14] Payandeh M, Nahidi F, Nasiri M, Fouladi A. Comparing the effects of transcutaneous electrical nerve stimulation and pharmaceutical hyoscine-promethazine compound on duration of second phase of labor. *The Iranian Journal of Obstetrics, Gynecology and Infertility*. 2019;22(8):19-25. doi.10.34172/mj.2019.042
- [15] Inamdar S, Agarwal H, Toshniwal S, Mishra A, Waigi R. Labour Outcome in “Programmed Labour” and “Expectant Management of Labour”: A Comparative Study. *Int J Cur Res Revl Vol*. 2020 Nov;12(22):27. doi.10.31782/IJCRR.2020.SP98.
- [16] Ejikeme Tb. Effect Of Hyosine Nebutylbromide In The Duration Of Labour In Term Pregnancies In Nnamdi Azikiwe University Teaching Hospital Nnewi South East Nigeria. *Faculty Of Obstetrics And Gynaecology*. 2018.
- [17] Puri S, Sunil I, Jaggi R. Programmed Labour: A Comparative Study. *JK Science*. 2019 Jul 1;21(3):130-3.
- [18] Alhafez L, Berghella V. Evidence-based labor management: first stage of labor (part 3). *American Journal of Obstetrics & Gynecology MFM*. 2020 Nov 1;2(4):100185. doi.10.1016/j.ajogmf.2020.100185
- [19] Kumar D, Kumar A, Malik JK, Semwal P. Process evaluation and in-vitro drug release study of fast dissolving uncoated tablets of Drotaverine HCl. *European Journal of Scientific Exploration*. 2019;2(6):1-8.
- [20] Maddady SM, Mohammad-Alizadeh-Charandabi S, Shafaei FS, Mirghafourvand M. Comparing the effects of hot shower and intravenous injection of hyoscine on the pain intensity and duration of active phase of labour in nulliparous women. *Journal of Clinical and Diagnostic Research*. 2018 Aug 1;12(8):QC07-11. doi.10.7860/JCDR/2018/35508.11950
- [21] Mehmood Y, Mahmood RK, Akram W. Development and validation of UV-spectrophotometric methods for quantitative estimation of Drotaverine HCl injection. *Pharm Methods*. 2017 Jan 1;8(1):169-73.
- [22] Rani P, Kalpana T. Development And Validation Of Analytical Method For Determination Of Drotaverine Hydrochloride And Mefenamic Acid In Bulk And Pharmaceutical Dosage Form By Using Rp-Hplc.
- [23] Kuralla H, Saripilli R, Kolapalli VR. Preparation and evaluation of drotaverine hydrochloride orally disintegrating tablets using melt granulation. *Journal of Applied Pharmaceutical Science*. 2018 Oct 31;8(10):039-46. Doi.10.7324/JAPS.2018.81006
- [24] Harwal NS, Melkundi MS. Assessment of maternal and perinatal outcome in pregnancy beyond 40 weeks of gestation. *Journal of Evolution of Medical and Dental Sciences*. 2017 Mar 6;6(19):1546-52. doi.10.14260/Jemds/2017/339
- [25] Payandeh M, Nahidi F, Nasiri M, Fouladi A. Comparing the effects of transcutaneous electrical nerve stimulation and pharmaceutical hyoscine-promethazine compound on duration of the first phase of labor. *Medical Journal of Tabriz University of Medical Sciences*. 2019 Sep 7;41(4):25-30. doi.10.34172/mj.2019.042



Original Article

The Effects of Conventional Physical Therapy with and Without Dry Needling on Pain, Range of Motions and Functional Disability in Patients with Shoulder Impingement Syndrome

Aqsa Maqsood¹, Muhammad Asim Arif¹, Hafiz Syed Ijaz Ahmed Burq², Rabia Jawa³, Muhammad Rizwan¹, Tooba Amin⁴

¹University Institute of Physical Therapy, The University of Lahore, Lahore, Pakistan

²Department of Physiotherapy, Lahore General Hospital, Lahore, Pakistan

³Physical Therapy Department, University of Management and Technology, Lahore, Pakistan

⁴Physical Therapy Department, Fatima Memorial Hospital, Lahore, Pakistan

ARTICLE INFO

Key Words:

Dry Needling, Physical Therapy, Shoulder Impingement, Shoulder Pain, Range of Motion

How to Cite:

Maqsood, A. ., Asim Arif, M. ., Ijaz Ahmed Burq, H. S. ., Jawa, R. ., Rizwan, M. ., & Amin, T. . (2022). The Effects of Conventional Physical Therapy with and Without Dry Needling on Pain, Range of Motions and Functional Disability in Patients with Shoulder Impingement Syndrome. *Pakistan BioMedical Journal*, 5(6).

<https://doi.org/10.54393/pbmj.v5i6.533>

***Corresponding Author:**

Aqsa Maqsood
University Institute of Physical Therapy, The University of Lahore, Lahore, Pakistan
aqsach46@gmail.com

Received Date: 8th June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Dry needling is a technique in which thin monofilament-based needles are inserted into soft tissues, especially trigger points in muscles. It is being used in a range of neuromuscular pain syndromes such as shoulder impingement syndrome in current study. In physical therapy, it is narrowly referred to as an intramuscular procedure for the treatment of myofascial trigger points (MTrPs). **Objective:** To compare the conventional physical therapy with and without dry needling on pain, range of motion, and functional disability in patients with shoulder impingement syndrome. **Methods:** It was randomized controlled trial conducted in 66 patients of shoulder impingement syndrome based on inclusion criteria and divided randomly allocated equally in two groups of 33 in each of conventional therapy and dry needling group. The outcome measures used were numeric pain rating scale for pain, DASH for hand arm function and shoulder ranges of motion. The SPSS 25.0 was used to analyse data. The descriptive statistics was applied, and inferential statistics was applied based on findings of tests of normality. **Results:** The results showed that the post interventional pain score was 1.43 ± 1.37 , 32.11 for conventional group and for experimental group that of 1.60 ± 1.02 , 34.89 with non-significant difference 0.544 , while DASH score was 27.02 ± 13.22 , 38.85 for conventional group and for experimental group that of 19.92 ± 11.20 , 28.15 with significant difference 0.024 . The results for flexion, abduction, internal and external rotation were non-significant with p value > 0.05 . **Conclusion:** It was concluded that although there was significant improvement in pain, range of motion and function in both of dry needling and conventional groups, however, pain and shoulder ranges improved equally in both groups without a statistically significant difference while that of disability improved significantly in dry needling group.

INTRODUCTION

Sub acromial pain syndrome refers to any shoulder problem that is not caused by an injury and causes pain around the acromion [1]. The pain typically intensifies during or after lifting the arm. It includes any kind of discomfort caused by damage to a structure or structures in the sub acromial space. SAPS is the most common shoulder condition [2,3]. SAPS accounts for 44 to 65 percent of all shoulder pain complaints, and its prevalence rises with age. The majority of cases occur within one's sixth decade of life. The majority of individuals affected are beyond the age of 40

and suffer from chronic pain that cannot be ascribed to an injury. Patients complain of pain while elevating the affected arm between 70 and 120 degrees, executing a "Painful Arc" over their heads, or sleeping on the affected side [4]. The symptoms may arise suddenly or gradually. Rather than a forceful outside force, most "impingement" is caused by a slow-growing sickness. Because of this, it may be hard for patients to figure out when their symptoms started. The patient's age, degree of exercise, and general health all influence the therapy. The goal is to relieve pain

and restore functioning. For up to a year, or until the patient heals and can return to work, conservative therapy should be the preferred choice. If the patient does not respond to non-surgical treatment, surgery may be the next step [5,6]. Conservative treatment includes resting the shoulder as much as possible; limiting activities that aggravate the pain, especially overhead activities, taking non-steroidal anti-inflammatory drugs to improve pain and swelling; managing the shoulder with physical therapy, and receiving a sub acromial injection. Cortisone is often used to reduce inflammation and pain, but it is controversial and should be avoided for tendon pain [7]. There is no conclusive evidence that surgical therapy is preferable to non-surgical treatments. If non-surgical treatment fails to relieve pain or restore function, surgery should be considered [8]. Depending on the kind and severity of the damage, many types of surgery may be done, but there is no clear favourite at this time [9]. Recent systematic reviews on this subject have emphasized the need of additional high-quality research, particularly studies that cover a range of modalities to reflect actual practice [10-12]. In this randomized controlled trial, the effects of standard physical therapy with and without dry needling on pain, range of motion, and functional impairment in people with shoulder impingement syndrome were studied. Parvaneh Jalilpanah et al., conducted to compare the effects of muscle energy and dry needling among shoulder impingement syndrome patients with activated trigger points in infra-spinatus. Both interventions found to be effective in improving range and pain, however, dry needling technique was superior in its success to improve function and ranges [13].

METHODS

It was a randomized clinical trial conducted at Physical Therapy department of University of Lahore Teaching Hospital. Non-probability purposive sampling was used. Patients having unilateral non traumatic shoulder pain for at least 3 months, age ranges from 30 to 65 years and pain intensity of 4 points or more on an 11-point numeric pain rating scale were included while patients with the history of shoulder dislocation or fractures, radiculopathy, fibromyalgia Syndrome, medical history of steroid injections in shoulder region or any past cervical or shoulder surgery were excluded. Patients were screened to meet inclusion criteria. Consent form was taken from patients than 33 Patients were randomly allocated in each group. The study was a single blinded Randomized Controlled Clinical Trial. Pain, function and range of motion were assessed at the baseline, after 1st week and 4th weeks of treatment. Range of motion of the shoulder was

assessed using a goniometer. Patients were assigned in two groups, control group was given conventional therapy and Group 2 was given dry needling with conventional treatment. The coin toss method of randomization was used to randomly allocate patients with 'Heads' going to dry needling group and 'Tails' going to control group. Dry needling was given once per week in the four weeks of treatment. NPRS for pain, DASH Scale for function and goniometer for range of motion were used. Data were analysed using SPSS 25.0. The categorical variables of Gender and 'affected side' were analysed as frequency tables. Based on tests of normality which showed it to be normative, independent samples T test was used to compare both groups at pre-interventional, post-interventional 1st and 4th week. p-value ≤ 0.05 was considered as significant.

RESULTS

The results regarding gender of the patients for frequency of the interventional group such as conventional group female 51.5% and male 48.5% and for the experimental group female 33.3% and male 66.7% were found whereas the frequency of the affected side of the limb for the conventional group right side 54.5% and left side 45.5% and for the experimental group right side 30.3% and left side 69.7% were found, Table 1.

	Intervention Group		Frequency	Percentage
Gender	Conventional	Female	17	51.5
		Male	16	48.5
	Experimental	Female	11	33.3
		Male	22	66.7
Affected side	Conventional	Right Side	18	54.5
		Left Side	15	45.5
	Experimental	Right Side	10	30.3
		Left Side	23	69.7

Table 1: Gender and Affected Side of the Patients

The results regarding the summary table of outcome measures such as NRPS at baseline for conventional group mean $6.59 \pm SD 1.5$, for the experimental group mean $6.98 \pm SD 1.3$ with p-value 0.327, at 1st week for conventional group mean $3.95 \pm SD 1.3$ and experimental group mean $3.85 \pm SD 1.1$ with p-value 0.739 and at 4th week for conventional group mean $1.44 \pm SD 1.1$ and for experimental group mean $1.61 \pm SD 1.1$ with p-value 0.544 were found whereas DASH score at baseline showed non-significant p value 0.653 and at 1st and 4th week of intervention it showed significant p values 0.023 and 0.024 respectively. Overall ROM for flexion, internal and external rotation at baseline, 1st and 4th week of intervention showed non-significant p values > 0.05 , Table 2.

	Intervention Group	Mean±SD	P-value
NPRS Baseline	Conventional	6.59±1.5	0.327
	Experimental	6.98±1.3	
NPRS 1st week	Conventional	3.95±1.3	0.739
	Experimental	3.85±1.1	
NPRS 4th week	Conventional	1.44±1.1	0.544
	Experimental	1.61±1.1	
DASH Baseline	Conventional	69.39±14.1	0.653
	Experimental	71.92±12.1	
DASH 1st week	Conventional	57.81±15.8	0.023
	Experimental	48.73±15.8	
DASH 4th week	Conventional	27.02±13.1	0.024
	Experimental	19.93±11.2	
ROM Baseline Flexion	Conventional	119.39±22.9	0.534
	Experimental	113.73±16.9	
ROM 1st week flexion	Conventional	144.24±18.5	0.001
	Experimental	121.54±20.3	
ROM 4th week flexion	Conventional	170.27±8.1	0.548
	Experimental	171.72±5.7	
ROM Baseline Internal Rotation	Conventional	44.64±16.3	0.555
	Experimental	42.76±19.2	
ROM 1st week Internal Rotation	Conventional	59.97±10.9	0.918
	Experimental	59.45±15.3	
ROM 4th week Internal Rotation	Conventional	72.39±8.9	0.585
	Experimental	73.36±10.4	
ROM Baseline External Rotation	Conventional	55.15±24.3	0.555
	Experimental	57.27±16.3	
ROM 1st week External Rotation	Conventional	68.18±11.8	0.123
	Experimental	72.51±12.8	
ROM 4th week External Rotation	Conventional	79.79±9.1	0.283
	Experimental	81.79±8.2	

Table 2: Summary of the Outcome Measures

DISCUSSION

Conservative treatment is the best option for patients with SIS. However, the most effective treatment method, known as the "Gold standard," hasn't been studied yet. A lot of different things, like injections and medication, as well as physical exercise and even cognitive therapy, are recommended by professionals because they have different levels of evidence. When the Visual Analogical Scale was used to measure pain, seven out of the eight trials showed a significant decrease in pain (VAS). Despite this, the addition of DN did not have any statistically significant effects on the level of pain at any time during the follow-up. It was also used in the study by Imani et al [14]. The numerical Pain Rating Scale (NPRS), which is the same as the VAS, was also used. At the end of the study, Gattie et al [15]. looked at data on night pain, pain at rest, and pain during activity. They found that the EG had unique effects across groups, with a big difference in night pain when compared to the other groups. The results of tests that used range of motion (as measured by goniometry) were very different. Halle et al [16]. found that the conventional

group did better at shoulder flexion than the group that did the experiment (conventional physiotherapy). People who had DN as part of their treatment had a lot more shoulder abduction [17]. They looked at how these two movements affected the shoulder joint. In six of the studies, the DASH questionnaire [18]. was used to measure how well people were doing as a result of the treatment they were getting. It was found statistically significant differences between the CG and EG at all the time points (immediately, 3–6 months, and 12 months after the intervention) [19]. To examine the effect of dry needling to the infraspinatus muscle function, pain sensitivity and shoulder range of motion in symptomatic and asymptomatic patients with unilateral sub-acromial shoulder pain and concluded that dry needling showed its beneficial effects on reducing pain and increasing range of motion in shoulder joint after 3–4 days of session in especially symptomatic patients with shoulder pain [20,21].

CONCLUSION

It was concluded that there were inconsistent findings regarding effect of dry needling in addition to conventional physical therapy. There was significant improvement in disability of arm and shoulder, however, there was no significant difference in level of pain and shoulder ranges of motion.

REFERENCES

- [1] de Witte PB, Nagels J, van Arkel ER, Visser CP, Nelissen RG, de Groot JH. Study protocol subacromial impingement syndrome: the identification of pathophysiologic mechanisms (SISTIM). *BMC musculoskeletal disorders*. 2011 Dec 14; 12:282. doi: 10.1186/1471-2474-12-282.
- [2] Lewis JS, Sandford FM. Rotator cuff tendinopathy: is there a role for polyunsaturated Fatty acids and antioxidants? *Journal of Hand Therapy*. 2009 Jan-Mar; 22(1):49-55; quiz 56. doi: 10.1197/j.jht.2008.06.007.
- [3] Charalambous CP, Eastwood S. Anterior Acromioplasty for the Chronic Impingement Syndrome in the Shoulder: A Preliminary Report. *Classic Papers in Orthopaedics*: Springer; 2014: 301-3.
- [4] Kachingwe AF, Phillips B, Sletten E, Plunkett SW. Comparison of manual therapy techniques with therapeutic exercise in the treatment of shoulder impingement: a randomized controlled pilot clinical trial. *Journal of manual & manipulative therapy*. 2008;16(4):238-47. doi: 10.1179/106698108790818314.
- [5] Kul A, Ugur M. Comparison of the Efficacy of

- Conventional Physical Therapy Modalities and Kinesio Taping Treatments in Shoulder Impingement Syndrome. *The Eurasian journal of medicine*. 2019 Jun; 51(2):139-144. doi: 10.5152/eurasianjmed.2018.17421.
- [6] Innocenti T, Ristori D, Miele S, Testa M. The management of shoulder impingement and related disorders: A systematic review on diagnostic accuracy of physical tests and manual therapy efficacy. *Journal of Bodywork and Movement Therapies*. 2019 Jul; 23(3):604-618. doi: 10.1016/j.jbmt.2018.08.002.
- [7] Min KS, St Pierre P, Ryan PM, Marchant BG, Wilson CJ, Arrington ED. A double-blind randomized controlled trial comparing the effects of subacromial injection with corticosteroid versus NSAID in patients with shoulder impingement syndrome. *Journal of Shoulder and Elbow Surgery*. 2013 May; 22(5):595-601. doi: 10.1016/j.jse.2012.08.026.
- [8] Rosa DP, Borstad JD, Ferreira JK, Gava V, Santos RV, Camargo PR. Comparison of specific and non-specific treatment approaches for individuals with posterior capsule tightness and shoulder impingement symptoms: A randomized controlled trial. *Brazilian Journal of Physical Therapy*. 2021 Sep-Oct; 25(5):648-658. doi: 10.1016/j.bjpt.2021.04.003.
- [9] Creech JA, Silver S. Shoulder impingement syndrome. *StatPearls [Internet]: StatPearls Publishing*; 2021.
- [10] Green S, Buchbinder R, Hetrick SE. Physiotherapy interventions for shoulder pain. *Cochrane database of systematic reviews*. 2003(2). doi.org/10.1002/14651858.CD004258
- [11] Kelly SM, Wrightson PA, Meads CA. Clinical outcomes of exercise in the management of subacromial impingement syndrome: a systematic review. *Clinical rehabilitation*. 2010 Feb; 24(2):99-109. doi: 10.1177/0269215509342336.
- [12] Kromer TO, Tautenhahn UG, de Bie RA, Staal JB, Bastiaenen CH. Effects of physiotherapy in patients with shoulder impingement syndrome: a systematic review of the literature. *Journal of Rehabilitation Medicine*. 2009 Nov; 41(11):870-80. doi: 10.2340/16501977-0453.
- [13] Jalilpanah P, Okhovatian F, Serri RA, Bagban AA, Zamani S. The effect of dry needling & muscle energy technique separately and in combination in patients suffering shoulder impingement syndrome and active trigger points of infraspinatus. *Journal of Bodywork and Movement Therapies*. 2021 Apr; 26:94-100. doi: 10.1016/j.jbmt.2020.12.030.
- [14] Imani M, Abbasi L, Taghizadeh S, Amiri M. Comparison of the effect of two different types of dry-needling techniques on subacromial impingement syndrome. *Journal of Bodywork and Movement Therapies*. 2021 Jan; 25:35-40. doi: 10.1016/j.jbmt.2020.10.018.
- [15] Gattie E, Cleland JA, Snodgrass S. The Effectiveness of Trigger Point Dry Needling for Musculoskeletal Conditions by Physical Therapists: A Systematic Review and Meta-analysis. *Journal of orthopaedic & sports physical therapy*. 2017 Mar; 47(3):133-149. doi: 10.2519/jospt.2017.7096.
- [16] Halle R, Crowell MS, Goss DL. Dry Needling And Physical Therapy Versus Physical Therapy Alone Following Shoulder Stabilization Repair: A Randomized Clinical Trial. *International journal of sports physical therapy*. 2020;15(1):81-102.
- [17] Lake AD, Myers H, Aefsky B, Butler R. immediate and short term effect of dry needling on triceps surae range of motion and functional movement: A randomized trial. *International Journal of Sports Physical Therapy*. 2018 Apr; 13(2):185.
- [18] Diercks R, Bron C, Dorrestijn O, Meskers C, Naber R, de Ruitter T, et al. Dutch Orthopaedic Association. Guideline for diagnosis and treatment of subacromial pain syndrome: a multidisciplinary review by the Dutch Orthopaedic Association. *Acta orthopaedica*. 2014 Jun; 85(3):314-22. doi: 10.3109/17453674.2014.920991.
- [19] Cha JY, Kim JH, Hong J, Choi YT, Kim MH, Cho JH, et al. A 12-week rehabilitation program improves body composition, pain sensation, and internal/external torques of baseball pitchers with shoulder impingement symptom. *Journal of exercise rehabilitation*. 2014 Feb; 10(1):35-44. doi: 10.12965/jer.140087.
- [20] Koppenhaver S, Embry R, Ciccarello J, Waltrip J, Pike R, Walker M, et al. Effects of dry needling to the symptomatic versus control shoulder in patients with unilateral subacromial pain syndrome. *Manual therapy*. 2016 Dec; 26:62-69. doi: 10.1016/j.math.2016.07.009.
- [21] Jalilpanah P, Okhovatian F, Serri RA, Bagban AA, Zamani S. The effect of dry needling & muscle energy technique separately and in combination in patients suffering shoulder impingement syndrome and active trigger points of infraspinatus. *Journal of Bodywork and Movement Therapies*. 2021 Apr; 26:94-100. doi: 10.1016/j.jbmt.2020.12.030.



Original Article

C-Reactive Protein levels in Acute Stroke: Ischemic vs Hemorrhagic in a Tertiary Care Hospital

Nighat Jamal¹, Iqra Jadoon¹, Ameer Hamza¹, Syed Affan Ali¹, Abdur Rauf¹, Hassan Mumtaz, Syed Muhammad Ismail³¹Ayub Medical College Abbottabad²Health Services Academy³Dow University of Medical Sciences

ARTICLE INFO

Key Words:

Epilepsy, Arrhythmias, EEG, Inter-ictal epileptic discharge, Focal epilepsy

How to Cite:

Jamal, N. ., Jadoon, I. ., Hamza, A. ., Affan Ali, S. ., Rauf, A. ., Mumtaz, H. ., & Muhammad Ismail, S. (2022). C-Reactive Protein levels in Acute Stroke: Ischemic vs Hemorrhagic in a Tertiary Care Hospital. Pakistan BioMedical Journal, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.513>

*Corresponding Author:

Abdur Rauf
 Associate Professor of Medicine: Ayub Medical College Abbottabad
abdulraufa646@gmail.com

Received Date: 16th June, 2022

Acceptance Date: 22nd June, 2022

Published Date: 30th June, 2022

ABSTRACT

There is growing evidence of the prognostic importance of C-reactive protein (CRP) in ischemic stroke. However, the independent value of CRP in ischemic vs hemorrhagic stroke has not been established. **Objective:** To assess the diagnostic value of CRP as biomarker in ischemic stroke in comparison to hemorrhagic stroke **Methods:** This prospective study was conducted from March 2020 to March 2022 in the Department of Medicine, Ayub Medical College. Sample size of 71 was calculated including patients of both genders having age 22-105 years admitted with first-ever acute stroke within the first 24 hours of onset. Data was analyzed using SPSS latest version. Quantitative variables are shown as frequency and percentages. Paired T Test was applied to see the association of CRP levels with effect on CT- Scan of Brain. *p value* less than 0.05 was considered significant **Results:** 69% of the participants were women, far outnumbering the men. 45 patients found to have ischemic stroke (63.38%) whereas 26 (36.62%) reported having Hemorrhagic stroke. *Paired t test* applied to see the association of CRP Levels with CT Scan Brain was found significant having *p value 0.002* **Conclusions:** CRP levels are important in the diagnosis of stroke based on data. CRP levels must be compared to those of other stroke biomarkers in order to make this determination. The serum CRP level within 24 hours can be used to predict severity in ischemic but not hemorrhagic stroke.

INTRODUCTION

C-Reactive Protein (CRP) levels may rise after an acute ischemic stroke because of an inflammatory response. CRP levels that are too high may indicate an inflammatory reaction or tissue damage, both of which can lead to a poor outcome [1]. An intracerebral hemorrhage-induced brain injury is thought to be the result of mechanical damage followed by ischemic, cytotoxic, and inflammatory changes in the tissue beneath and around it. Inflammatory biomarkers and growth factors secreted during intracerebral hemorrhage have piqued researchers' interest in recent years [2]. Blood CRP levels rise during the

acute phase of ischemic stroke as a result of ischemic brain damage. In patients with acute ischemic stroke, plasma CRP levels are elevated because of the underlying vascular lesions and the inflammation caused by brain infarction. CRP administration in an adult rat model of middle cerebral artery occlusion led to significantly larger infarcts than control subjects. In addition, a specific small-molecule inhibitor of CRP was administered to rats undergoing acute myocardial infarction to prevent the increase in infarct size and cardiac dysfunction induced by injection of human CRP [3]. After adjusting for confounding

variables, some studies found that CRP was associated with post-stroke functional outcomes, while others found that the association disappeared. As a result, the relationship between CRP levels in the blood and clinical outcomes in patients with acute ischemic stroke remains inconclusive [4]. Haemorrhagic Stroke has a worse prognosis in terms of long-term disability and mortality. Many studies have been done to find suitable markers for stroke diagnosis, but none of them are universally accepted. A population-specific biomarker for stroke could be identified based on these findings[5]. Our aim was to assess the diagnostic value of CRP as biomarker in ischemic stroke in comparison to hemorrhagic stroke.

METHODS

This prospective study was conducted from March 2020 to March 2022 in the Department of Medicine, Ayub Medical College. Sample size of 71 was calculated using WHO calculator keeping confidence interval 95% & margin of error 5%. Non-probability consecutive sampling technique was used. Patients of both genders having age 22-105 years admitted with first-ever acute stroke within the first 24 hours of onset were included in our study. Patients admitted more than 24 hours after symptoms onset were excluded from our study. Patients with recent history of traumatic brain injury, unstable angina, Aspiration pneumonia, autoimmune disease, liver failure, acute or chronic renal and diabetic foot were also excluded from study. The study protocol was approved by the institutional review board at Ayub Teaching Hospital Abbottabad and written informed consent to participate and publish data were obtained from all participating patients or first degree relatives. A CT scan plain of brain was done on admission differentiate between ischemic and hemorrhagic stroke. Three ml of venous blood was taken through a venipuncture and sent to the laboratory. The CRP assay was done using solid phase enzyme-linked immunosorbent assay. Normal reference of CRP was less than 5 mg/L. Data was analyzed using SPSS latest version. Quantitative variables are shown as frequency and percentages. Paired t test was applied to see the association of CRP levels with effect on CT- Scan of Brain. p value less than 0.05 was considered significant

RESULTS

A total of 71 individuals were in harmony with the inclusion criteria. The demographics section included the names, age, gender and medical record number. Names were just taken for the marking of data; it neither adds nor decreases the weight of this research. The ages ranged from 22-105 years, but the mean age was 62 years. More than were females (69%) overshadowing males. The medical record

number was taken to ease the process of data keeping a track and follow up the patients and doesn't have any other significance, as shown in Table 1.

Gender	Frequency
Male	22 (31.0)
Female	49 (69.0)
Age	
22-50	20 (28.17)
51-105	51 (71.83)

Table 1: Patient Demographics

Upon arrival in an emergency, the customary vitals blood pressure and blood sugar levels were taken and noted. A major portion of $\frac{2}{3}$ lied in the category of less than 140/90 mmHg (40.8%), meanwhile, the mean systolic pressure was found to be around 150 and diastolic was 98 mmHg approximately. Tests for random blood glucose highlighted that half of the numbers had normal levels of glucose i.e. <160mg/dl. In addition, more than of the study population were known diabetics, as shown in Table 2.

Characteristics	Frequency (%)
Blood Pressure on Arrival	
Less than 140/90mmHg	29 (40.8)
140/90 to 159/99	14 (19.7)
160/100 to 179/109	12 (16.9)
Equal to or more than 180/110	16 (22.5)
Blood Glucose Levels	
Less than 200 mg/dl	Less than 200 mg/dl
More than 200 mg/dl	More than 200 mg/dl

Table 2: Frequency of Blood Pressure & Glucose Levels

The CT scan conducted on patients revealed that almost suffered from hemorrhagic stroke and the rest endured ischemic stroke. Furthermore, the basis and defining factor of this research is the CRP levels, CRP levels were measured within 24 hours of admission, results depicted a balance distribution, almost half of the patients had CRP levels less than 5mg/dl and the other half had levels more than 5mg/dl. Paired t test was applied to see the association of CRP Levels with CT Scan Brain and was found significant having p value 0.002, as shown in Table 3. A total of 45 patients were found to have ischemic stroke (63.38%) whereas 26 (36.62%) reported having Hemorrhagic stroke, shown in Figure 1.

C-Reactive protein levels	CT scan (brain)	Hemorrhagic Ischemic	Total	P-value
Less than 5 mg/d	20	18	38	0.002
More than 5 mg/dl	6	27	33	

Table 3: C-Reactive protein levels & CT scan(brain)Association

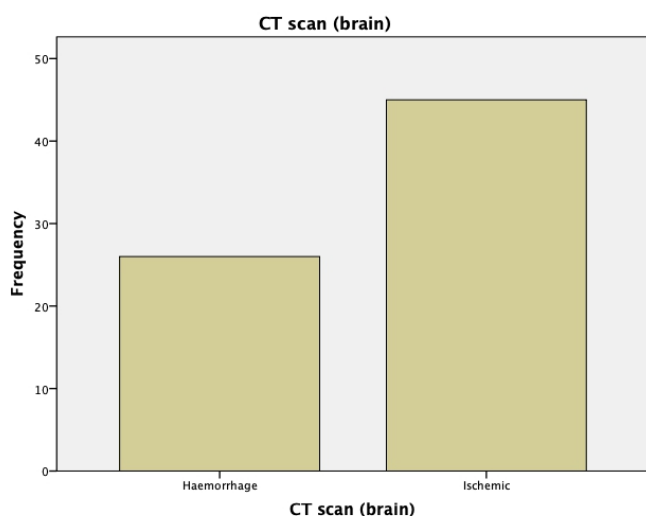


Figure 1: Frequency of Ischemic & Hemorrhagic Stroke

DISCUSSION

As prevalence of stroke in South Asia countries is high, it is important to determine the easy diagnostic tools. Based on blockage or rupture strokes are categorized as being hemorrhagic or ischemic. This research is designed to signify and emphasize on the decisive and diagnostic distinction of CRP levels in patients with a stroke. Multiple associations were made to endorse the findings, patients with age 50 or above were at higher risk of getting a stroke, study by Mehta et al., strengthened by providing strongly abiding evidence with a $p=0.001$ [6]. Similar evidence was extracted in case of age and blood pressure that with an increasing age blood pressure abnormalities were more eminent. The fact that the older patients suffered more from strokes may be because there were more known diabetics in the same age groups. Debrah et Al highlighted the age-related association of type 2 diabetes mellitus [7]. On the other hand, Nicolas et al., reported the correlation among elderly age and the development of hypertension [8]. Gender based approach was taken and percentages were compared to signify and eliminate the bias of females being greater in numbers. Gender differences were not remarkable in terms of ischemic or hemorrhagic stroke, this depicts no gender predisposition. Though more females were found to be hypertensive on arrival than males but it may be physiological. This was an ambiguous finding as usually males are prone to hypertension, females tend to show high blood pressure symptoms after menu pause [9]. Coming onto the core or bedrock of our study chi-square test revealed significant results, patients with hemorrhagic stroke had a value of $<5\text{mg/dl}$ and with ischemic stroke had a value of $>5\text{mg/dl}$ with a p value of 0.300 and Fisher test showing a value of 0.005. Napoli et al., braced and aided the discoveries of our study, moreover, a

meta-analysis by Zhou et al., affirmed that the higher CRP levels were found in patients with ischemic heart stroke [10,11]. Contrary to this, Erdal et al., portrayed a different dimension in which hemorrhagic group of both males and females showed higher CRP levels, with values of ≥ 0.74 mg/dL [12]. Kristine et al., researched the usefulness of CRP levels in diagnosis and prognosis of cancer patients and the higher CRP values are found to be related to poor prognosis. Studies identified the association of CRP levels with smoking and intake of anti-inflammatory compounds like coffee etc., [13,14]. Neither Blood pressure on admission had an impact on CRP values nor the diabetes was able to grasp the attention. In Texas, a secondary study found that patients admitted to inpatient rehabilitation centres and skilled nursing facilities for post-acute rehabilitation had distinct demographic and clinical characteristics. When it comes to patient and facility characteristics, a closer assessment of ischemic and hemorrhagic stroke discharges implies a need for more comprehensive comparisons of inpatient rehabilitation centres vs skilled nursing facilities [15]. According to systematic review published in 2021, persons with AIS treated with IVT who had elevated levels of plasma CRP had a bad 3-month prognosis. Risk categorization of AIS patients as candidates for IVT or other alternative therapies, such as mechanical thrombectomy, may be aided by CRP levels [16]. HsCRP levels were found to be high in both ischemic and hemorrhagic strokes, suggesting an inflammatory response in acute stroke. The greater the hsCRP levels, the worse the prognosis and neurological damage, according to a study conducted in 2022 India [17]. High CRP levels were found to be independently related with poor clinical outcomes and greater in-hospital mortality in patients with ICH, according to research from the Chinese Stroke Center Alliance (CSCA) [18]. Whereas a prospective population-based study in Sweden shows CRP has been found to be a major risk factor for first-time ischemic stroke, particularly in patients with small-vessel disease. A polymorphism in CRP 1444C>T did not have a significant connection with any type of stroke [19]. Serum CRP levels, according to researchers at the University of Ulsan College of Medicine, have little discernible utility in diagnosing acute stroke in patients with dizziness but no obvious neurological abnormalities [20]. Factors such as obesity or cholesterol levels, genetic makeup, ethnicity and socioeconomic conditions were not accounted. Relying on the available literature and knowledge CRP levels may be to be a breakthrough and effective method serving in diagnostic and prognostic domains.

CONCLUSION

The role of CRP in the early diagnosis of type of stroke in ER

is crucial in this context and will be helpful in setting where facilities of early CT scan or MRI brain is not available. Moreover, our research will lay the foundation for future research projects in our area and future studies are warranted to find if CRP can serve as a prognostic factor in stroke or not.

REFERENCES

- [1] den Hertog HM, van Rossum JA, van der Worp HB, et al. C-reactive protein in the very early phase of acute ischemic stroke: association with poor outcome and death. *J Neurol*. 2009 Dec;256(12):2003-8. doi: 10.1007/s00415-009-5228-x.
- [2] Bernstein J E, Savla P, Dong F, et al. (October 31, 2018) Inflammatory Markers and Severity of Intracerebral Hemorrhage. *Cureus* 10(10): e3529. doi:10.7759/cureus.3529
- [3] Matsuo R, Ago T, Hata J, Wakisaka Y, Kuroda J, Kuwashiro T, et al. Plasma C-Reactive Protein and Clinical Outcomes after Acute Ischemic Stroke: A Prospective Observational Study. *PLoS ONE*, 2016,11(6): e0156790. <https://doi.org/10.1371/journal.pone.0156790>
- [4] Cucchiara BL, Messe SR, Sansing L, MacKenzie L, Taylor RA, Pacelli J, et al. Lipoprotein-associated phospholipase A2 and C-reactive protein for risk-stratification of patients with TIA. *Stroke*. 2009; 40: 2332-2336.
- [5] Fang C, Lou B, Zhou J, et al. Blood biomarkers in ischemic stroke: Role of biomarkers in differentiation of clinical phenotype. *European Journal of Inflammation*. January 2018. doi: [10.1177/2058739218780058](https://doi.org/10.1177/2058739218780058)
- [6] Mehta RH, Rathore SS, Radford MJ, Wang Y, Wang Y, Krumholz HM. Acute myocardial infarction in the elderly: differences by age. *Journal of the American College of Cardiology*. 2001 Sep;38(3):736-41.
- [7] Asiimwe D, Mauti GO, Kiconco R. Prevalence and risk factors associated with type 2 diabetes in elderly patients aged 45-80 years at Kanungu District. *Journal of diabetes research*. 2020 Oct;2020.
- [8] R Robles N, F Macias J. Hypertension in the elderly. *Cardiovascular & Hematological Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Cardiovascular & Hematological Agents)*. 2014 Dec 1;12(3):136-45.
- [9] Reckelhoff JF. Gender differences in the regulation of blood pressure. *Hypertension*. 2001 May;37(5): 1199-208.
- [10] Di Napoli M, Slevin M, Popa-Wagner A, Singh P, Lattanzi S, Divani AA. Monomeric C-reactive protein and cerebral hemorrhage: from bench to bedside. *Frontiers in immunology*. 2018:1921.
- [11] Zhou Y, Han W, Gong D, Man C, Fan Y. Hs-CRP in stroke: a meta-analysis. *Clinica chimica acta*. 2016 Jan 30;453:21-7.
- [12] Erdal GS, Hursitoglu M, Erdogan HA, Yildirim G, Yayla V, Issever H, Isiksacan N, Kural A, Cirak M, Kansu AD, Karandere F. Serum C-Reactive Protein and Sex Hormone Levels in the Early Hyperacute Phase of Stroke. *Clinical Laboratory*. 2021 Feb 1;67(2).
- [13] Allin KH, Nordestgaard BG. Elevated C-reactive protein in the diagnosis, prognosis, and cause of cancer. *Critical reviews in clinical laboratory sciences*. 2011 Aug 1;48(4):155-70.
- [14] Moua ED, Hu C, Day N, Hord NG, Takata Y. Coffee consumption and c-reactive protein levels: A systematic review and meta-analysis. *Nutrients*. 2020 May;12(5):1349.
- [15] Hong I, Karmarkar A, Chan W, et al. Discharge Patterns for Ischemic and Hemorrhagic Stroke Patients Going From Acute Care Hospitals to Inpatient and Skilled Nursing Rehabilitation. *Am J Phys Med Rehabil*. 2018 Sep;97(9):636-645.
- [16] Jiang J, Tan C, Zhou W, et al. Plasma C-Reactive Protein Level and Outcome of Acute Ischemic Stroke Patients Treated by Intravenous Thrombolysis: A Systematic Review and Meta-Analysis. *Eur Neurol*. 2021;84(3):145-150. doi: 10.1159/000514099.
- [17] Pinniboyana VK, Pinniboyana SH, Gridhati S. A study of C-reactive protein in cerebrovascular accident (stroke) in a tertiary care hospital. *European Journal of Molecular & Clinical Medicine*. 2022, 9(1).
- [18] Wang D, Wang J, Li Z, Gu H, Yang K, Zhao X, Wang Y. C-Reaction Protein and the Severity of Intracerebral Hemorrhage: A Study from Chinese Stroke Center Alliance. *Neurol Res*. 2022 Apr;44(4):285-290. doi: 10.1080/01616412.2021.1980842.
- [19] Andersson J, Johansson L, Ladenvall P, Wiklund PG, Stegmayr B, Jern C, Boman K. C-reactive protein is a determinant of first-ever stroke: prospective nested case-referent study. *Cerebrovasc Dis*. 2009;27(6): 544-51. doi: 10.1159/000214217.
- [20] Hong SI, Kim JS, Bae HJ, Kim WY. C-reactive Protein for Stroke Detection in the Emergency Department in Patients With Dizziness Without Neurological Deficits. *Front Neurol*. 2021 May 31;12:662510. doi: 10.3389/fneur.2021.662510



Original Article

Assessment of Frequency of EEG Findings In Children With Epilepsy

 Faiqa Hassan¹, Shazia Ali², Misbah munir³, Ali Masood⁴, Munazza Suharwardy Obaid⁴, Ramsha Urooj Baig⁵ & Faiza Zakaria⁵
¹Memon Medical Institute Hospital, Karachi, Pakistan²Shaheed Nawab Ghos Bakhsh Raisani Memorial Hospital, Mastung, Pakistan³Mekran Medical College, Balochistan, Pakistan⁴DOW Hospital, Karachi, Pakistan⁵DOW University of Health Sciences, Karachi, Pakistan

ARTICLE INFO

Key Words:

Epilepsy, Arrhythmias, EEG, Inter-ictal epileptic discharge, Focal epilepsy

How to Cite:

 Hassan, F. ., Ali , S. ., Munir, M. ., Masood, A. ., Suharwardy Obaid, M. ., Urooj Baig, R. ., & Zakaria, F. . (2022). Assessment Of Frequency of EEG Findings in Children with Epilepsy in A Tertiary Care Hospital in Karachi, Pakistan: Frequency of EEG Findings in Children With Epilepsy. Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.565>

*Corresponding Author:

 Faiqa Hassan
 Memon Medical Institute Hospital, Karachi, Pakistan
faiqa.kashif@yahoo.com

Received Date: 16th June, 2022

Acceptance Date: 22nd June, 2022

Published Date: 30th June, 2022

ABSTRACT

Epilepsy impacts around 46 million individuals worldwide, with an exacerbated incidence and mortality in lower-income settings Objective: To evaluate the use of EEG in determining the diagnosis of epilepsy, with its particular subtypes. This study also assessed the vital correlation between age and sex with subnormal EEG findings. Methods: It is a cross-sectional study conducted at MMI Pead's Memon Hospital, Karachi, from January 2020 to December 2020. Age ranges between 1 month and 18 years. Study evaluated the correlation of EEG findings. The EEG patterns was also assessed. EEG patterns were categorized as normal, abnormal with either background slowing or interictal epileptiform discharges (IED) or both, types of seizure and day of admission when the EEG was performed. Using SPSS latest version, association of age, and sex with abnormal EEGs was determined Results: Two-third of the children reported normal EEG, whereas abnormal background findings were observed in the remaining one-third. Inter-ictal epileptic discharge was noted on 18 EEG reports. This finding was most frequent in children within the age bracket of 30 months to more than 67 months. A combination of inter-ictal epileptic discharge and abnormal background findings were noted in children older than 49 months. However, hypsarrhythmia was noted in 2 subjects, both under 30 months of age. With regards to diagnosis, majority of the children categorized as having generalized epilepsy were over 67 months of age. Focal epilepsy was the second most frequent diagnosis, with majority under 30 months of age. On the association of EEG findings with sex, out findings were insignificant. Conclusions: EEG has been determined as the investigation of choice among patients with epilepsy, however it may have certain limitations in providing an accurate diagnosis, and must not be relied on as the sole determinant of epilepsy.

INTRODUCTION

Epilepsy is a neurological disorder characterized by paroxysmal episodes of unprovoked seizures, which occur due to exorbitant discharge of electrical activity in the brain. This alteration in the activity of neurons results in temporary abnormalities of muscle tone, movements, or behavior [1]. Epilepsy exhibits bimodal distribution, with children and the elderly most frequently afflicted with the disease [2]. A systematic analysis for the Global Burden of Disease Study revealed a staggering number of 45.9 million individuals afflicted with all-active epilepsy worldwide in

2016 [3]. In the United States, one in 26 people develop epilepsy during their lifetime England [4]. In comparison, the incidence, as well as the excess premature mortality associated with epilepsy is exacerbated in lower-income settings. Within Pakistan, the prevalence of Epilepsy has been quantified as 9.99 in a population of 1,000 [5]. In addition to examining the patient, as well as obtaining a detailed history, an electroencephalogram (EEG) serves as the cornerstone of the diagnosis, classification of the seizure, and subsequent prognosis of the patient. Interictal

epileptiform discharges—such as spikes and sharp waves—along with ictal EEG findings provide a strategic roadmap for an effective treatment plan in patients, particularly children, with epilepsy [6]. Among children, EEG not only assists in distinguishing between varying childhood epileptic syndromes, Interestingly, EEG results must be taken with caution, due to the occurrence of abnormal findings in normal individuals, and normal findings in patients afflicted with the disease [7]. Primary aim of study included an assessment of the proportion of epilepsy patients with abnormal EEGs and the subsequent diagnosis of the patients.

METHODS

A cross-sectional study was conducted at MMI Pead's Memon Hospital, Karachi from January 2020 to December 2020. The sample size was 105, which was calculated using the standard formula for calculating the sample size on the basis of prevalence. Prevalence was taken at 50% because no relevant data was available. The bound of error was 5% with a 95% confidence interval. Non-probability consecutive sampling technique was utilized. Inclusion criteria consisted of all patients between the age of 1 month to 18 years referred to the neurology department for an EEG, while patients who either refused to give consent or had an EEG done outside of hospital were excluded from study. Children with known structural brain anomalies or space-occupying lesions were also excluded. A self-designed questionnaire was used for the collection of data. The questionnaire contained information such as the patient's demographics (age, sex), pertinent history (drug, family, substance abuse, if an activation procedure was performed during EEG), provisional diagnosis made by the physician referring for EEG. Additionally, the EEG records were reviewed for relevant findings. The data was analyzed using Statistical Package for the Social Sciences (SPSS) latest version. Quantitative variables were presented as mean and standard deviation, while qualitative variables were presented as frequency and percentages. The outcome variable was the correlation of EEG with the provisional diagnosis. Independent Chi-square tests were conducted to assess the association of abnormal EEGs with age and sex.

RESULTS

A total of 117 individuals were selected for the study, with the majority being males (56.8%) followed by 42.4% females. In terms of age, almost 2/3rd of the subjects (61.7%) fell under the age bracket of fewer than 30 months, whereas only about 12% of the participants lay in the 49–66 months age bracket with the mean age of 36.15 months being reported. As for the EEG diagnosis, a significant majority of study sample had a normal EEG with

generalized and focal epilepsy having more or less the same frequencies at 13 and 12 respectively in study (Table 1).

Variables	Frequency	Percentage
Sex		
Male	67	56.8
Female	50	42.4
Age in Months		
<30	61	61.7
31–48	22	18.6
49–66	14	11.9
>67	20	16.9
Mean age	36.15	
S.D	+22.15	
Diagnosis on EEG		
Normal	67	56.8
Generalized Epilepsy	13	11
Focal epilepsy	12	10.2
Other	25	21.2

Table 1: Demographic data

	Epileptic Discharges	Sex		Total	P-value
		Male	Female		
EEG findings	Normal	39	27	66	0.216
	Abnormal background	12	14	26	
	Interictal epileptic discharge	12	6	18	
	Presence of Abnormal background and Interictal epileptic discharge	4	1	5	
	Hypsarrhythmia	0	2	2	
	Total	67	50	117	
	Seizure Types	Sex		Total	P-value
		Male	Female		
Diagnosis on EEG	Normal	40	27	67	0.221
	Generalized Epilepsy	09	04	13	
	Focal Epilepsy	08	04	12	
	Other	10	15	25	
	Total	67	50	117	

Table 2: EEG findings and their diagnosis in relation to sex

On the superficial evaluation of the data, a majority of males (39) females (27) reported a normal EEG. The number of abnormal background findings on the EEG was more or less the same among both sexes. Inter-ictal discharges on their EEG were more commonly seen among male subjects/children as opposed to only 6 female children. Likewise, the presence of abnormal background and interictal epileptic discharge together was also predominant among male children (4) as compared to females (only 1). In contrast, Hypsarrhythmia was only found in the female subjects (2). However, on analysis, these findings were observed to be insignificant (p value=0.216) (Table 2). With regards to the diagnosis of epilepsy in relation to sex, male subjects were found to have a greater number of normal (40), generalized epilepsy (9), and focal epilepsy diagnosis on EEG. Other diagnoses

including infantile spasms and febrile seizures were more common in female subjects. However, on analysis, these findings were observed to be insignificant (p value=0.221) (Table 3).

	Epileptic Discharges	Range of Ages*(in months)				Total	P-value
		1	2	3	4		
EEG Findings	Normal	44	14	3	5	66	0.001
	Abnormal background	8	5	7	6	26	
	Interictal epileptic discharge	7	2	2	7	18	
	Presence of Abnormal background and Interictal epileptic discharge	0	1	2	2	5	
	Hypsarrhythmia	2	0	0	0	2	
	Total	61	22	14	20	117	
	Seizure Types	Range of Ages*(in months)				Total	P-value
		1	2	3	4		
Diagnosis on EEG	Normal	44	15	03	05	67	0.000
	Generalized Epilepsy	02	01	01	09	13	
	Focal Epilepsy	05	02	04	01	12	
	Other	10	04	06	05	25	
	Total	61	22	14	20	117	

Table 3: EEG findings and associated diagnosis with respect to age

Ranges in months *1=<30, 2=31-48, 3=49-66, 4=>67

A variety of findings were observed on the EEG. Even though around 2/3rd (66 in total) of the children reported normal EEG, abnormal background on the EEG was noted in around 1/3rd of the EEG reports with the majority of children falling under 30 months of age in both EEG findings. Other findings included inter-ictal epileptic discharge which was noted on 18 EEG reports. This finding was dispersed along with all age groups with the most falling under less than 30 months and more than 67 months age group. A few (5 in total) reported both inter-ictal epileptic discharges along with an abnormal background on the EEG with the majority of children being in the more than 49 months age bracket. Hypsarrhythmia was only noted in 2 subject both being under 30 months of age. On analysis, these findings were significant (P value=0.001). In terms of the diagnosis on EEG, most children (13 in total) were diagnosed with generalized epilepsy with the majority being over 67 months of age. Focal epilepsy was the second most common diagnosis with a total of 12 children, with the majority of them lying under 30 months of age. These findings were found to be significant (p value=0.000).

DISCUSSION

EEG is one of the most significant modality of choice when it comes to the diagnosis of epilepsy [8]. Study was solely based on the diagnosis from EEG findings. As per our data, 56.8% (39) were boys contrasting to 42.4% (27) of females who were a part of study. From findings during EEG data collection, out of the total of 117 subjects who came in for an EEG, the majority reported a normal EEG with a greater number being male children. This trend is to similar

findings being reported in studies from Estonia, Germany, and others [9]. Regardless of the fact that more boys had a normal EEG, they also had a greater number of abnormal EEG findings as compared to girls, such as interictal epileptic discharge with or without abnormal background were predominantly seen in males. An analogous trend of males having more reported cases than females with general epilepsy (9 boys) and focal epilepsy (8 boys) being more prevalent in male subjects than females (4 and 4 respectively). A similar pattern was noted in a study that dealt with idiopathic generalized epilepsy which reported a stark male preponderance in syndrome diagnosis on EEG [10]. Other diagnosis infantile spasm and febrile seizures were slightly more prevalent in females (15 girls as compared to 10 boys). A significant majority of participants lied in the youngest age bracket of study which was less than 30 months. Generalized epilepsy and focal epilepsy shared more or less the same number of cases however other diagnosis were more prevalent in study subjects. The highest number of normal EEGs were 44 in number. These findings are in line with similar findings observed in a study that reported a prevalence of only 0.76% in their cohort of children less than 5 years of age [11]. According to a study interictal epileptic discharges may be the only abnormal finding on an EEG done routinely [12] and in this study interictal epileptic discharges were noted to be present the most in age groups of less than 30 months and greater than 67 months (7 cases in each age group) while the least number of interictal discharges were seen in the EEG of children aged between 31-49 months (4 cases). However, the presence of abnormal background along with interictal epileptic discharges grew in number with the increasing age of our subjects as only 1 case finding was observed in the 31-48 months of age bracket which increased to 4 cases in the age brackets of 49-66 and >67 months. Interestingly, hypsarrhythmia was only noted in 2 children younger than 30 months of age. A study reported hypsarrhythmia in association with infantile spasms in all of their subjects, so further evaluation of the type of seizure in showing hypsarrhythmia can be initiated in the future [13]. Coming towards diagnosis on EEG with respect to age, the youngest age group of less than 30 months reported the highest number of normal EEGs (44), 30 months age bracket reported the highest number of focal epilepsy cases diagnosed on EEG (5 cases) followed by generalized epilepsy with only 2 cases diagnosed. This trend is established by a study that says that focal seizures are more likely to be seen than generalized [14]. There should be proper evaluation and need to be discussed by researcher regarding the roles of genes versus acquired causes in seizure; that a normal brain can develop epilepsy by any insult or any congenital cause [15] so further

research in the molecular genetics will guide and provide the details regarding classification of epilepsy and will help in disease specific treatment [16]. Provocation techniques such as hyperventilation and photic stimulation [17,18], anti-epileptic drug reduction [19], sleep derived EEGs, and long-term EEG monitoring or ambulatory EEG, could potentially assist medical personnel in catering to patients presenting with diagnostic and therapeutic challenges. Further, multi-centre studies within populations with varying demographic profile are essential in determining the correlation of EEGs with variables such as sex and age, and the efficacy of EEGs in the diagnosis and long term treatment of a patient with epilepsy [20]. Since there is a dearth of studies evaluating the correlation of EEG with varying socio demographic profiles, as well as alternative measures such as ambulatory EEGs in accurately determining diagnosis and treatment of epilepsy within Pakistan we must look into such studies in future.

CONCLUSION

Study findings have important implications. It has been seen that EEG is a standard investigative procedure for epilepsy diagnosis following a seizure, but in this study, it was seen that EEG findings present with certain limitations, and must not be taken as a confirmed diagnosis of epilepsy.

REFERENCES

- [1] Sirven JI. Cold Spring Harbor Perspectives in Medicine. 2015,5. doi:10.1101/cshperspect.a022848
- [2] Milligan TA. Epilepsy: A clinical overview. The American Journal of Medicine, 2021, 134(7), 840-847. doi:10.1016/j.amjmed.2021.01.038
- [3] GBD 2016 Epilepsy Collaborators. Global, regional, and national burden of epilepsy, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurology, 2019,18(4), 357-375. doi:10.1016/S1474-4422(18)30454-X
- [4] England MJ, Liverman CT, Schultz AM & Strawbridge LM. Epilepsy across the spectrum: promoting health and understanding. A summary of the Institute of Medicine report. Epilepsy & Behavior: E&B, 2012,25 (2), 266-276. doi:10.1016/j.yebeh.2012.06.016
- [5] Khatri IA, Iannaccone ST, Ilyas MS, Abdullah M & Saleem S. Epidemiology of epilepsy in Pakistan: review of literature. JPMA. The Journal of the Pakistan Medical Association, 2003,53(12), 594-597.
- [6] Chen H & Koubeissi MZ. Electroencephalography in epilepsy evaluation. Continuum (Minneapolis, Minn.), 2019,25(2), 431-453. doi:10.1212/CON.0000000000000705
- [7] Rana KS. Rational use of EEG in childhood epilepsy. Indian Journal of Pediatrics, 2000,67(1 Suppl), S22-31.
- [8] Eze CO, Afolabi OF et al. Electroencephalography: Experience at Abakaliki Nigeria. 2021, 13(9): 1-71.
- [9] Sillanpää M & Helen Cross J. The psychosocial impact of epilepsy in childhood. Epilepsy & Behavior: E&B, 2009, 15 Suppl 1(2), S5-10. doi:10.1016/j.yebeh.2009.03.007
- [10] Asadi-Pooya AA & Homayoun M. Sex differences in characteristics of idiopathic generalized epilepsies. Neurological Sciences: Official Journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology, 2021,42(6), 2421-2424. doi:10.1007/s10072-020-04834-3
- [11] Bihege CJ, Langer T, Jenke ACW, Bast T & Borusiak P. Prevalence of epileptiform discharges in healthy infants. Journal of Child Neurology, 2015,30(11), 1409-1413. doi:10.1177/0883073814565457
- [12] Chen H and Koubeissi MZ. Electroencephalography in Epilepsy Evaluation. Continuum (Minneapolis, Minn). 2019 Apr;25(2):431-453. doi: 10.1212/CON.0000000000000705.
- [13] Hani AJ. T20. EEG characteristics affecting response to therapy in selected patients with infantile spasms and hypsarrhythmia. Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology, 2018,129, e9. doi:10.1016/j.clinph.2018.04.021
- [14] Beghi EJN. The epidemiology of epilepsy. 2020, 54(2): 185-191.
- [15] Stafstrom CE and Carmant L. Seizures and epilepsy: an overview for neuroscientists. Cold Spring Harbor perspectives in medicine, 2015, 5(6): a022426.
- [16] Falco-Walter JJ, Scheffer IE et al. The new definition and classification of seizures and epilepsy. Epilepsy research, 2018, 139: 73-79.
- [17] Das JC. Electroencephalogram (EEG) in the management of epilepsy in children. Mymensingh Medical Journal: MMJ, 2014,23(2), 406-411.
- [18] Doose H & Sitepu B. Childhood epilepsy in a German city. Neuropediatrics, 1983, 14(4), 220-224. doi:10.1055/s-2008-1059582
- [19] Smith SJM. EEG in the diagnosis, classification, and management of patients with epilepsy. Journal of Neurology, Neurosurgery, and Psychiatry, 2005,76 Suppl 2(suppl_2), ii2-7. doi:10.1136/jnnp.2005.069245
- [20] Seneviratne U, Cook MJ et al. Electroencephalography in the Diagnosis of Genetic Generalized Epilepsy Syndromes. Frontiers in Neurology, 2017,8: 499-499



Original Article

Sonographic Evaluation of Fetal Complications in Gestational Diabetes During 3rd Trimester of Pregnancy

Gull E Hina¹, Syeda Khadija-Tul-Sughra Murrium¹, Syed Amir Gilani¹, Mehreen Fatima¹, Qurat ul Ain Khalid², Maham Shahid², Noraiz¹, Maryam Sania², Hafsa Talat¹ and Taiba Suleman¹¹Department of Radiological Sciences and Medical Imaging Technology, The University of Lahore, Pakistan²Department of Radiology, Gujranwala Institute of Medical and Emerging Sciences, Gujranwala, Pakistan

ARTICLE INFO

Key Words:

Gestational diabetes mellitus, fetal complications, third trimester, macrosomia, polyhydramnios, ultrasound.

How to Cite:

Hina, G. E. ., Murrium, S. K.-T.-S. ., Gillani, S. A. ., Fatima, M. ., Khalid, Q. ., Shahid, M. ., Noraiz, ., Sania, M. ., Talat, H. T., & Suleman, T. . (2022). Sonographic Evaluation of Fetal Complications in Gestational Diabetes During 3rd Trimester of Pregnancy: Fetal Complications in Gestational Diabetes. Pakistan BioMedical Journal, 5(6).

<https://doi.org/10.54393/pbmj.v5i6.554>

*Corresponding Author:

Gull E Hina

University Institute of Radiological Sciences and Medical Imaging Technology, The University of Lahore, Lahore, Pakistan
gullehina08@gmail.com

Received Date: 12th June, 2022

Acceptance Date: 23rd June, 2022

Published Date: 30th June, 2022

ABSTRACT

Gestational Diabetes (GDM) is becoming more common everywhere around the globe.

Objective: To sonographically assess the complications of gestational diabetes in fetuses associated with gestational diabetes during 3rd trimester of pregnancy **Methods:** A cross-sectional investigation has been carried out in Mother Care Hospital, Gujranwala. All subjects signed an informed consent form in written prior to ultrasound examination. 700 participants were enrolled in this study, among them 60(8.1%) pregnant women during 3rd trimester and at term diagnosed with GDM by glucose tolerance tests as diabetics. Patients were 29.5 years old on average, and the average Gestational age was 30.4 weeks. Estimated fetal weight was derived from ultrasound measures using the Hadlock2 equation. Patients were assessed for eligibility in inclusion criteria. **Results:** Out of a total of 700 women, 60(8.1%) were diagnosed as GDM and studied. Their minimum age was 21 years and maximum age was 40 years, the mean age was 32±4.04 years. Other studies have found that increasing maternal age is connected with an increase in the prevalence of GDM. Among the studied cases, most frequent complication was macrosomia 27(45%) and 12(20%) have no fetal complication by GDM. LGA 7(11.7%), polyhydramnios 5(8.3%), SGA and placental changes 3(5%), SGA 2(3.3%) and placental changes 2(3.3%) was evaluate. **Conclusion:** 8.1 percent of pregnant women were diagnosed with GDM. The majority of the ladies were beyond the age of 25 and had many children. Macrosomia and Polyhydramnios were the most prevalent fetal complications, hence caesarean surgery was a typical technique of birth.

INTRODUCTION

Gestational Diabetes Mellitus (GDM) is characterized as glucose intolerance that develops or is discovered during gestational time period. Overall, the prevalence of GDM prevalence normally ranges between 2 and 6%, although it can be substantially higher in certain groups; there is a general trend toward rising prevalence [1]. The prevalence and risk factors of GDM, as well as its influence on maternal and newborn outcomes in the population, are being studied in more depth, as are the benefits of GDM's present universal screening. GDM is a laboratory plasma glucose

measurement that is abnormal, not a disease. Therefore, general conclusions cannot be drawn, especially since subgroups analysis show inter-population differences, particularly according to ethnicity [2]. The recent increase in the frequency of GDM has been considered to be an artefact of universal screening, with no indication of benefit to pregnancy outcomes [3]. The incidence of GDM in the overall population varies according to the origin country and the indigenous people's nature [4]. Pre-eclampsia (18%), polyhydramnios (4.8%), and impending

abortion (3.5%) were the most common maternal problems. Fetal problems included macrosomia (15.1%), intrauterine growth retardation (7.2%), and intrauterine deaths (5.5%) were noted [5]. The premise for using ultrasonography for pregnant diabetic women is the early detection of congenital abnormalities and the observation of abnormal fetal development [6]. Furthermore, ultrasonography gives a tool for assessing the baby's aberrant development and weight in order for the baby to be born at period. This editorial investigates how ultrasonography can assist clinicians in treating a diabetic pregnancy [7]. Perinatologists are particularly concerned in fetal growth and development in diabetic women. The glucose will transfer to the fetus and produce increased insulin generation in the fetus in diabetics, pregnancy, and due to maternal hyperglycemia. This fetal hyperinsulinemia will affect insulin-dependent organs and result in macrosomia [8]. Macrosomia is currently defined as a baby weight of 4,500 g or more. Figure 1, In diabetic individuals, macrosomia is a big problem [9]. The intervention group had 4.3 percent macrosomia compared to 13% women with hyperglycemia discovered during pregnancy are more likely to have unfavorable pregnancy outcomes, including such macrosomia of the baby and increased perinatal death in children of GDM female, demonstrating the necessity of diagnosing and treating gestational diabetes [10]. GDM has been associated with numerous of pregnancy complications, the most common of which are fetal hyperinsulinism, macrosomia, and increased fetal growth, because maternal blood sugar have been highly related with the risk of increasingly rapid fetal development growth and neonatal morbidity [11].



Figure 1: Obstetrical ultrasound shows macrosomia in 32 weeks of gestation

Ultrasound can detect fetuses at low hazard for macrosomia and associated perinatal issues in women who come with fasting low blood sugar in the range of 106–120 mg/d [12]. However, fetal abdominal circumference enlargement and faster growth velocity in the 3rd trimester are believed to indicate large gestational age (LGA) body mass [13]. Furthermore, whereas the amniotic fluid index

AFI falls in non-diabetic moms from late mid-trimester to late pregnancy, it remains stable in diabetes mothers throughout the third trimester. However, predicting macrosomia solely on the basis of the AFI parameter is problematic. It is, however, tough to estimate macrosomia just utilizing the AFI parameter [14]. The major hormone involved for intrauterine fetal development is known to be maternal insulin [15]. Body Mass Index (BMI) was expressed, the weight in kilogram divided by the body height in meters square (kg / m^2) and regarded as per the WHO guide as underweight ($18 \text{kg} / \text{m}^2$), normal weight ($18.5\text{--}25 \text{kg} / \text{m}^2$), overweight ($25\text{--}30 \text{kg} / \text{m}^2$), and obese (30.0 or above kg / m^2) [16]. GDM treatment is useful in lowering macrosomia, major during gestation, shoulders dystocia, or pre-eclampsia and hypertensive problems in the pregnancy [17]. It is generally known that prenatal morbidity and death are higher in diabetes pregnancies than in nondiabetic pregnancies [18]. USG is the best modality of choice. Perinatologists are concerned with fetal growth and development in diabetic women. Most obstetricians, if not all, depend on U/S to calculate estimated fetal weight (EFW) [19].

METHODS

A cross-sectional investigation has been carried out in Mother care hospital, Gujranwala. All subjects signed an informed consent form in written prior the ultrasound examination. A sample size of 60 was estimated. The sample size was calculated using the 95% confidence level, 0.05 absolute precision, and the estimated percentage of fetal problems in gestational diabetes as 0.96 (20). 700 patients underwent in this study, among them 60 (8.1%) pregnant women during 3rd trimester and at term diagnosed with GDM by glucose tolerance tests as diabetics and calculated. Patients were 29.5 years old on average, and the average Gestational age was 30.4 weeks in those patients. Estimated fetal weight was derived from ultrasound measures using the Hadlock2 equation. Patients were assessed for eligibility in inclusion criteria. Inclusion Criteria: was all pregnant females of 3rd trimester and term, all age groups would include and Singleton pregnancy. Exclusion Criteria of this study was Twins pregnancy and Congenital anomalies. Doppler ultrasound machine (Toshiba) frequency ranging 3 to 7.5 MHz was used. All pregnant females were assessed according to eligibility in inclusion criteria. Patients who were not meeting the inclusion criteria was excluded and that non-consented patients were bared who were not meeting the consideration standards. Fetal complications diagnosed by GDM were monitored according to a data collection sheet and ultrasonography. Random blood sugar was

checked by glucometer for separation of GDM patients after sonographic assessment. Pre-delivery inspections were done for maternal complications. Collected data was analyzed.

RESULTS

A cross-sectional study of 60 pregnant women in their third trimester and at term was conducted. The average patient age was 29.5 years, and the average GA was 30.4 weeks in those patients. We scanned 700 pregnant females and among them 60 pregnant females during 3rd trimester and at term have GDM. Data of these 60 participants was analyzed and their minimum age was 21 years and maximum age was 40 years. The mean \pm SD of age was 32 ± 4.04 years as shown in table 1. According to descriptive statistics, the calculated minimum maternal BMI was 18.00 kg/m² and maximum was 27kg/m² with average of 23 ± 2.03 kg/m² and maternal BSR with minimum and maximum of 191 mg/dl and 378 mg/dl respectively, with average of 251 ± 50.36 mg/dl, as shown in Table 1.

Descriptive Statistics	N	Range	Maximum	Minimum	Mean+SD
Age	60	18.00	22.00	40.00	32.2500 4.04896
Maternal BMI	60	9.00	18.00	27.00	23.0283 2.03745
Maternal BSR	60	187.00	191.00	378.00	251.1333 50.36526

Table 1: Descriptive Statistics of age, maternal BMI and BSR

Frequency of GDM with respect to GA	
weeks	GDM (%)
24.00	1(1.7)
25.00	1(1.7)
26.00	2(3.3)
27.00	4(6.7)
28.00	6(10.0)
29.00	6(10.0)
30.00	9(15.0)
31.00	9(15.0)
32.00	8(13.3)
33.00	4(6.7)
34.00	2(3.3)
35.00	3(5.0)
36.00	2(3.3)
37.00	2(3.3)
38.00	1(1.0)
Total	60(100.0)

Table 2: Frequency of GDM with respect to Gestational age

Fetal complication on USG	
Fetal complications	Frequency (%)
LGA	7(11.7)
Macrosomia	27(45.0)
Macrosomia and LGA	1(1.7)
Macrosomia and polyhydoamnios	1(1.7)
No complication	12(20.0)
Placental changes	2(3.3)
Polyhydoamnios	5(8.3)
SGA	2(3.3)
SGA and Placental changes	3(5.5)
Total	60(100.0)

Table 3: Frequency of fetal complications on USG

Table 4 illustrates the Correlation between BMI Group, Fetal complication on USG, Previous Unexplained fetal demise and Family history of diabetes. In this table among 60 patients 32 have no history of previous unexplained fetal demise and no family history of diabetes under 23-27 BMI group. Rest of 21 patients have history of previous unexplained fetal demise and family history of diabetes under 18-22 BMI group.

Correlation between BMI Group, Fetal complication on USG, Previous Unexplained fetal demise and Family history of diabetes						
Family history of diabetes	Previous Unexplained fetal demise	Fetal complication on USG				
		MACROSOMIA	POLYHYDO AMNIOS	Total		
NO	NO	BMI Group	23--27	32	0	32
		Total		32	0	32
	Total	BMI Group	23--27	32	0	32
		Total		32	0	32
YES	NO	BMI Group	18--22	21	0	21
			23--27	0	7	7
	Total		21	7	28	
	Total	BMI Group	18--22	21	0	21
23--27			0	7	7	
Total		21	7	28		
Total	NO	BMI Group	18--22	21	0	21
			23--27	32	7	39
	Total		53	7	60	
	Total	BMI Group	18--22	21	0	21
23--27			32	7	39	
Total		53	7	60		

Table 4: Correlation between BMI Group, Fetal complication on USG, Previous Unexplained fetal demise and Family history of diabetes

DISCUSSION

This was a cross-sectional study of 60 pregnant women during 3rd trimester and at term. Among those cases, the mean patient age was 29.5 years and the mean GA was 30.4 weeks. We scanned 700 pregnant females and among them 60(8.1%) pregnant females during 3rd trimester and at term have GDM. We analyzed our data of these 60 patients and their minimum age was 21 years and maximum age was 40 years. The mean \pm SD of age was 32 ± 4.04 years. Increase in maternal age was associated with higher frequency of GDM, which was in accordance with other studies [21]. The mother's advanced age is a well-defined risk factor for the development of GDM [22]. Zargar et al. demonstrated 1.7% prevalence of gestational diabetes in subjects belonging to Indian subcontinent and aged less than 25 years. These findings are much in line with low prevalence of gestational

diabetes observed in our study. The authors believe that our study has several positive attributes that could explain the extremely low incidence rate of gestational diabetes mellitus [23]. According to descriptive statistics, the calculated minimum maternal BMI was 18.00 kg/m² and maximum was 27 kg/m² with average of 23±2.03kg/m² and maternal BSR with minimum and maximum of 191 mg/dl and 378 mg/dl respectively, with average of 251±50.36mg/dl. Our study agrees with Ali Jawa et al., that the average BMI of the subjects was 24 of their study, suggesting a normal pre-pregnancy body weight. Pre-gravid BMI is a known predictor of development of gestational diabetes with far reaching metabolic implications. Frequency distribution of patient age of 60 females with average age of 32±4.04 years in 24weeks of G.A there was 1(1.7%) patient lie. Similarly, in 26,27,28,30,32,36 weeks there was 2(3.3%), 4(6.7%), 6(10%), 9(15%), 8(13.3%) and 2(3.3%) patients lie respectively and the mean of GA was 30.4 weeks [24]. The frequency of fetal complication followed by GDM in 60 pregnant patients during third trimester of pregnancy and term. Among the studied cases, most frequent complication was macrosomia 27(45%) and 12(20%) have no fetal complication by GDM. LGA 7(11.7%), polyhydramnios 5(8.3%), SGA and placental changes 3(5%), SGA 2(3.3%) and placental changes 2(3.3%) was evaluate. Present study agrees with the Akin Usta et al., who concluded that there was an increased incidence of macrosomic newborns in the world. Out of 4246 pregnant women were 399 diagnosed with fetal macrosomia (8.6%). Compared with control women, statistically correlation between fetus macrosomia and pre-pregnancy BMI, gestational weight gain, proportion, age of mother, and gender of male child. Maternal BMI and GWG were the two risk factors most strongly associated with macrosomia. Our study also agrees with the Farooq, Ayaz et al., who concluded that total of 1429 women delivered, 50(3.5%) were diagnosed as GDM and studied. Most frequent fetal complications were polyhydramnios 9(18%) and macrosomia 18(36%). Macrosomia and jaundice were most prominent complications among neonates [20]. The reported incidence of macrosomia is 25-40%, comparable to our study with 27% but more in another developing world study, i.e. 46.6% [25]. this high figure in the current study might be due to the effect of hyperglycemia which largely manifests in the third trimester, leading to fetal overgrowth during that period [26]. And in lower rates of LGA and SGA in a study by Bonomo et al. [27]. The Correlation between BMI Group, fetal complication on USG, Previous Unexplained fetal demise and Family history of diabetes. In this table among 60 patients 32 have no history of previous unexplained fetal demise and no family history of diabetes

under 23-27 BMI group. Rest of 21 patients have history of previous unexplained fetal demise and family history of diabetes under 18-22 BMI group. Compared with control women, statistically correlation between fetus macrosomia and pre-pregnancy BMI, gestational weight gain, proportion, age of mother, and gender of male child. Maternal BMI and GWG were the two risk factors most strongly associated with macrosomia. Our study agrees with the GDM resulted in similar rates of cesarean section, LGA, SGA, neonatal hypoglycemia, and neonatal admission compared to management based on strict glycemic criteria.

CONCLUSIONS

GDM was discovered in 8.1% of pregnant women. The majority of the participants in the trials were above the age of 25, and the majority were multiparous. Polyhydramnios and Macrosomia were the most prevalent fetal complications, hence caesarean surgery was a typical technique of birth. Ultrasound is a noninvasive, generally available technology for assessing and monitoring the fetus, and use of it in diabetes pregnancy is now globally accepted, allowing for early diagnosis of defects by birth and measurement of fetal development to optimize timing and mode of delivery. Future research should compare management regimens addressing appropriate time, frequency of ultrasonography tests, and glycemic objectives. Great trials are with greater sample size required to truly assess the impact of diabetes on pregnant women in Pakistan.

REFERENCES

- [1] Galtier F. Definition, epidemiology, risk factors. *Diabetes Metab.* 2010 Dec; 36(6 Pt 2):628-51. doi: 10.1016/j.diabet.2010.11.014.
- [2] Seshiah V. *Contemporary Topics in Gestational Diabetes Mellitus*: Jaypee Brothers, Medical Publishers Pvt. Limited; 2014.111(8):94-112.
- [3] Xiong X, Saunders LD, Wang FL, Demianczuk NN. Gestational diabetes mellitus: prevalence, risk factors, maternal and infant outcomes. *International Journal of Gynecology & Obstetrics.* 2001 Dec; 75(3):221-8. doi.10.1016/S0020-7292(01)00496-9
- [4] Di Cianni GV, Lencioni C, Miccoli R, Cuccuru I, Ghio A, Chatzianagnostou K, Bottone P, Teti G, Del Prato S, Benzi L Prevalence and risk factors for gestational diabetes assessed by universal screening. *Diabetes Res Clin Pract.* 2003 Nov; 62:131-7. doi.10. 1016/j.diabres.2003.07.004
- [5] Akhter J, Qureshi R, Rahim F, Moosvi S, Rehman A, Jabbar A, Islam N, Khan MA. Diabetes in pregnancy in

- Pakistani women: prevalence and complications in an indigenous south Asian community. *Diabetic medicine*. 1996 Feb; 13(2):189-91. doi.10.1002/(SICI)1096-9136(199602)13:2<189::AID-DIA32>3.0.CO;2-4
- [6] Lapolla A, Metzger BE, editors. *Gestational Diabetes: A Decade After the HAPO Study*. Karger Medical and Scientific Publishers; 2019 Dec 19; 5(4):99-105. doi.10.1159/isbn.978-3-318-06612-8
- [7] Langer O. Ultrasound biometry evolves in the management of diabetes in pregnancy. *Ultrasound in Obstetrics and Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology*. 2005 Nov; 26(6):585-95. doi.10.1002/uog.2615
- [8] Association A D. *Gestational Diabetes: What to Expect*: American Diabetes Association; 1997.11(5):94-110.
- [9] Ahmed B, Abushama M, Khraisheh M, Dudenhausen J. Role of ultrasound in the management of diabetes in pregnancy. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2015 Oct 13; 28(15):1856-63. doi.10.3109/14767058.2014.971745
- [10] Ferrara CKA. *Gestational Diabetes During and After Pregnancy*: Springer-Verlag London.13(9):33-40.
- [11] Kim C. *Gestational Diabetes During and After Pregnancy*: Springer London. 2010; 11(8):118-120. doi.10.1007/978-1-84882-120-0
- [12] Kjos SL, Schaefer-Graf U, Sardesi S, Peters RK, Buley A, Xiang AH, et al. A randomized controlled trial using glycemic plus fetal ultrasound parameters versus glycemic parameters to determine insulin therapy in gestational diabetes with fasting hyperglycemia. *Diabetes care*. 2001 Nov; 24(11):1904-10. doi.10.2337/diacare.24.11.1904
- [13] Schaefer-Graf UM, Wendt L, Sacks DA, Kilavuz Ö, Gaber B, Metzner S, et al. How many sonograms are needed to reliably predict the absence of fetal overgrowth in gestational diabetes mellitus pregnancies?. *Diabetes Care*. 2011 Jan 1; 34(1):39-43. doi.10.2337/dc10-0415
- [14] Nizard J, Ville Y. The fetus of a diabetic mother: sonographic evaluation. In *Seminars in Fetal and Neonatal Medicine*. WB Saunders. 2009 Apr; 14(2):101-5. doi.10.1016/j.siny.2008.10.001
- [15] Project CIHD, Cherokee Nation D H, Services H. *Gestational Diabetes: How to Have a Healthy Baby*: Claremore Indian Hospital, Diabetes Project; 1986.100(8):105-112.
- [16] Usta A, Usta CS, Yildiz A, Ozcaglayan R, Dalkiran ES, Savkli A, et al. Frequency of fetal macrosomia and the associated risk factors in pregnancies without gestational diabetes mellitus. *The Pan African Medical Journal*. 2017; 26:62. doi.10.11604/pamj.2017.26.62.11440
- [17] World Health Organization. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy. WHO/NMH/MND/132: Zugegriffen; 2013.11(6):24-26
- [18] Ahmed B, Abushama M, Khraisheh M, Dudenhausen J. Role of ultrasound in the management of diabetes in pregnancy. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2015 Oct; 28(15):1856-63. doi.10.3109/14767058.2014.971745
- [19] Dupak JD, Trujillo AL. Ultrasound surveillance in pregnancy complicated by diabetes. *Diabetes Spectrum*. 2007 Apr; 20(2):89-93. doi.10.2337/diaspect.20.2.89.
- [20] Farooq MU, Ayaz A, Bahoo LA, Ahmad I. Maternal and neonatal outcomes in gestational diabetes mellitus. *International Journal of Endocrinology and Metabolism*. 2007 Jul 31; 5(3):109-15.
- [21] Randhawa MS, Moin S, Shoaib F. Diabetes mellitus during pregnancy: a study of fifty cases. *Pakistan Journal of Medical Sciences*. 2003; 19(4):277-82.
- [22] Najma P. Gestational diabetes and pregnancy outcome: experience at shaikh zayed hospital. 1996; 34: 83-8
- [23] Zargar AH, Sheikh MI, Bashir MI, Masoodi SR, Laway BA, Wani AI, et al. Prevalence of gestational diabetes mellitus in Kashmiri women from the Indian subcontinent. *Diabetes research and clinical practice*. 2004 Nov; 66(2):139-45. doi.10.1016/j.diabres.2004.02.023
- [24] Jawa A, Raza F, Qamar K, Jawad A, Akram J. Gestational diabetes mellitus is rare in primigravida Pakistani women. *Indian journal of endocrinology and metabolism*. 2011 Jul; 15(3):191. doi.10.4103/2230-8210.83404
- [25] Ferchiou M, Zhioua F, Hadhri N, Hafsia S, Mariah S. Predictive factors of macrosomia in diabetic pregnancies. *Revue Francaise de Gynecologie et Obstetrique*. 1994 Feb; 89(2):73-6.
- [26] Diabetes Control and Complications Trial Research Group. The effect of pregnancy on microvascular complications in the diabetes control and complications trial. *Diabetes Care*. 2000 Aug 1; 23(8):1084-91. doi.10.2337/diacare.23.8.1084
- [27] Bonomo M, Cetin I, Pisoni MP, Faden D, Mion E, Taricco E et al. Flexible treatment of gestational diabetes modulated on ultrasound evaluation of intrauterine growth: A controlled randomized clinical trial. *Diabetes & metabolism*. 2004 Jun; 30(3):237-43. doi.10.1016/S1262-3636(07)70114-3



Original Article

Etiological Aspects of Hoarseness of Voice Among Patients Attending A Tertiary Care Hospital in Peshawar

Bakht Zada¹, Sobia Humerah^{2*}, Muhammad Habib³, Javed Iqbal⁴, Muhammad Nadeem⁵ and Ali Khan⁶

¹Department of ENT Head & Neck Surgery, Lady Reading Hospital MTI Peshawar, Pakistan

²Department of Physiology, Al Nafees Medical College, Islamabad, Pakistan

³Department of ENT, Peshawar Medical College Peshawar, Pakistan

⁴Department of ENT, Sahara Medical College, Narowal, Pakistan

⁵Department of ENT Department, M. Islam Medical & Dental College, Gujranwala, Pakistan

⁶Department of ENT, Gomal Medical College, Dera Ismail Khan, Pakistan.

ARTICLE INFO

Key Words:

laryngitis and hoarseness, laryngeal neoplasms, laryngeal tuberculosis.

How to Cite:

Zada, B. ., Humerah, S. ., Habib, M. ., Iqbal, J. ., Nadeem, M. . & Khan, A. . (2022). Etiological Aspects of Hoarseness of Voice Among Patients Attending in A Tertiary Care Hospital: Etiological Aspects of Hoarseness . Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.570>

***Corresponding Author:**

Sobia Humerah
 Department of Physiology, Al Nafees Medical College,
 Islamabad, Pakistan
doctorsobiarwp@gmail.com

Received Date: 19th June, 2022

Acceptance Date: 26th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Hoarseness of voice is much frequent in recent times and it alters the normal quality of voice

Objective: To understand and assess the etiological factors of hoarseness. **Methods:** A Non-randomized, longitudinal and cross-sectional study was conducted in the ENT Head & Neck Surgery, Lady Reading Hospital Peshawar and Al Nafees Medical College and Hospital, Islamabad for six months duration from September 2021 to February 2022. All subjects with a history of hoarseness underwent routine specific clinical evaluation to establish diagnosis. The simple manual analysis was applied for final outcomes assessment with percentage and frequency using SPSS 21.0. **Results:** Participants enrolled were 150, amongst them, the patients of 21-30 and 31-40 years of age suffered from hoarseness. Likewise, 98 (72%) were males, 52 (28%) were females with a M: F proportion of 1.45: 1. According to the distribution, the utmost communal etiology observed in this study was acute laryngitis (30%), trailed by acid peptic laryngitis in 25.3%, laryngeal neoplasms in 8.7% and other includes laryngeal tuberculosis, intubation granuloma, and very rarely trauma. **Conclusions:** There was an etiological variability of hoarseness, varies from simple laryngitis to malignant neoplasms. For this reason, it is significant not to overlook hoarseness and a thorough examination, investigation and proper history should be taken.

INTRODUCTION

Hoarseness is a term that ordinary people frequently use to describe changes in the quality of their voice [1,2]. In fact, the voice of human is an extra-ordinary realization, which have capacity to convey not only multifaceted thoughts, but also refined emotions [3]. Baby cry's is the most commonly expected sign of life at the time of birth. Crying refers to the full physiological capacity necessary for a baby to survive [4]. Perhaps no other organ system of human body function so quickly after the birth. Although the sound

is not visible during speech production, its absence or malfunction is obvious. Hoarseness is the alteration in the normal voice quality. This is a non-generic term, comparable to a patient complaining of dizziness when telling signs ranging from light-headedness to true vertigo [5,6]. It can include shortness of breath, hoarseness, stiffness, crackles in the voice, or unusual variations in pitch of voice. Otolaryngologists use the word dysphonia to describe abnormal sound quality [7,8]. Hoarseness

complaints can be a serious illness and should not be ignored. As Chevalier Jackson said, "Hoarseness is a very important symptom and deserves to be treated as a separate issue because of the frequency." The reasons of hoarseness can be assessed if a careful history taken before the hoarseness occurs and a complete physical examination is performed [9]. The later may involve the vocal cords visualization, probably flexible nasal endoscopy, indirect laryngoscopy or video-laryngoscopy. In the absenteeism of URTI, the patient with hoarseness >2 weeks should be fully assessed. If the patient has smoked in the past, neck and head cancer should be evaluated and must be ruled out. Voice overuse is the utmost communal reasons of hoarseness and result in added pathologies of vocal cords like vocal nodules [10,11]. Therapy with voice is a fundamental pillar in the treatment of some hoarseness. Well-recognized causing factors for disorders of voice are age (40-59 years), female gender, loud voice demand, vocal abuse, exposure to chemicals, extra-esophageal reflux, frequent colds, smoking and sinusitis [12]. Females are much predisposed to developing functional disorders of voice because of vulnerability, such as coping with anxiety, stress, negative emotions and depression. Professional voice users such as teachers, singers, politicians, actors, telephone workers, call center worker and broadcasters are at jeopardy of progressing towards occupational disorders of voice [13,14].

METHODS

This is a cross-sectional, longitudinal and non-randomized study held in In the ENT Head & Neck Surgery, Lady Reading Hospital Peshawar and Al Nafees Medical College and Hospital, Islamabad for six months duration from September 2021 to February 2022. All subjects with a history of hoarseness endured routine, specific clinical evaluation to establish diagnosis. In order to establish the diagnosis, a detailed interview, clinical examination, routine and special examination (direct laryngoscopy and nasopharyngo-laryngoscopy) were performed. The psychological, surgical issues like patients done with thyroidectomy or other problems other than the neck (i.e. RLN paralysis due to a malignant tumor of the lung or the thoracic oesophagus) were omitted from the study. Final outcomes analysis was done using SPSS 21.0 software.

RESULTS

Age (years)	Number of patients (%)
0 -10	3 (2)
11 - 20	15 (10)
21 -30	49 (32.7)
31 -40	40 (26.7)
41 - 50	21 (14)
51 - 60	12 (8)
>60	10 (6.6)

Table 1: Distribution of patients with reference to the age group

Likewise, of the 150 subjects, 98 (65.3%) were male, 52 (34.7%) were female with a M: F proportion of 1.45: 1, as given in Table 2.

Sex	Number of patients (%)
Male	98 (65.3)
Female	52 (34.7)

Table 2: Gender wise distribution of patients

According to the distribution, the utmost communal reason was acute laryngitis (30%) trailed by acid peptic laryngitis in 25.3%, laryngeal neoplasms in 8.7% and others include laryngeal tuberculosis, intubation granuloma, and very rarely trauma as given in Table 3.

Presentation	No. of cases
Cough	31
Change of voice	15
Vocal fatigue	15
Fever	39
Weight loss	19
Irritation/Sore throat	31
Dysphagia	6
Painful vocalization	8
Painful Swallowing	5
Neck mass	3
Heart burn/vomiting	61
URTI	16
Haemoptysis	4
Respiratory distress	10
Stridor	3

Table 3: Clinical features of the patients

Presentation	No. of cases
Inflammatory Acute laryngitis	45 (30%)
Chronic simple laryngitis	22 (14.7%)
Acid peptic laryngitis	38 (25.3%)
Reinke's edema	2 (1.3%)
Vocal cord nodule	6 (4%)
Vocal cord polyp	4 (2.7%)
Chronic specific laryngitis	4 (2.7%)
Tuberculosis of larynx	2 (1.3%)
Carcinoma Hypopharynx	5 (3.33%)
Carcinoma larynx	13 (8.7%)
Papilloma of vocal cord	2 (1.3%)
Papillary carcinoma thyroid	1 (0.7%)
Laryngeal trauma	1 (0.7%)
Neurological	4 (2.7%)
Intubation granuloma	1 (0.7%)
Hypothyroidism	2 (1.3%)

Table 4: Patients distribution conferring to etiology (n=150)

The distribution of patients according to etiology is given I

Table-4. Inflammatory acute laryngitis was the most common etiology in 45(30%) of patients followed by acute peptic laryngitis in 38(25.3%) and Chronic simple laryngitis in 22 (14.7%) of cases. The least common cause was Papillary carcinoma thyroid, Laryngeal trauma and Intubation granuloma in 1 patient each category.

DISCUSSION

In this research, hoarseness in the 31-40 age group was 40%. The male-to-female ratio in our study was 1.45: 1, similar to the study by Baitha et al., [12] and Saeed M and Ramazan [13]. The reason for such a big difference between the men and women in our study may be that the society is dominated by men, they are exposed to cigarettes, alcohol, pollution and voice abuse, while women in rural areas are unaware of what they are going through their health issues [14,15]. In our analysis, the incidence of acid peptic laryngitis was 25.3%, and Shrestha BL et al., [16] showed only 1.9%. This high incidence in this study may be due to the fact that the majority of patients suffered from GERD. Similarly, the incidence of acute laryngitis in our study was 30%, analogous to the study by Kivekäs I et al. [17]. As in other studies, the incidence of simple chronic laryngitis in this study was 14%. The incidence of Reinke's edema, vocal nodules and vocal polyps was 1.3%, 4%, and 3%, correspondingly. Our results differed from various other studies that presented a slightly lower or higher incidence of these ailments. In this study, only 1.3% have laryngeal tuberculosis, considerable lesser than the study by Zang et al., study [18]. This may be due to the higher incidence of pulmonary tuberculosis in Southeast Asia, but earlier diagnosis and treatment results in less incidence rate. The neurological and neoplastic causes reported here are 2.7% and 12%. The incidences were lesser than in other various analyses. In this analysis, the incidence of granuloma by intubation was 0.7%. In our study, hypothyroidism was the same as Maselli et al. [19], but differed from Hussain et al., [20] who presented 84.1%. The study showed that the prevalence of hypothyroidism is not higher in the Pakistani people.

CONCLUSIONS

Hoarseness is an emerging problem. It can be less dangerous as in the simple laryngitis to the most dangerous form the malignant tumor. The need of the hour is to pay more attention to the hoarseness. The proper examination investigation and history of the patient provide with the knowledge necessary to treat hoarseness.

REFERENCES

- [1] Lechien JR, Saussez S, Harmegnies B, Finck C, Burns JA. Laryngopharyngeal Reflux and Voice Disorders: A Multifactorial Model of Etiology and Pathophysiology. *J Voice*. 2017 Nov; 31(6):733-752. doi: 10.1016/j.jvoice.2017.03.015
- [2] Fortes HR, von Ranke FM, Escuissato DL, Araujo Neto CA, Zanetti G, Hochegger B, Souza CA, Marchiori E. Recurrent respiratory papillomatosis: A state-of-the-art review. *Respir Med*. 2017 May; 126:116-121. doi: 10.1016/j.rmed.2017.03.030
- [3] Srirangaprasad K, Mahajan R, Kanithavalli K, Deepa P. A Prospective Study to Determine Clinico-Etiological Factors in Hoarseness of Voice. *Journal of Evolution of Medical and Dental Sciences*. 2020 Feb 17; 9(7):374-8. doi: /10.14260/jemds/2020/86
- [4] Saha K, Maikap MK, Maji A, Moitra M, Jash D. Demographic, clinical, biochemical, radiological and etiological characteristics of malignant pleural effusions from Eastern India. *Indian J Cancer*. 2017 Jan-Mar; 54(1):257-261. doi: 10.4103/0019-509X.219575.
- [5] Reddy PH. Psychogenic Status as a Risk Factor in Minimal Pathological Conditions of the Vocal Cords-A Clinical Study in a Tertiary Teaching Hospital of Telangana. *International Journal of Scientific Study*. 2018; 5(12):26-30.
- [6] Joshi AA, Singh V, Rajani SZ. A prospective study to evaluate the etiologies and parameters of voice assessment in patients of vocal cord paralysis. *Otolaryngol Head Neck Surg*. 2017 Sep 22; 3(4):962-7.
- [7] Chatterjee S, Pal N, Chakraborty S, Majhi B. An unusual cause of hoarseness of voice in an immunocompetent individual. *Journal of Medical Sciences*. 2017 Jan 1; 37(1):29. doi:10.4103/1011-4564.200740
- [8] Van Stan JH, Mehta DD, Ortiz AJ, Burns JA, Marks KL, Toles LE, Stadelman-Cohen T, Krusemark C, Muise J, Hron T, Zeitels SM, Fox AB, Hillman RE. Changes in a Daily Phonotrauma Index After Laryngeal Surgery and Voice Therapy: Implications for the Role of Daily Voice Use in the Etiology and Pathophysiology of Phonotraumatic Vocal Hyperfunction. *J Speech Lang Hear Res*. 2020 Dec 14; 63(12):3934-3944. doi: 10.1044/2020_JSLHR-20-00168.
- [9] Minu M. A clinical study on etiopathogenesis of hoarseness of voice (Doctoral dissertation, PSG Institute of Medical Sciences and Research, Coimbatore).
- [10] Ханчи М, Маткеримов АЖ, Демеев ТН, Баубеков АА, Жакубаев МА, Тергеусизов АС, Таджибаев ТК, Еркинбаев НН, Маккамов РО, Садуакас АС, Шамшиев АС. CLINICAL AND ACADEMIC ASPECTS OF PERIPHERAL ARTERY ANEURISM (literature review) part one. *Вестник хирургии Казахстана*. 2020(3):36-47.

- [11] Samuel HT, Varghese L, Kurien R, Thomas M. Human papilloma virus induced oropharyngeal inverted papilloma as a precursor to laryngeal papillomatosis in A 1 year old child. *Int J Pediatr Otorhinolaryngol.* 2020 Nov;138:110335. doi: 10.1016/j.ijporl.2020.110335.
- [12] Baitha S, Raizada RM, Singh AK, Puttewar MP, Chaturvedi VN. Clinical profile of hoarseness of voice. *Indian journal of otolaryngology and head and neck surgery.* 2002 Jan;54(1):14-8.
- [13] Saeed Muhammad, Rahman, Taous A, Hossain MM. Aetiological factors of hoarseness of voice in patients attending in a district level hospital. *Bangladesh Journal of Otorhinolaryngology.* 2018;24(2):125-30.
- [14] Anil HT, Lasya Raj N, Pillai N. A Study on Etiopathogenesis of Vocal Cord Paresis and Palsy in a Tertiary Centre. *Indian J Otolaryngol Head Neck Surg.* 2019 Sep;71(3):383-389. doi: 10.1007/s12070-018-1502-5.
- [15] Kaur G, Singh M, Kaur M, Singh B, Gupta RK. A clinicopathological study of upper aerodigestive tract cancers. *Niger J Clin Pract.* 2019 Sep;22(9):1208-1212. doi: 10.4103/njcp.njcp_131_19.
- [16] Shrestha BL, Amatya RC, Sekhar KC, Shrestha I, Pokharel M. Aetiological factors of hoarseness in patients attending at Kathmandu University Hospital. *Bangladesh Journal of Otorhinolaryngology.* 2013 May 3;19(1):14-7.
- [17] Kivekäs I, Rautiainen M. Epiglottitis, acute laryngitis, and croup. *Infections of the ears, nose, throat, and sinuses.* 2018:247-55.
- [18] Zang J, Tian Y, Jiang X, Lin XY. Appearance and morphologic features of laryngeal tuberculosis using laryngoscopy: A retrospective cross-sectional study. *Medicine.* 2020 Dec 12;99(51).
- [19] Maselli M, Inelmen EM, Giantin V, Manzato E. Hypothyroidism in the elderly: diagnostic pitfalls illustrated by a case report. *Arch Gerontol Geriatr.* 2012 Jul-Aug;55(1):82-4. doi: 10.1016/j.archger.2011.05.003.
- [20] Hussain I, Ahmad S, Aljammal J. Radiofrequency ablation of parathyroid adenoma: a novel treatment option for primary hyperparathyroidism. *AACE Clinical Case Reports.* 2021 May 1;7(3):195-9.



Original Article

Attitude of Final Year Doctor of Physical Therapy Students Towards Direct Access

Armaghan Tahir¹, Muhammad Saad Hassan¹, Muhammad Jawwad Mohammad Latif², Saadia Batool Mohammad Latif², Sheikh Fahad Khalid³, Muhammad Faizan Hamid⁴¹Rawal Institute of Health Sciences (RIHS), Rawalpindi²Riphah International University Islamabad (RIU)³Specialist Clinic Islamabad, Pakistan⁴Department of Allied Health Sciences University of South Asia Cantt Campus Lahore, Pakistan

ARTICLE INFO

Key Words:

Direct access, Physical therapy, DPT students

How to Cite:

Tahir, A. ., Saad Hassan, M. ., Muhammad Latif, M. J., Muhammad Latif, S. B., Fahad Khalid, S. ., & Faizan Hamid, M. (2022). Attitude Of Final Year Doctor of Physical Therapy Students Towards Direct Access: Attitude of Final Year DPT Students Towards Direct Access. Pakistan BioMedical Journal, 5(6), 271-275. <https://doi.org/10.54393/pbmj.v5i6.567>

*Corresponding Author:

Muhammad Faizan

Department of Allied Health Sciences, University of South Asia, Cantt Campus, Lahore, Pakistan
biostats1000@gmail.comReceived Date: 17th June, 2022Acceptance Date: 21st June, 2022Published Date: 30th June, 2022

ABSTRACT

Direct access in physical therapy means the removal of a medical practitioner's referral directed by the country's law to access services of physical therapists for patient evaluation and treatment. students are the future of any country. **Objective:** To describe the attitude of physical therapy students in their final year towards direct access in Pakistan. **Methods:** A cross-sectional study was conducted on a sample size of 500, over a period of six months. A semi-structured questionnaire was developed to determine the desired objectives. Data was analyzed by using SPSS 21. **Results:** 62.8% students agreed and 30% students strongly agreed to practice under direct access after graduating. **Conclusions:** The study concludes that most physical therapy students are ready to practice under direct access in Pakistan after graduating.

INTRODUCTION

Physiotherapy or Physical therapy is defined as an independent health care profession that deals with identifying and increasing the current quality of life and the ability to move freely to prevent, examine, evaluate, and treat certain conditions to promote patient rehabilitation [1]. Physical therapy employs primarily physical agents and techniques to deliver efficient treatment sessions for patients and clients suffering from various musculoskeletal and neuromuscular disorders and pathologies [2]. Physical therapy may be defined as the management of pain, movement dysfunctions and/or

physical disabilities (caused by one or many disorders), by employing certain exercises, manual techniques, and manoeuvres, without employing medicines (drugs) or surgical procedures [3]. Physical therapists are a key part of the health care system and play a vital role in the life of many patients suffering from life threatening and debilitating disabilities that may be a result of some underlying pathology or disease condition [4]. Such disabilities and disorders may lead to faulty biomechanics which in turn could lead to abnormal movement patterns and imbalances. These factors may impose abnormally

increased stresses upon various muscular, neural, or vascular tissues leading to difficulty performing activities of daily life (ADLs) and as a result, may decrease or adversely affect a person's quality of life [5]. Direct access to physical therapy is defined as the act of visiting or seeing a physical therapist without the use of physician or medical specialist referral dictated by an area's law or rules and regulations to approach physical therapy services for the patient's assessment and treatment [6]. To restrict direct access services would result in delays in providing the physical therapy services to those individuals who would greatly benefit from treatment by a physical therapist [7]. In one study, only 34–38% students in the final year of their Masters' programme felt that they were ready to practice physical therapy via direct access [8]. Lack of amount of clinical hands-on skills and insufficient knowledge of non-musculoskeletal pathologies and conditions appeared to be the main reasons for their lowered perceptions regarding direct access [9]. Direct access denotes the ability of patients and/or clients to seek treatment from physical therapists without a prescription or referral from any other health care provider, primarily a physician [10]. Direct access allows physical therapists to act as a primary entry-point into the health care system [11]. Physical therapists provide care via direct access in different states. Greater perceived competence with direct access among students is critical as they are the future of the profession. There is a significantly increased student perceived competence with direct access to physical therapy [12]. This descriptive cross-sectional survey determines the attitude of final year DPT students towards direct access in Pakistan.

METHODS

This is a descriptive cross-sectional survey to assess the attitude of physical therapy students towards direct access in Pakistan. This study was completed in 6 months i.e., from August 2019 to January 2020. The chosen sample size was 500 participants (students) in different universities from all over Pakistan including Rawalpindi, Islamabad, Sargodha, and Lahore. Non-probability convenient sampling technique was used for recruiting individuals (students) into the study. DPT students in their final year (9th and 10th semester). Only those students who were willing to take part in this study were included. DPT students from 1st to 4th year (1st to 8th semester) were excluded. DPT students who were unwilling to take part in the study were excluded. The research was conducted to determine the attitude of final year physical therapy students towards direct access in Pakistan. To fulfil this requirement, a semi-structured questionnaire was developed based on basic demographic questions and 20

questions related to our study. The inclusion criteria were based on all the students being in their final year (9th and 10th semester) of DPT. The exclusion criteria based on all students who did not meet the inclusion criteria. The data was also analysed using SPSS 21.

RESULTS

There was a total sample of 500, 120 (24%) males and 380 (76%) females participated in the study. Figure 1 show that the frequency of people aged 18, 20, 21, 22, 23, 24, 25 and 26 years is 1, 4, 20, 123, 188, 158, 5 and 1 respectively. Figure 2 shows that 255 participants belong to 9th semester and 245 participants belong to 10th semester.

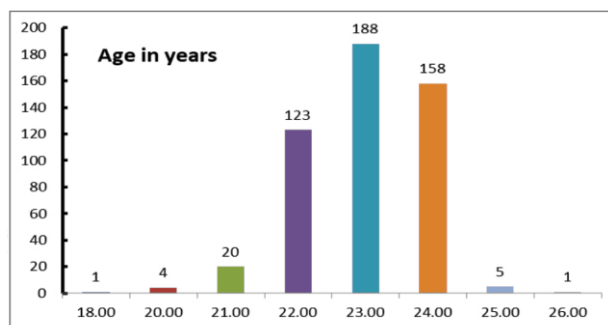


Figure 1: Frequency distribution of age

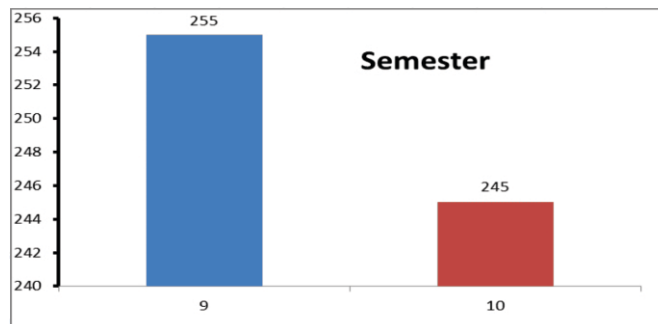


Figure 2: Frequency distribution of semester

	id	Age_in_yrs	Gender	CGPA1	University_category	Semester	Interest_before_admission	college_university
Mean	250.5000	22.9820	1.7600	1.6390	1.8080	1.4900	1.4660	4.41803
SD	144.48183	.95052	.42751	.48025	.41410	.50040	.49934	.43495

Table 1: Frequency distribution of Demographics

Table 1 shows that out of the total of 500 participants the mean values of age in years, gender, cGPA, university category, semester, interest before admission and college/university name are 22.982±0.95052, 1.76±0.42751, 1.639±0.48025, 1.8080±0.4141, 1.49±0.50040, 1.466±0.49934 and 4.418±3.43495 respectively.

Valid	Frequency	Percent	Valid Percent	Cumulative Percent
SD	16	3.2	3.2	3.2
D	16	3.2	3.2	6.4
U	78	15.6	15.6	22.0
A	197	39.4	39.4	61.4
SA	193	38.6	38.6	100.0
Total	500	100.0	100.0	

Table 2: Frequency of adequate preparedness to practice under direct access

Table 2 shows that 18(3.6%) strongly disagree, 42(8.4%) disagree, 66(13.2%) are undecided, 235(47%) agree and 139(27.8%) strongly agree of being adequately prepared to practice under direct access. Figure 3 shows that 18 strongly disagree, 42 disagree, 66 are undecided, 235 agree and 139 strongly agree of being adequately prepared to practice under direct access

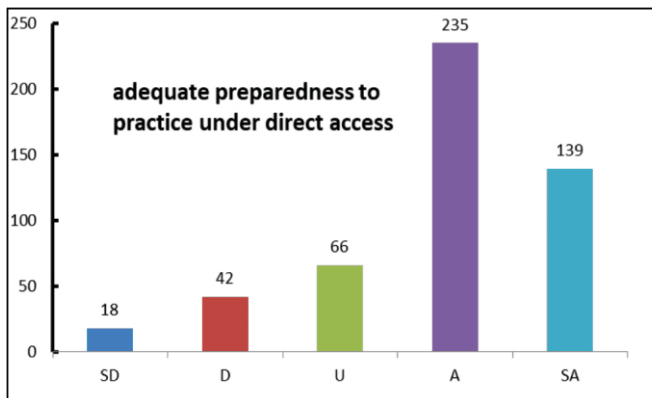


Figure 3: Frequency of adequate preparedness to practice under direct access

Valid	Frequency	Percent	Valid Percent	Cumulative Percent
SD	7	1.4	1.4	1.4
D	19	3.8	3.8	5.2
U	53	10.6	10.6	15.8
A	185	37.0	37.0	52.8
SA	236	47.2	47.2	100.0
Total	500	100.0	100.0	

Table 3: Frequency of Nation-wide direct access

Among the research participants 7(1.4%) strongly disagree, 19(3.8%) disagree, 53(10.6%) are undecided, 185(37%) agree and 236(47.2%) strongly agree to nation-wide direct access being important to the PT profession. 25(5.0%) strongly disagree, 62(12.4%) disagree, 113(22.6%) undecided, 177(35.4%) disagree and 123(24.6%) strongly agreed to having knowledge of non-musculoskeletal pathologies to detect serious medical problem outside treatment capabilities. 10(2.0%) strongly disagree, 37(7.4%) disagree, 88(17.6%) have not decided, 229(45.8%) agree and 136(27.3%) strongly agree that were informed about common diagnostic procedures performed by other professionals. 15(3%) strongly disagree, 25(5%) disagree, 72(14.4%) have not decided, 232(46.4%) agree and

156(31.2%) strongly agree that they have ample information about direct access and its implication. 12(2.4%) strongly disagree, 28(5.6%) disagree, 82(16.4%) have not decided, 226(45.2%) agree and 152(30.4%) strongly agree that they would like to practice in direct access setting after graduation. 86(17.2%) strongly disagree, 138(27.6%) disagree, 94(18.8%) have not decided, 117(23.4%) agree and 65(13%) strongly agree that they would not be capable of practicing under direct access immediately after graduation. 14(2.8%) strongly disagree, 26(5.2%) disagree, 90(18%) have no decided, 202(40.4%) agree and 167(33.4%) strongly agree that they would like to legalize direct access in all provinces. Out of 500 participants, the attitude towards direct access was a minimum of 36, maximum of 98.

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	D (21-40)	1	.2	.2	.2
	U (41-60)	35	7.0	7.0	7.2
	A (61-80)	314	62.8	62.8	70.0
	SA (80-100)	150	30.0	30.0	100.0
	Total	500	100.0	100.0	

Table 4: Frequency of the attitude towards direct access

Table 4 shows that out of 500 participants, 1(0.2%) disagree, 35(7.0%) have not decided, 314(62.8%) agree and 150(30%) strongly agree.

DISCUSSION

A survey was conducted by Kristina Scheuneman in 1994 to investigate the perceptions of physical therapy students to see patients via direct access without requiring physician referral. The study targeted final year students of master's program. This study used *Chi square* to test and analyze the data. The study found that a few students thought that they could practice directly without using medical referral. According to the study, the cause came out to be lack of knowledge and skills regarding non-musculoskeletal issues and disorders as well as less know how of side effects of various medicines. This study differs in its results significantly from ours. It must be noted that the study is old and many advances in the field of physical therapy have been made including changes and revision in the curriculum to enhance student knowledge and know how on non-musculoskeletal and systematic diseases and pathologies[9]. A study was done by Kelly L Crout in 1998 to determine the different physical therapist's beliefs regarding the use of direct access in Massachusetts and in Connecticut. The survey was among 329 therapists from Massachusetts and 179 from Connecticut. Questionnaires were mailed to the therapists. The study employed independent t testing and chi square to analyze the difference of opinion between two states. They found that most of the physical therapists were in favour of treating

their patients via direct access instead of referral. As according to our study, the future physical therapists of our country (our students) mostly agree with the use of direct access to evaluate and treat their patients and clients [13]. A systematic review was done by Heidi A. Ojha in 2014 to determine cost of health care and prognosis of patients with the use of direct access as compared to referral from a medical practitioner. The study extracted 8 articles of level 3 and 4 studies. The data was collected via CINAHL, Web of Science and Pedro. The study found that the average cost of health care without direct access went up as compared to practicing with direct access. As in our study, most of our students favour direct access [14]. A retrospective study was done by Joseph H. Moore in 2005 to determine if practicing via direct access in physical therapy was associated with increased risk or not as compared to practicing without it. 6 army, 11 navy and 8 air force locations were selected as target. The study lasted for 40 months (October 1999 to January 2003). The study found that there was no probable risk or danger on practicing physical therapy via direct access. As in our study, most of the students prefer direct access over referral from other health care professionals [15]. A pilot study was performed by Chantal J Leemrijse in 2008 to determine if the patients who visited physical therapists via direct access were different from those who used referral system in Netherland. The data was collected via National Information Service for Allied Health Care. 12,369 patients were included in the study. The study made use of chi square test and Mann-Whitney U test and found that those patients who had recurring problems and were young used direct access more than others. As in our study, students prefer to use direct access instead of referral from medical practitioner [16]. A survey was done by William G. Boissonault in 2016 to find the level of use of direct access by hospitals in Wisconsin. 89 questionnaires were mailed to directors of hospitals. The study employed the 5-point Likert scale and used the Fischer exact test. The study concluded a lack of use of direct access in hospitals. It must be kept in mind that biasness was limitation of this study. Hence, the results come out to be different from our study in which most physical therapy students agreed that they would like to use direct access for patients [17]. A study was done by Diane U. Jette in 2006 to investigate the skills of physical therapists in working via direct access. 394 people took part in this study. A logistic regression model was used. The study concluded that most physical therapists were well versed regarding musculoskeletal and non-critical medical conditions. As in our study, most of our physical therapy students agreed that they had sufficient knowledge to handle musculoskeletal conditions [18]. A descriptive study was done by Christine A. McCallum in

2012 to find out the factors that affect direct access in physical therapy in Ohio. 32 physical therapists were selected for this study. Descriptive analysis was used such as chi square test, frequency, and percentages. Most participants favoured direct access instead of medical referral to see their patients if they had the means to do so. As in our study, most students agreed to support direct access instead of referral system [19]. A survey was conducted by to find out how students in college perceive physical therapy as a career. A total of 703 students participated in the study. The study employed descriptive statistics and *Pearson Chi square test*. The study found that most students were of view that the public should be seen by physical therapists via direct access [20]. As in our study, we found that most physical therapy students agree and support direct access environment for physical therapy.

CONCLUSIONS

The results of the study conclude that many final year physical therapy students have difficulty in making differential diagnosis of medical conditions causing musculoskeletal issues and disorders. Many students agree that they are ill-prepared to identify problems in patients inappropriate for physical therapy. Many students agree to be doubtful of their education to serve as first point of contact for the patients. In general, most students agree to practice under direct access.

REFERENCES

- [1] Khalid MT, Sarwar MF, Sarwar MH, Sarwar M. Current role of physiotherapy in response to changing healthcare needs of the society. *International Journal of Education and Information Technology*, 2015;1(3): 105.2015;110.
- [2] Higgs J, Refshauge K, Ellis E. Portrait of the physiotherapy profession. *J Interprof Care*. 2001 Feb;15(1):79-89. doi: 10.1080/13561820020022891
- [3] Li LC, Bombardier C. Physical therapy management of low back pain: an exploratory survey of therapist approaches. *Phys Ther*. 2001 Apr;81(4):1018-28. doi:10.1093/ptj/81.4.1018
- [4] Orlin MN, Cicirello NA, O'Donnell AE, Doty AK. The continuum of care for individuals with lifelong disabilities: role of the physical therapist. *Phys Ther*. 2014 Jul;94(7):1043-53. doi: 10.2522/ptj.20130168.
- [5] Jankovic J, Lang AE. Movement disorders: Diagnosis and assessment. *Neurology in Clinical Practice*'de. Ed Bradley WG, Daroff RB, Fenichel GM, Jankovic J. 4. Bask>.
- [6] Berglund J, Poepping E. Physical Therapists' Role in Health Promotion as Perceived by the Patient: A

- Descriptive Study.
- [7] Demont A, Bourmaud A, Kechichian A, Desmeules F. The impact of direct access physiotherapy compared to primary care physician led usual care for patients with musculoskeletal disorders: a systematic review of the literature. *Disabil Rehabil.* 2021 Jun;43(12):1637-1648. doi: 10.1080/09638288.2019.1674388.
- [8] Robert G, Stevens A. Should general practitioners refer patients directly to physical therapists?. *British Journal of General Practice.* 1997 May 1;47(418):314-8.
- [9] Scheuneman K. Physical therapy students' views of preparation to practice under direct access (Doctoral dissertation, Grand Valley State University).
- [10] Scheele J, Vijfvinkel F, Rigter M, Swinkels IC, Bierman-Zeinstra SM, Koes BW, Luijsterburg PA. Direct access to physical therapy for patients with low back pain in the Netherlands: prevalence and predictors. *Phys Ther.* 2014 Mar;94(3):363-70. doi: 10.2522/ptj.20120330.
- [11] Boissonnault WG, Badke MB, Powers JM. Pursuit and implementation of hospital-based outpatient direct access to physical therapy services: an administrative case report. *Phys Ther.* 2010 Jan;90(1):100-9. doi: 10.2522/ptj.20080244.
- [12] Owens SC, Tucker P, Rainey Y, Edmunds B, Shetty A. Student perceived competence in direct access to physical therapy in a doctor of physical therapy program at a historically black university. *J Health Care Poor Underserved.* 2014 Nov;25(4):1966-81. doi: 10.1353/hpu.2014.0192.
- [13] Crout KL, Tweedie JH, Miller DJ. Physical therapists' opinions and practices regarding direct access. *Phys Ther.* 1998 Jan;78(1):52-61. doi: 10.1093/ptj/78.1.52..
- [14] Ojha HA, Snyder RS, Davenport TE. Direct access compared with referred physical therapy episodes of care: a systematic review. *Phys Ther.* 2014 Jan;94(1):14-30. doi: 10.2522/ptj.20130096.
- [15] Moore JH, McMillian DJ, Rosenthal MD, Weishaar MD. Risk determination for patients with direct access to physical therapy in military health care facilities. *J Orthop Sports Phys Ther.* 2005 Oct;35(10):674-8. doi: 10.2519/jospt.2005.35.10.674.
- [16] Leemrijse CJ, Swinkels IC, Veenhof C. Direct access to physical therapy in the Netherlands: results from the first year in community-based physical therapy. *Phys Ther.* 2008 Aug;88(8):936-46. doi: 10.2522/ptj.20070308.
- [17] Boissonnault WG, Lovely K. Hospital-Based Outpatient Direct Access to Physical Therapist Services: Current Status in Wisconsin. *Phys Ther.* 2016 Nov;96(11):1695-1704. doi:10.2522/ptj.20150540.
- [18] Jette DU, Ardleigh K, Chandler K, McShea L. Decision-making ability of physical therapists: physical therapy intervention or medical referral. *Phys Ther.* 2006 Dec;86(12):1619-29. doi: 10.2522/ptj.20050393.
- [19] McCallum CA, DiAngelis T. Direct access: factors that affect physical therapist practice in the state of Ohio. *Phys Ther.* 2012 May;92(5):688-706. doi: 10.2522/ptj.20100358.
- [20] Wilson AM. Integrated clinical experiences in a campus onsite clinic: A self-contained model of physical therapy clinical education. *Internet Journal of Allied Health Sciences and Practice.* 2014;12(3):8.



Original Article

The Evaluation of Treatment Efficacy of the Laparoscopic Interventions for Hepatic Cystic Echinococcosis

Deedar Ahmad Mian¹, Saifullah Brohi^{2*}, Fazal-E-Nauman³ and Aftab Ahmad Baig⁴

¹Department of Anatomy, Bannu Medical College, Bannu, Pakistan

²Department of Surgery, Bilawal Medical College for Boys LUMHS, Jamshoro, Pakistan

³Department of Surgery, Islam Medical College Sialkot, Pakistan

⁴Department of Surgery, Akhtar Saeed Trust Hospital, Lahore, Pakistan

ARTICLE INFO

Key Words:

Laparoscopic interventions, hepatic cystic echinococcosis, abdominal pain, hydatid cyst

How to Cite:

Ahmad Mian, D., Brohi, S., Nauman, F.-E., & Ahmad Baig, A. (2022). The Evaluation of Treatment Efficacy of The Laparoscopic Interventions for Hepatic Cystic Echinococcosis: Laparoscopic Interventions for Hepatic Cystic Echinococcosis. *Pakistan BioMedical Journal*, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.484>

*Corresponding Author:

Saifullah Brohi
 Department of Surgery, Bilawal Medical College for Boys LUMHS, Jamshoro, Pakistan
drsaifullahbrohi@hotmail.com

Received Date: 8th June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

For the treatment of the Cystic Echinococcosis (CE) different surgical and non-surgical approaches are present. Laparoscopy has replaced the conventional open surgeries that were highly used in the past. This chronic liver infection is caused by the cestode. This disease is increasing the mortality and morbidity cases. **Objective:** To evaluate the treatment efficacy and complications in patients experienced during the postoperative period. The recurrence rate of the laparoscopic treatment was also calculated. **Methods:** A total of 24 patients visited the Islam Medical College Sialkot from June 2019 to March 2021 were included in the study. The patients were pre-treated with the albendazole (10mg/kg) for almost one week. Then the Palanivelu hydrated system was used for the laparoscopic partial peri cystectomy. Postoperative complication was classified on the basis of the Clavien-Dindo classification system. **Results:** The calculated mean age of the 24 patients that participated in the study was 34 ± 15.6 years. The included patient's age was between 17-76 years. Out of 24, 17 were males and other 7 were females. The 21 patients belonged to the hilly areas. The 19 patients reported the complaint of abdomen pain. While cyst at the right side of the liver was observed in the 90% cases. Abdominal pain and cyst formation were the most common symptoms and pathology reported in the patients. The 10.4 ± 3.1 was the calculated mean size of the cyst. The calculated mean operative time was 80.8 ± 19.8 (60-20) minutes. According to WHO grading of cyst the 4 patients were included in the group with unilocular cyst, while the 7 patients were included in the CE1 hydatid group. **Conclusions:** The study proved that the laparoscopic treatment is an effective treatment for the hepatic CE. This treatment has reduced the risks of recurrences, mortality and conversion in the treated patients.

INTRODUCTION

Cystic Echinococcosis (CE) is also commonly known as hydatid disease. The larval stage of the taenid cestode is involve in causing this chronic infection. The metacestode belong to the genus echinococcus. This disease is highly observed in the temperate countries of Australia, Europe and South America [1,2]. It is an endemic disease. Because of the close association between the cultural and socioeconomic in the hilly areas of Pakistan, the people are more prone to the development of the infection [3]. Homo sapiens are the intermediate host of the cestode. This germ transmits through contaminated water, improperly

cooked food and hand to mouth fecal transmissions. The cyst is developed from the larval stage of the tapeworm. These cysts develop in different organ of the human body. Liver are more prone to cyst development with the incidence of 70%, while lungs share the second highest rank with the 20% probability. Kidney, spleen and heart show less incidence of cyst development [4,5]. The most commonly observed symptoms in the hepatic CE infected patients are abdominal pain and jaundice. Despite of the advances in the field of diagnostic and intervention therapies surgery is usually recommended to the patients

for the removal of the large cyst before rupture. Different types of surgeries such as open, laparoscopic total and partial per cystectomy are suggested to the different patients [6]. Sometimes the combination of chemotherapy with puncture injection and aspiration also used to percutaneous drainage of the cysts. The Magnetic Resonance Imaging (MRI) and computed tomography (CT) has enhanced the in-depth understanding of anatomical segmentation and imaging. For the radical resection of the lesion the total per cystectomy partial hepatectomy are considered more effective treatment therapies with fewer complications and little trauma. Fewer studies have reported it as the non-invasive or minimally invasive treatment therapy [7,8]. Because of the increased risk of residual cavity complications associated with the laparoscopic surgery, its acceptance is limited. Anaphylaxis, improper evacuation of the cyst and recurrence fears have further limited these approaches. Few centers in Pakistan are practicing these laparoscopic interventions. This study has evaluated the recurrences and post-operative outcomes associated with laparoscopic interventions [9,10].

METHODS

This was a prospective study conducted at Department of Surgery, Islam Medical College Sialkot. The 24 patients attended the surgery department of our institute teaching hospital were included in the study. In this prospective study the patients presented with the hepatic CE from June 2019 to March 2021 were treated by partial per cystectomy. The patients diagnosed with the hepatic CE by either enzyme linked immunosorbent assay, Ultrasonography or computed tomography passed the inclusion criteria of the study. The ethical committee of the hospital approved the study. The exclusion standards were applied on the patients having general anesthesia complication, cyst biliary communications and posteriorly located cysts. The patients younger than 16 years were also excluded from the study. Clinical, radiological and serological approaches were used to diagnose the hepatic CE. The WHO-IWGE classification were used for the classification of the cyst size, location and type. The patients included in the study were pre-treated with the albendazole (10mg/kg) for one week before the surgical interventions. This treatment remains continue after the surgery for four weeks (three cycles) at the interval of the two weeks. By using general anesthesia, the umbilical and epigastric ports were created. The fluid was aspirated by using palanivelu hydatid system, the 10% betadine solution was filled in the cavity and re-aspirated. The monopolar diathermy and laparoscopic hook facilitated the partial per cystectomy surgery. The Endoscopic Retrograde

Cholanigio-pancreatography (ERCP) with sphincterotomy and Common Bile Duct CBD stenting was performed for the patients in which persistent and bilious drain were seen for more than two weeks. The surgical, intraoperative and radiological findings were reported for each patient. The patients were followed up for the six months to twelve months. The recurrences were reported for such patients. The re-appearance of the cyst or development of new cyst is defined as the recurrence. The complications were classified according to the Clavien-Dindo classification system. The Grade III complications were labeled as major, while other lower than the grade III were marked as minor complications. The statistical analyses were carried out by using SPSS latest version. The 0.05 p-value were labelled as significant value.

RESULTS

There were total 24 patients that contributed in this study. Written consent was taken from the patients. There were 17 females (70%) and remaining 7 (30%) patients were male. The mean age of the participating candidates was also calculated and it came out to be 34 ± 15.6 yr. the age ranged from 17-76 years in case of patients. Most of the participating patients were from northern and other hilly areas. The patients belonging to hilly areas were 22 (91%) and the remaining patients were from other regions. As far as clinical presentation is concerned, the participating individuals mostly complaint about abdominal pain (n=19) that is 40%. These patients also complaint that the slight abdominal pain led them to face issues like lump in the abdomen in case of 41% of the participating patients. Fever was found only in one of the patients. There was only one case where incidental detection took place while doing ultrasonography for some other disease, Table 1.

Clinical parameters	No. of patients (%)
Pain in the abdomen	19 (40%)
Abdominal lump	20 (41%)
Incidental finding	1 (4%)
Fever	1 (4%)

Table 1: Clinical parameters of the patients suffering from hepatic CE

The procedure of ELISA was found to be in only 12 cases in almost 45% of the population. There were more than 20 patients (90%) that had detection of cyst in their right side of hemi liver. Whereas there were 2 patients that had cyst present in the left side of the liver lobe, Table 2.

Cyst location	Single	Multiple	No. of patients (%)
Right hemi-liver	18	5	23 (95%)
Left hemi- liver	1	0	1 (4%)
Both sides cysts	1	0	1 (4%)
Total	20	4	24 (100%)

Table 2: The general features of the cyst present in the liver

The number of patients that had cyst found in both sides were 20 while multiple of them (80%) had cysts in the hemi liver region. Most of the cysts were from class CE3 while there were 26%, 27% and 5% of other categories of cyst also found like CE2 and CE1 respectively, Table 3.

WHO grading	No. of patients (%)
CL that includes (No wall, cyst that is unilocular)	1(4%)
Ce1 hydatid sand	7(24%)
Ce2 (multiseptated and multivesicular cyst)	7(24%)
Ce3 having detached membrane	10(41%)
CE4 with no daughter cyst	0(0%)
CE5 with full wall calcification	0(0%)
Total	24(100%)

Table 3: The WHO grading of the cyst

DISCUSSION

Laparoscopic surgeries are very much prevalent in the whole world as they provide patients with multiple advantages as compared to old form of surgeries. Not only it provides cosmetic advantages but also helps them get rid of issues like pain after operation. So, there are multiple advantages of laparoscopic surgeries already known [11]. The improvement in the skills of surgeons and the recent advances in the field of technology has enabled scientists to multiply the skills of old and conventional hydatid form of cyst surgery by making use of laparoscopic principles. One problem that surgeons face while undergoing the conventional sort of surgery is that there is spillage of cysts content that ultimately leads to inflammation and infection in the abdomen. Later on, problems like concomitant anaphylaxis makes it difficult for patient to recover [12,13]. There are many articles that has studies where it is proved that the use of laparoscopic surgery has improved the older ways of operation for doctors and patient faced no anaphylaxis and spillage of cyst content in this case. In the present study there were 24 patients taken 23 of them had undertaken partial peri cystectomy by using laparoscopic method. But one of the participating patients had to face severe bleeding as his cyst was very close to the hepatic vein [14]. That's why there was need to shift to open surgery method for that patient. The rate of conversion was almost same as found according to studies carried out by Shrestha et al., where the team reported that there were 8% patients converted due to hemorrhage. But the conversion of one patient towards open surgery didn't make this one a failure. As the safety of the participating patients was the most important thing that's why they were shifted to open surgery method [15,16]. The mean age of the patients in the study was 34 which was same as the average age taken by other studies as well. However, there were more female patients included in our study which were just according to another study. However, it was seen that many studies had

either male or female dominance [17]. The mean time of operating the surgery was quite high in our study it was 81 minutes as compared to another study [13] and Gurusamy (53 minutes) and Shrestha et al. [15] (40 minutes). Our surgery timing was more than others because the time was calculated from the time the patient was given anesthesia and also because the learning curve was decreasing slowly as the surgery was progressed. There were some studies that had their operating time near 117, minutes as shown in Li et al., [18]. After surgeries it was found that among all patients 7 had minor problems like 4 of them had some superficial port inflammation and 3 of them had to face bilious drainage from the drain of peri cysts. But all of these 7 patients recovered from these complications shortly after few days of procedure. One of the patients faced Clavein - Dindo problems of 1 and 2 grades that required some sort of intervention. One of the patients was found suffering from persistent bile in the drain of peri cysts region even after two weeks of the Clavein- Dindo complication [19,20]. There was recurrence of the cyst in almost 5% of the participating patients. The rate of recurrence in other studies ranged from 0-10% in the patients. However, the total recurrence rate was found to be 2% after laparoscopic treatment. Despite all these efforts acute kidney inflammation was observed in one of the patients. The cause of this complication was not identified however, it was seen that the parasitic nephropathy mediated by immune system even without any attack by parasite on the kidney took place which was unexplained sort of kidney injury [21]. According to a study carried out by Kumar et al., the cause of acute kidney injury was iodine toxicity during the procedure in case of hydatid cyst cavity. As there was no testing available that can prove the iodine level of the serum the study could not prove that the risk of these complications is due to iodine level while installing the iodine povidone in the surgery. However, it was found that the kidney functioning of the patient became improved after 16 cycles of dialysis in the health care unit [22].

CONCLUSION

The study showed that the laparoscopic treatment can be done for hepatic CE as it is possible even if there are limited recourses. The rate of conversion of the patient from this surgery to the old conventional procedure is low, the recurrence rate is low and the post-operative complications are very much less than the conventional therapies. It is safer, cheaper and effective treatment for the patients suffering from hepatic CE.

REFERENCES

- [1] Rajbhandari AP, Maharjan S, Adhikari SS. A Laparoscopic management of Hepatic cystic

- echinococcosis in Nepal: A single center experience. *Journal of Society of Surgeons of Nepal*. 2020 Dec; 23(1): 2-8. doi.org/10.3126/jssn.v23i1.33513
- [2] Koirala R, Rajbhandari AP, Maharjan S, Adhikari SS. Laparoscopic management of Hepatic cystic echinococcosis in Nepal: A single center experience. *Journal of Society of Surgeons of Nepal*. 2020 Dec; 23(1): 2-8. doi.org/10.3126/jssn.v23i1.33513
- [3] Joshi BD, Koirala U, Joshi A, Dhital SP, Dhoubadhel P. Experience of Hydatid Cyst Management in a Tertiary Care Center in Kathmandu Nepal. *Journal of Institute of Medicine Nepal*. 2020 Apr; 42(1): 26-30. doi.org/10.3126/jiom.v42i1.37421
- [4] Hazra NK, Batajoo H, Ghimire S, Sathian B. Open Conservative Surgical Management of Cystic Echinococcosis in a Tertiary Care Hospital, Nepal. *Journal of clinical and diagnostic research: Journal of Clinical and Diagnostic Research*. 2015 Jul; 9(7): PC01.
- [5] Sah SP, Adhikary S, Agrawal CS, Gupta R, Ghimire A. Laparoscopic management of liver echinococcal cyst at BP Koirala Institute of Health Sciences Dharan, Nepal an institutional review. *Health Renaissance*. 2015 Aug; 13(1):86-94. doi.org/10.3126/hren.v13i1.17952
- [6] Mansy W, Mohamed M, Saber S. Outcomes of radical surgical management in liver hydatid cysts: 7 years' center experience. *Mini-invasive Surgery*. 2018 Oct; 2:36. doi.org/10.20517/2574-1225.2018.48
- [7] Senthilnathan P, Inamdar S, Nalankilli VP, Vijay A, Rajapandian S, Parthasarathi R, et al. Long-term results of hepatic hydatid disease managed using palanivelu hydatid system: Indian experience in tertiary center. *Surgical endoscopy*. 2014 Oct; 28(10):2832-9. doi:10.1007/s00464-014-3570-2.
- [8] Manterola C, Claros N. Long-Term Results After Laparoscopic Pericystectomy in Patients with Hepatic Echinococcosis: Case Series with Follow-up. *Indian Journal of Surgery*. 2022 Jan: 1-6. doi.org/10.1007/s12262-021-03202-5
- [9] Gohil VB, Thakur SU, Mehta SM, Dekhaiya FA. Comparative study of laparoscopic and open surgery in management of 50 cases of liver hydatid cyst. *International Surgery Journal*. 2020 Mar; c7(4):1099-105. doi.org/10.18203/2349-2902.isj20201170
- [10] Shaikh AS, Tandur AE, Pathrabe YS, Patil DS, Bhandarwar AH, Shaikh NA. Laparoscopic management in hydatid disease of liver: a series of 35 cases. *International Surgery Journal*. 2021 Mar; 8(4): 1134-42. doi.org/10.18203/2349-2902.isj20211097
- [11] Marom G, Houry T, Gazla SA, Merhav H, Padawer D, Benson AA, et al. Operative treatment of hepatic hydatid cysts: A single center experience. *Asian Journal of Surgery*. 2019 Jun; 42(6):702-7. doi.org/10.1016/j.asjsur.2018.09.013
- [12] Gupta N, Javed A, Saravanan MN, Kalayarsan R, Puri S, Agarwal AK. Laparoscopic resectional surgery for hydatid disease of the liver. *Tropical Gastroenterology*. 2019 Mar; 38(4): 211-7. doi.org/10.7869/tg.439
- [13] Gurusamy, K. S., Aggarwal, R., Palanivelu, L., & Davidson, B. R. (2009). Virtual reality training for surgical trainees in laparoscopic surgery. *Cochrane database of systematic reviews*,(1).
- [14] Rashid MM, Rabbi H, Ahmed AT, Goni O, Joya M, Hussain MS, et al. Outcome of Surgically Treated 79 Patients of Hepatic Hydatidosis: A Single Center Tertiary Care Hospital Experience in Bangladesh. *Journal of Surgical Sciences*. 2018; 22(2):118-24. doi.org/10.3329/jss.v22i2.44076
- [15] Shrestha SK, Thapa PB, Maharjan DK, Tamang TY. Laparoscopic Approach for Management of Hydatid Cyst of Liver. *Journal of Nepal Health Research Council*. 2017 Jan; 15(1):67-70. doi: 10.3126/jnhrc.v15i1.18017. doi.org/10.3126/jnhrc.v15i1.18017
- [16] Sah R, Calatri M, Neupane S, Poudyal S, Toledo R, Acosta L. A case of Echinococcus granulosus hepatic hydatid cyst together with pyogenic liver abscess in a Nepali patient. *Journal of Parasitic Diseases*. 2020 Jun; 44(2):472-5. doi.org/10.1007/s12639-020-01213-9
- [17] Farhat W, Ammar H, Rguez A, Harrabi F, Said MA, Ghabry L, et al. Radical versus conservative surgical treatment of liver hydatid cysts: A paired comparison analysis. *The American Journal of Surgery*. 2021 Dec: S0002-9610(21)00742-X. doi: 10.1016/j.amjsurg.2021.12.014.
- [18] Li, Y. P., Ma, Z. G., Tuxun, T., Li, Z. D., Meng, Y., & Chen, X. (2020). The application of laparoscopy combined with indocyanine green fluorescence imaging technique for hepatic cystic echinococcosis. *BMC surgery*, 20(1), 1-8.
- [19] Talaiti T, Shao Y, Zhang R, Wen H, Jiang T, Kasimu A, et al. A study on the clinical outcomes using different laparoscopic methods to treat hepatic cystic hydatidosis. *Chinese Journal of Hepatobiliary Surgery*. 2019: 664-7.
- [20] Joshi U, Subedi R, Jayswal A, Agrawal V. Clinical Characteristics and Management of the Hydatid Cyst of the Liver: A Study from a Tertiary Care Center in Nepal. *Journal of Parasitology Research*. 2020 Sep; 2020:8867744. doi: 10.1155/2020/8867744.
- [21] Al-Saeedi M, Khajeh E, Hoffmann K, Ghamarnejad O, Stojkovic M, Weber TF, et al. Standardized

endocystectomy technique for surgical treatment of uncomplicated hepatic cystic echinococcosis. *PLoS Neglected Tropical Diseases*. 2019 Jun; 13(6): e0007516. doi: 10.1371/journal.pntd.0007516.

- [22] Kumar, R., Kaur, K., & Hastir, A. (2017). Laparoscopic treatment of hydatid cyst of liver. *Journal of evolution of medical and dental sciences-jemds*, 6(41), 3260-3263.



Original Article

Bacteriological Profile and Drug Resistance Pattern of Isolates of ICU Patients In Hospital Of Peshawar

Muhammad Nabi^{1*}, Shah Zaman², Amna Umar², Erum Rehman², Zakia Subhan³, Nighat Aziz⁴, Nabiha Naeem⁵, Ambreen Anjum⁶, Irfan Ullah⁵

¹Institute of Pharmaceutical Sciences, Khyber Medical University, (IPS-KMU), Peshawar, Pakistan

²Department of Pharmacology, Peshawar Medical and Dental College, Peshawar, Pakistan

³Department of Pharmacology, Khyber Medical University Institute of Medical Sciences (KMU-IMS), Kohat, Pakistan

⁴Department of Pharmacology, Gomal Medical College, Medical Teaching Institute, Dera Ismail Khan, Pakistan

⁵Department of Life Sciences, School of Science, University of Management and Technology (UMT), Lahore, Pakistan

⁶Department of Psychology, Virtual University of Pakistan

ARTICLE INFO

Key Words:

Multidrug-resistant, infectious diseases, morbidity, death, intensive care units

How to Cite:

Nabi, M. ., Zaman, S. ., Umar, A. ., Rehman, E. ., Subhan, Z. ., Aziz, N. ., Naeem, N. ., Anjum, A. ., & Ullah, I. (2022). Bacteriological Profile and Drug Resistance Pattern of Isolates of ICU Patients In Hospital Of Peshawar: Bacteriological Profile and Drug Resistance Pattern. *Pakistan BioMedical Journal*, 5(6), 281-285. <https://doi.org/10.54393/pbmj.v5i6.603>

*Corresponding Author:

Muhammad Nabi
Institute of Pharmaceutical Sciences, Khyber Medical University, Institute of Medical Sciences (KMU-IMS), Kohat, Pakistan
mnabipharmacist@gmail.com

Received Date: 20th June, 2022

Acceptance Date: 28th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Multidrug-resistant infectious diseases are one of the top causes of death and morbidity among hospitalized patients worldwide. **Objective:** This study's aim was to assess the frequency of common bacterial pathogens, as well as their antibiotic sensitivity & resistance, in various intensive care unit tertiary care hospitals. **Methods:** The current investigation was conducted from February to May 2021 in multiple ICU at a primary care hospital in Peshawar. Patients who were admitted to any of the hospital's four intensive care units (ICUs) and patients medically speculated of having an infection within 48 hours of arrival were included. Patients' laboratory samples were selected based on clinical suspicion. Antibiotic sensitivity testing was performed on the samples. **Result:** E. coli 33(26) was the most commonly isolated bacteria across all samples. "In NICU, CONS 17(67.78), in 7(28.28), in MICU, PICU E. coli, E. coli, Pseudomonas spp and Acinetobacter spp.11(22.39), and in E. coli, SICU 17(46.82) were predominantly isolated" "Amikacin 29(88.6), Cefuroxime 21(65), Klebsiella sp. to Cefoperazone+Salbactam 15(79), Pseudomonas to Tazobactam+Piperacillin 12(66), and Acinetobacter sp. to Sulbactam+Cefoperazone 12(66) are commonly used antibiotics against E. coli 12(56)". Citrobacter spp. (67.8) was observed more followed by Proteus spp. (34.4) and Enterococcus (34.4). **Conclusion:** In the ICUs, infectious diseases and antimicrobial resistance are key barriers to patient outcome multidrug-resistant as well as expenditure. All intensive care units throughout the world face the issue of lowering the same.

INTRODUCTION

Multidrug-resistant infectious diseases are major reasons of mortality and morbidity worldwide, putting a significant strain on patients and the healthcare structure of countries [1,2]. Patients in the ICU who are critically unwell are at the highest risk of getting these infections [3,4]. An ICU patient has a 5 to a 7 percent greater risk of nosocomial pathogens than the usual patient, and ICU infections account for 20% - 25% of all nosocomial pathogens in a

hospital [5]. Factors such as the increased use of invasive equipment and immunosuppressive drugs. All of these factors, as well as the inappropriate use of antibiotic treatment in ICUs, are leading to the same outcome [6,7]. Resistance to antibiotics among surgery center organisms is spread by antibiotic abuse, overuse, and illogical and fraudulent pharmaceutical market company as well as irregular intake brought on by either a bad medication or

poor compliance [8]. Infection-causing organisms and their antibiotic-resistant patterns differ greatly from one country to the next, various ICUs within the same hospital as well as between different hospitals. Irrational antibiotic use in ICUs, as well as medications and status, are now all leading to the same problem [9-11]. This study aimed to determine incidence of mostly identified bacterial pathogens and resistance patterns face in treatment among patients. So, Patients were included admitted to various Intensive care units (ICU) in Peshawar, Pakistan.

METHODS

A tertiary medical hospital in Peshawar's ICUs provided the data for this investigation. This Hospital has four Main ICUs i.e. Surgical ICU (SICU), Medical ICU (MICU), Neonatal ICU (NICU) and Pediatric ICU (PICU). Data was collected from the patients admitted to the ICU from February 2021 to May 2021. ICU-related infections are those that arise within 48 hrs. of admission to the hospital or within 48 hrs. of Hospital discharge, according to the Control and Prevention (CDC). During the three-month study period, patients hospitalized in ICUs of these four hospitals patients clinically speculated for infection after 48 hours of admittance were part of this study. Patients with clinical symptoms of infection diagnosed at the time of admission were not included in this study. "Clinical signs and symptoms of infections are described i.e. Leukocytosis $>10000/\text{mm}^3$, plained fever $>38^\circ\text{C}$, Dysuria, New infiltrates on chest X-ray, persistent Tracheal aspirates/secretions, Suprapubic tenderness, Turbid urine, Thrombophlebitis, Burning micturition, Abdominal pain or tenderness, Cloudy effluent containing more than 100 Polymorphonuclear cells/ mm^3 , and Microorganisms in peritoneal dialysis fluid" To test samples i.e. sputum, urine, pus, swabs, body fluids (ex Cerebro - spinal fluid, "Pleural fluid, Ascitic fluid, feces and blood" were obtained from the patients based on clinical suspicion. In this investigation, only bacteria hospital-acquired infections were examined in depth. *Candida* sp. was also found on gram stain. Antibiotic sensitivity testing was performed on the samples. The following antibiotics were tested for sensitivity "Gatifloxacin, Cefazolin, Imipenam, Cefuroxime, Gentamycin, Cefotaxime, Amikacin, Ampicillin, Ampicillin+Sulbactam, Cefoperazone+Sulbactam, Piperacillin+Tazobactam, Imipenam, Gatifloxacin, Cefazolin, Cefuroxime, Cefotaxime, Gentamycin, ". Furthermore, patients' details, such as gender, age, and admission day, were obtained from their medical records.

RESULTS

Table 1 shows the gender and age profiles of the patients in the research.

ICU	Neonate less than 28 years		Post neonate 1 year		Preschool 1-5 years		School 6-12 years		Adolescent 20-19 years		Adult 20-60 years		Elderly Greater than 60 years		Total 324 participants
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
NICU															
PICU	78	74			12	14	8	10	3	10					152
SICU			6	5											70
MICU							1	2	2	2	12	22	11	5	58
					1	3					20	15	15	3	44

Table 1: The gender and age characteristics of patients

Blood 198 (66.77), swab 40 (13.77), bodily fluids 28 (10), pus 12 (4.77), urine 21 (7.7), and sputum 8 (3.44) were among the 324 patient samples examined (Table 2).

Sample collection	Total amount of samples n= 324 %	Yield growth organism samples n=100 %
Urine	21 (7)	12 (56)
Blood	198 (66.77)	31 (16.33)
Sputum	08 (3.44)	7 (86.62)
Swab	39 (13.77)	35 (90.58)
Pus	12 (4.77)	9 (73.83)
Fluids	28 (9)	7 (19.92)

Table 2: Sample profile and culture rate obtained from different samples

A total of 100 (32.44) samples were found to be positive for organism growth, yielding a total of 129 (43.77) distinct isolates. In table 3 there were 96 (75.32) gram-negative bacteria, 28 (22.10) gram-positive and gram bacteria, and 7 (5.79) Candida sp. bacteria. Out the of 100 samples, 76 (80.79) revealed single isolates, while 20 (21.42) revealed multiple isolates (maximum to 3). E. coli 33 (26) was the most commonly isolated bacterium from all samples, followed with Acinetobacter species, 21 (16.73), Coagulase Negative Staphylococci (CONS) 22 (17.51), Klebsiella sp. 19 (15.17), Pseudomonas sp. 18 (14.39), Candida sp. 7 (5.79).

Microbe	Blood (n=) (%)	Urine (n=) (%)	Sputum (n=) (%)	Swab (n=) (%)	Pus (n=) (%)	Fluid (n=) (%)	Total (n=) (%)
E Coli	3(7.7)	5(29.6)	3(19.2)	15(26.5)	7(57.)	5(9)	37(26)
Acineto bacteria so	4(11)			17(30.08)	2(8.88)		23 (16.73)
CONS	19(71)	2(8.25)		3(4.75)			24(17.5)
PSEUDOMONAS SP		2(8.25)	4(28.28)	12(21)	3(16.49)		21(15.17)
CANDIDA		4(22.54)	2(10.10)	2(2.93)	2.(878)		10(5.79)
KLEBSIELLA	4(11)	4(22.54)	4(28.28)	9(15.66)		2(2)	23 (15.17)
CITO BACTER SP	2(4.44)	2(8.25)		2(93)			6(3.45)
STAPH AUREUS	2(4.44)			2(93)	2(8.78)		6(3.45)
PROTEUS	2(4.44)		2(29.29)				6(3.45)
ENTERO COCCUS	2(4.44)	2(8.25)		2(93)	2(8.78)		6(3.45)
ENTERO BACTER SP				2(2.93)	2(2.93)		4(2.657)

Table 3: Types of organisms secluded from different samples

Table 4 illustrates the distribution of strains isolated from various ICU. The majority of CONS 17(77.78) was identified in the NICU, closely by Klebsiella sp. 5 (17.78). The most common bacteria found in PICU were E. coli 7(28.28), Acinetobacter spp., Klebsiella spp., and Candida spp (12.75).

Microbe	NICU (%)	PICU (N=)(%)	SICU (N=)(%)	MICU (N=)(%)	Total (%)
E Coli		7(28.28)	17(46.72)	11(22.28)	36(26)
Acineto bacteria so	2(5.8)	2(14.75)	7(18.28)	11(22.39)	22(16.73)
CONS	17(77.78)	3(10.10)	2(3.36)	3(4.36)	25(17.5.28)
PSEUDOMONAS SP		2(10.10)	6(15.39)	11(22.39)	3(16.49)
CANDIDA		4(14.75)		4(7.49)	8.(5.79)
KLEBSIELLA	5(17.78)	4(14.75)	4(9.68)	9(18.13)	22(15.17)
CITO BACTER SP	2(4.28)		2(3.97)	2(93)	6(3.97)
STAPH AUREUS	2(4.28)	2(5.65)	2(3.97)	2(93)	6(3.97)
PROTEUS			2(3.97)	4(5.56)	6(3.97)
ENTERO COCCUS	2(4.28)	2(5.65)			6(3.97)
ENTERO BACTER SP		2(5.65)	2(3.97)	2(93)	4(2.67)
Total	29(19.86)	28(18.20)	44(28.45)	58(37.83)	159(100)

Table 4: Microbes Patterns isolated from various Intensive Care Units

Table 5 shows the antibiotic sensitivity trend of the major five isolates in MICU. E. coli is most usually sensitive to Amikacin 29(88.6), Cefotaxime 21(96), Klebsiella sp. is most frequently resistant to Cefoperazone+Salbactum 15(79), E coli, Pseudomonas spp, and Acinetobacter spp. were most usually secluded in 11(22.29), followed by E. coli 17(46.82) Klebsiella. 9 (18.03). was the most commonly isolated organism in SICU, followed by Acinetobacter spp. 7(18.15), and Pseudomonas spp. 6 (15.39). Piperacillin+Tazobactam 12(66) was usually sensitive to Pseudomonas, and Cefoperazone+Sulbactam 12(66) was commonly sensitive to Acinetobacter sp 12(66).

Antibiotic	E Coli	CONS (n=) (%)	KLEBSIELLA (n=) (%)	PSEUDOMONAS SP (n=) (%)	Acineto bacteria (%)
Amikacin	29 (88.6)	7(39)	12(62)	9(48)	2(6)
Cefo perezone +sulbactum	27(82)	27(49)	15(79)	10(54)	12(56)
Amphicillin	3(7.36)	18(82)		2(7)	4(16)
Amphicillin +sulbactum	3(7.36)	6(25)		2(7)	4(16)
Piperacillin +tazobactum	27(82)	12(53)	10(51)	12(66)	
Gatifloxan	10(29.2)	9(39)	9(45)	4(19)	2(6)
Cefzoline	2(4.2)	9(39)		2(7)	
Imipenem	3(7.36)	18(82)		2(7)	
Cefuroxime	4(10.4)	15(68)			
Gentamycin	12(35.4)	13(58)	3(12)	4(19)	2(6)
Cefotaxime	5(13.6)	21(96)			
Cipro floxacin	6(15.6)	18(82)		7(4)	3(11)

Table 5: Antibiotic sensitivity pattern

Table 6 shows the percentage of different organisms that are completely resistant to all drugs studied. Citrobacter spp. (77.8%), Proteus spp. (44.4), and Enterococcus spp. (44.4) were the most prevalent multidrug resistant species (44.4).

Microorganisms	Antibiotic-resistant to all n-18 (%)
Klebsiella	5 (23.23)
Acinetobacter sp.	3 (11)
Citrobacter sp.	3 (67.68)
Proteus sp.	2 (34.34)
Pseudomonas sp.	2 (6.90)
Enterococcus	2 (34.34)

Table 6: Multidrug-Resistant Organisms' Frequency

DISCUSSION

findings of this study showed that rate of infection in patients admitted in ICU due to microbes was 32.44 percent. The percentage of *E. coli* was identified 26 (33 cases), following *Acinetobacter sp.* 16.73% (21 cases). Furthermore, the percentage of Coagulase-negative staphylococci was found 17.51% (22cases), *Klebsiella sp.* 15.17% (19 cases), *Pseudomonas sp.* in 14.29% (18cases), and *Candida sp.* 5.79% (7 cases). *E. coli* isolates were 14 percent in one study published in the Eastern Mediterranean Health Journal [12]. *Pseudomonas aeruginosa* was found most common isolates (26.5%) in the ICU of hospitals in Pakistan from from January 2010 to March 2011., *Klebsiella pneumonia* (15.3), and *Staphylococcus epidermidis* were the most common isolates in the ICU of hospitals in Pakistan (14.9)[12]. In the same study Another study found percentage of *Pseudomonas spp.* 29.1%, *Acinetobacter spp.* Percentage with 27, *Candida spp.* Percentage 12.8%, *Escherichia coli* percentage 10.3, and *Klebsiella spp.* Percentage 9.7 as were *Staphylococcus aureus*, *Enterobacter spp.*, *Citrobacter spp.*, *Enterococcus spp.*, *Providentia* (10.7%) [13]. However, in a European Intensive care unit, one of the most frequently identified organisms were *Staphylococcus aureus* with the percentage of 30.1, *Pseudomonas aeruginosa* percentage 28.7%, Coagulase-negative staphylococcus percentage 19%, and yeast percentage with 17.1% [14]. A study conducted in the hospital of Jordan University and found the following percentage e.g., *Acinetobacter spp.* 28%, *Staphylococcus aureus* 40, *Pseudomonas spp.* 23, Coagulase-negative staphylococcus 19, *Enterobacter spp.* 20, *Candida spp.* 19, *Escherichia coli* 15, *Klebsiella spp.* 17 and *Enterococcus* 11 [15]. In the ICUs, nosocomial infections and antibiotic resistance are a major impediment to patient outcomes, lengthening patient stays and raising costs. Most intensive care units throughout the world face the issue of implementation of such measures that can control infections for example safeguards measures and strictly adhering to wash hand practice [16,17]. antibiotic plan; surveillance deeds, [18]. and employment of experts to control infections, [19-20] may be essential, for that more study is recommended.

CONCLUSION

E. coli was found to be the most frequent in all samples. *Acinetobacter spp.* and *Pseudomonas sp.* were the most frequently isolated bacteria in PICU *E. coli*, NICU CONS, SICU *E. coli* and MICU *E. coli*. Furthermore, *E. coli* was the highest susceptible to CONS to Cefotaxime, Amikacin, *Pseudomonas* to Tazobactam+Piperacillin, *Klebsiella sp.* to Cefoperazone+Salbactam, & *Acinebacter sp.* to Sulbactam+Cefoperazone and *Acinetobacter sp.* from Cefoperazone+Sulbactam. *Citrobacter sp.*, *Proteus sp.*, and *Enterococcus sp.* were the most prevalent multidrug-resistant species.

REFERENCES

- [1] 1. Eskander HG, Morsy WYM, Elfeky Haajp. Intensive care nurses' knowledge & practices regarding infection control standard precautions at a selected Egyptian cancer hospital. *Prevention*. 2013;4(19):160-74.
- [2] 2. Eggimann P, Pittet D. Infection control in the ICU. *Chest*. 2001 Dec;120(6):2059-93. doi: 10.1378/chest.120.6.2059.
- [3] 3. Kumhar GD, Ramachandran VG, Gupta P. Bacteriological analysis of blood culture isolates from neonates in a tertiary care hospital in India. *Journal of Health, Population and Nutrition*. 2002 Dec 1:343-7.
- [4] 4. Abbas SH, Naeem M, Adil M, Naz SM, Khan A, Khan Mujoamca. Sensitivity patterns of *Pseudomonas aeruginosa* isolates obtained from clinical specimens in Peshawar. *Journal of Ayub Medical College Abbottabad*. 2015 Jun;27(2):329-32.
- [5] 5. Hecini-Hannachi A, Bentchouala C, Lezzar A, Laouar H, Benlabed K, Smati FJAJoMR. Multidrug-resistant bacteria isolated from patients hospitalized in Intensive Care Unit in University Hospital of Constantine, Algeria (2011-2015). *African Journal of Microbiology Research*. 2016 Sep; 10(33):1328-36. doi.org/10.5897/AJMR2016.8257
- [6] 6. Ullah O, Khan A, Ambreen A, Ahmad I, Akhtar T, Gandapor AJ, et al. Antibiotic sensitivity pattern of bacterial isolates of neonatal septicemia in Peshawar, Pakistan. *Archives of Iranian medicine*. 2016 Dec;19(12):0.
- [7] 7. Nasim O, Rustam Z, Mufarrih Smjjormi. Bacteriological profile and antimicrobial susceptibility pattern of sputum samples in patients presenting to the pulmonology ward of a tertiary care hospital of Peshawar. *Journal of Rehman Medical Institute*. 2018; 4(2):16-9.
- [8] 8. Rafiq MS, Rafiq MI, Khan T, Rafiq M, Khan MM. Effectiveness of simple control measures on

- methicillin-resistant *Staphylococcus aureus* infection status and characteristics with susceptibility patterns in a teaching hospital in Peshawar. *Journal of Pakistan Medical Association*. 2015 Sep; 65(9):915-20.
- [9] Abbas S, Sabir AU, Khalid N, Sabir S, Khalid S, Haseeb S, et al. Frequency of Extensively Drug-Resistant Gram-Negative Pathogens in a Tertiary Care Hospital in Pakistan. *Cureus*. 2020 Dec; 12(12): e11914. doi: 10.7759/cureus.11914.
- [10] Ahmed W. Microorganisms related with ventilator Associated pneumonia (VAP) and their antibiotic sensitivity pattern. *Journal of Rawalpindi Medical College*. 2014 Jun; 18(1):45-8.
- [11] Ahmed A, Lutfi S, Al-Hail M, Al-Saadi Mjajpcr. Antibiotic susceptibility patterns of microbial isolates from blood culture in the neonatal intensive care unit of Hamad Medical Corporation (HMC), Doha, Qatar. *Asian Journal of Pharmaceutical and Clinical Research*. 2013;(6):191-5.
- [12] Pattanayak C, Patanaik SK, Datta PP, Panda P. Assessment of Antibiotic Sensitivity Pattern of Bacterial Isolates in the Intensive Care Unit of a Tertiary Care Hospital in Eastern India. *Issues and Developments in Medicine and Medical Research*. 2022 Feb; 10:71-81. doi.org/10.9734/bpi/idmmr/v10/2590C
- [13] Saxena S, Priyadarshi M, Saxena A, Singh R. Antimicrobial consumption and bacterial resistance pattern in patients admitted in I.C.U at a tertiary care center. *Journal of infection and public health*. 2019 Sep; 12(5):695-699. doi: 10.1016/j.jiph.2019.03.014.
- [14] Setu SK, Sattar Anijejob. Antimicrobial Resistant Profile of Bacterial Isolates in The Intensive Care Unit of a Tertiary Care Hospital in Bangladesh. *European Journal of Biomedical*. 2021;8(2):06-12.
- [15] Ennab R, Al-Momani W, Al-Titi R, Elayan A. Antibiotic Profile of Pathogenic Bacteria Isolated from Postsurgical Site Infections in Public Hospitals in Northern Jordan. *Infection and Drug Resistance*. 2022 Feb 2; 15:359-366. doi: 10.2147/IDR.S350406.
- [16] Loftus RW, Dexter F, Robinson ADM. High-risk *Staphylococcus aureus* transmission in the operating room: A call for widespread improvements in perioperative hand hygiene and patient decolonization practices. *American Journal of Infection Control*. 2018 Oct; 46(10):1134-1141. doi: 10.1016/j.ajic.2018.04.211.
- [17] Vermeil T, Peters A, Kilpatrick C, Pires D, Allegranzi B, Pittet D. Hand hygiene in hospitals: anatomy of a revolution. *Journal of Hospital Infection*. 2019 Apr; 101(4):383-392. doi: 10.1016/j.jhin.2018.09.003.
- [18] Organization WH. Core competencies for infection prevention and control professionals. 2020.
- [19] Choe PG, Lim J, Kim EJ, Kim JH, Shin MJ, et al. Impact of national policy on hand hygiene promotion activities in hospitals in Korea. *Antimicrobial Resistance & Infection Control*. 2020 Sep; 9(1):157. doi: 10.1186/s13756-020-00817-3.
- [20] Zingg W, Storr J, Park BJ, Ahmad R, Tarrant C, Castro-Sanchez E, et al. Geneva IPC-Think Tank. Implementation research for the prevention of antimicrobial resistance and healthcare-associated infections; 2017 Geneva infection prevention and control (IPC)-think tank (part 1). *Antimicrobial Resistance & Infection Control*. 2019 May; 8:87. doi: 10.1186/s13756-019-0527-1.



Original Article

Practices of Medical Device Usage Among Nurses Working in The Critical Care

Samreena Ghafoor¹, Hajra Sarwar¹, Adnan Yaqoob¹ and Saida Khan¹Lahore School of Nursing, The University of Lahore.

ARTICLE INFO

Key Words:

Medical Device, Practices, Intervention, Education

How to Cite:

Ghafoor, S., Sarwar, H., Yaqoob, A., & Khan, S. (2022). Practices Of Medical Device Usage Among Nurses Working in The Critical Care: Practices of Medical Device Usage Among Nurses. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.568>

*Corresponding Author:

Corresponding Author:
Samreena Ghafoor
samreenaghafloor@gmail.com

Received Date: 17th June, 2022Acceptance Date: 23rd June, 2022Published Date: 30th June, 2022

ABSTRACT

Ventilator is widely used medical device in the critical care to deal with multiple life emergencies. So, nurses must be trained regarding usage of ventilator to provide excellent care without any complication. **Objective:** To analyze the effect of educational training program on nurses' practices regarding the usage of medical devices (Ventilator). **Methods:** Quasi experimental research design with pre- and post-was used followed by educational intervention. Research was conducted in Critical Care Unit (CCU) of public tertiary care Hospital. Total 36 nurses were selected. Nurses who have attended any training session regarding ventilator care were excluded from the study **Results:** Paired sample t-test showed a significant difference in the pre and post scores of nurse's practices regarding the usage of the ventilator, with paired sample t test, $t(34) = -20.4$, $p < .05$ was significant. Pre-test mean scores ($M=10.00$, $SD= 0.00$) compared with post -test scores ($M=17.42$, $SD=2.14$) which showed highest differences in mean. The value of *Cohen's d* was 0.12 showing a lower effect size. **Conclusions:** Educational interventional program has a positive effect on nurse's practices regarding the usage of ventilator. During Pre-program evaluation of ventilator nurse's practices were unsatisfactory which improved to 95% after the educational intervention.

INTRODUCTION

Medical Devices (MD) are considered as one of most important essential facility in critical care units. Critical care is not possible without medical device like ventilator [1]. It is evident by research that 80% of total patients in critical care unit need ventilator support to restore their life. Which shows that nurses have a dire need to be expert in providing the ventilator associated care. Nursing care of ventilated patients is very important and nurses must be trained before entering in the critical care unit about all basic practices and techniques of medical devices. Specially, ventilator [2]. Moreover, every critical care nurse should encounter the best possible nursing care to the patients. In Pakistan according to recent statistic. Approximately, 28% to 35% patients develop irreversible complication due to unsatisfactory nursing care practices. Because more than 90% critical care unit are managed in Pakistan by the untrained critical care nurses. That's why, In

Pakistan, mortality rate of mechanically ventilated is more than 60%. This mortality can be control by improving the nursing care practices with the help of regular teaching and learning sessions and giving the proper training to the novice nurses before coming in direct contact of ventilated patients [3]. Moreover, nurses don't have proper practices about the medical devices and do not report any adverse event to the higher authorities as even professional deficiencies can be corrected by reporting the hurdle which nurses are facing during the usage of ventilator [4]. As novice nurses don't practice the standard pre-cautions usually, due lacking of proper training, education and experience. Globally, ventilators are extensively used in the critical care units for multiple life threatening emergencies. As nurses play an abundant role throughout mechanical ventilation process from intubating to extubating. So, nurses must be trained to have satisfactory practices

about operating the ventilator like adjustment settings according to physician and anesthetic orders [5]. Training session can improve the nursing care and practices to satisfactory level [6]. Only experienced and qualified nurses can handle quickly all ventilator associated problem. Professional requirements of nursing profession nurses must have teaching sessions in real setting with patients and clinical teaching sessions are revolutionary steps for the enhancement critical care nurses' practices [7]. It is prime responsibility of the nurses to identify the any complication throughout the ventilator support and suitable management in order to provide the best quality care and life saving assistance to the patients [8]. Critical care unit (CCU) is always equipped with multiple Medical devices. Nurses are the first line user of these medical devices and in critical care unit patients are totally depended on the nurses. As nurses plays an essential role in CCU that's why nurses should have professional expertise to handle the medical devices while taking care of critically ill patients. Nurses have knowledge of these device but their practices are not up to the mark. Specially, novice nurses use the medical devices for the first time. Nurses face multiple issues regarding the usage of the medical devices [9]. Another study was carried out in Ireland by Sowan et al., (2017), results showed that 61% nurses don't know the reasons of ventilator alarm and appropriate practices according the alarm. Due unsatisfactory practices, medical errors occur which lead to the death untimely. Alarms in the medical devices act like a safeguard because every alarm is the indication of specific urgent need to be fulfilled by the nurses e.g. blocked endotracheal (EET) can be assess by the alarm but if blockage of the EET is ignored this may cause sudden death of the ventilator depended patient [10]. A research study was conducted in Pakistan at Islamabad in which 62% nurses express that there is no proper training regarding the nursing practices of ventilator that's why nurses face multiple issues in using the ventilator which leads to professional deficiencies. Organizations and clinical faculty of nursing colleges should focus on clinical practices regarding the use ventilator. There should be proper clinical and education training sessions for novice nurses to make them expert in using the ventilator [5]. Dipaanjali et al., observed in their research study that nurses don't have satisfactory practices regarding the care of mechanically ventilated patient. Unsatisfactory Practices score was 76% regarding the patients' position, proper suctioning techniques and endotracheal tube care. Education training session proved improvement in the unsatisfactory score of practices [11]. Educational training session is most powerful strategy to improve the nurse's practices and their performance regarding the usage of

ventilator. likewise, a research study concluded that post training session has a positive effect on the nurse's practices regarding the usage of the ventilator [12]. The purpose of current study is to explore practices of the critical care nurses regarding the usage of the medical devices.

METHODS

The quasi experimental design was used with pre -post design. 36 nurses were selected as research participant from critical care unit. Duration of the study was 9 months after inter research review board approval. Ethical approval was also obtained from ethical committee of The University of Lahore. Nurses who had attended any training session before or who were on leave were excluded from the study. Demographic tool and observational check list containing 42 items were the 2 adopted tools used in this study. Observational check list had 5 domains: ventilator setting, EET care, emergency equipment and safety check, infection control practices, suction care practices. Response was measured by research as Done and Not done pre and post-test mean, Standard deviation, sample t test and Pearson product moment co- relation analysis was done. Intervention: PHASE 1 Self- introduction was given to the participants and written consent was obtained. Pre-test was conducted by researcher after filling out the observational check list by observing the nurse's practices regarding the ventilator without interrupting the participant. PHASE 2 the educational program was implemented for 16 weeks which included lecture, discussion, and teaching on spot and practical exercises. Teaching materials in form of hand out, data base, power point presentation, pictures, laptop, videos, and booklets. Each study session was given in 30 to 45 minutes which induces discussion for extra 10 minutes. PHASE 3 After 4 months, post test was conducted data was collected by the same observational check list. Statistical analysis as performed by using SPSS 21.

RESULTS

Results showed that there were 21(60.0%) females and 14(40.0%) males. 27(71.1%) participants belonged from 25-30 years of age group which showed that majority were novice nurses in young age. Education of nurses was measured through a diploma in Nursing, 4 years BS genetics, and 2 years BS nursing. Statistics showed that 17(48.6%) of nurses were those who acquired nursing diplomas. According to their work experience, 28(80.0%) participants had less than six month of work experience in ICU and CCU. Results of the paired sample t-test concluded in the table blow which showed a significant difference in pre and post scores of nurse's practices regarding the usage of the ventilator. Values of paired sample t test and p

value, $t(34) = -20.4$, $p < .05$ were found significant Findings showed that pre-test mean scores compared with post-test educational intervention for Ventilator ($M=10.00$, $SD=0.00$) ($M=17.42$, $SD=2.14$) and for showing the highest differences in mean. Thus, the hypothesis of difference has been approved. The value of Cohen's d was 0.12 showing a lower effect size (Table 1).

Variables	Pre-scores (n=35)		Post-scores (n=35)		99% CI				Cohen's d
	M	SD	M	SD	t	p	LL	UL	
Ventilator	10.00	0.00	17.42	2.14	-20.4	.000	-8.16	-6.69	0.1

Table 1: Pre and Post scores of nurse's practices regarding the usage of the ventilator

Note. M= Mean, SD= Standard Deviation, p= Significant value, LL= Lower Limit, UL= Upper Limit, CI= Confidence Interval, Cohen's d = Effect Size

Variables	n	M	SD	1	2	3	4	5	6	7	8	9
1. Gender	35	1.11		-	-1*	-1	-9*	.03*	.231	.04*	.10*	.6*
2. Age	35	3.10		-	-	.71	.32	.131	.2	.216	.251	.35
3. Education	35	3.23		-	-	-	.39	.118	.254	.242	.323	.41
4. Experience	35	4.11		-	-	-	-	.497	.332	.785	.927	.92
5. NPOC	35	3.98		-	-	-	-	-	.45	.644	.460	.46
6. VC	35	4.05		-	-	-	-	-	-	.33	.28	.33
7. ETC	35	4.11		-	-	-	-	-	-	-	.72**	.73**
8. ICRC	35	4.13		-	-	-	-	-	-	-	-	-

Table 2: Analysis of correlation between demographic characteristics, and practices of ventilator medical devices (n=35)

Note. m= mean, SD= standard deviation, *correlation is significant at the 0.05 level (2-tailed). **correlation is significant at the 0.1 level (2-tailed) and ***correlation is significant at the 0.01 level (2-tailed), gender (male=1, female=2), experience (less than 6 months=1, more than month=2), (npoc= nurses practice observational checklist), vc= ventilator care, etc= endotracheal tube care, eesc= emergency equipment and safety check, icrc= infection control related care, icrc= infection control related care, scp= suction care practices

DISCUSSION

Descriptive were calculated in two main steps. Individual personal characteristics i.e., age, gender, education and experience of work in critical care unit was estimated in first step while descriptive of nurse's practice and observational checklist was calculated in second step. Analysis of the demographic characteristics showed that different age group, experience level and educational background effects the nurse's practices and their professional capabilities. Similar, findings were also supported by another research study [13]. The results suggest that there is a significant relationship between the level of age, years of experience and education. Nurses who have more work experience in critical care unit and

higher educational degree like BSN. Specially, young nurses have the great potential of learning advance skill. Similar findings were also supported by the Kramer that year experience in critical care unit make nurses practices perfect [14]. Meanwhile, current research study showed that 80% nurses have less than six month experience that's why nurse's practices are not satisfactory. Because perfection always come with time. Similar results were agreed by another research study that more experienced nurses can perform nursing care with perfection [15]. Ventilator is considered as life-saving therapy in critical care unit but ventilator usage needs expert practices to functional well. Nurses are consider as back bone of the ventilator care. Research finding suggest that nurses have unsatisfactory practices regarding the usage of ventilator as pre - test score showed that 81% have unsatisfactory practices, as have less than 6 month experience in the critical care unit and regarding the usage of medical devices specially ventilator similar finding were also indicated in a study published in 2021 which observed that 70% nurses have unsatisfactory practices regarding the usage of ventilator [16,2]. Research finding showed that educational taring session is most powerful strategy to improve the nurse's practices and their performance regarding the usage of ventilator Likewise, a research study concluded that post training session has a positive effect on the nurse's practices regarding the usage of the ventilator [12]. Research findings showed that Ventilator depended patients' needs round the clock strict monitoring of all physical needs and ventilator parameters and only nurses are responsible for whole task with doctor. Moreover, suddenly specific decisions and actions are needed to handle life threatening emergencies like air leakage, unexpected shutdown, low oxygen saturation, blockage or displacement of endotracheal tube (EET). There is significant positive effect of educational training session on nurse's practices regarding the endotracheal care of ventilated patients as post-test results confirmed that 95% nurse's practices were found satisfactory. Likewise, another research was agreed with the similar findings that training session is helpful in improvement of nurse's practices [17,18]. Research findings indicated that educational training sessions has a positive effect on the nurse's practices. Pre and post test results were found significant statistically and results of the paired sample t-test showed a significant difference in pre and post scores for nurse's practices regarding ventilator. It was found significant differences with paired sample test $t(34) = -20.4$, $p < .05$. Findings showed pre and post mean scores compared with post -educational session for Ventilator ($M=10.00$, $SD=0.00$) ($M=17.42$, $SD=2.14$). and for showing the highest differences in mean. Thus, the hypothesis of

difference has been approved. The value of Cohen's d was 0.12 showing a lower effect size. Similar research results were agreed with another research study [19,20].

CONCLUSION

Most of the nurses have unsatisfactory practices regarding the usage of medical devices. Specifically, ventilator practices were not up to the mark in the pre- test implementation. Meanwhile, in post-test it was found that educational intervention has significant positive effect on nurse's practices.

REFERENCES

- [1] Sole ML, Klein DG, Moseley MJ. Introduction to Critical Care Nursing E-Book: Elsevier Health Sciences, 2020.
- [2] Hesham S. Assessment of nurses' performance regarding management of patients on mechanical ventilator. *Port Said Scientific Journal of Nursing*, 2016;3(1): 161-177. doi:10.21608/PSSJN.2019.32327
- [3] Rafiq MY, Ikram A, Afzal A, Zaman G, Usman B, Ayyub M. Ventilator associated pneumonia among patients on mechanical ventilation at tertiary care centres. *PAFMJ*, 2018, 68(1), 75-79. doi: 10.1086/502151.
- [4] Alsohime F, Temsah MH, Hasan G, Al-Eyadhy A, Gulman S, Issa H, et al. Reporting adverse events related to medical devices: A single center experience from a tertiary academic hospital. *PLoS One*. 2019 Oct 24;14(10):e0224233. doi:10.1371/journal.pone.0224233.
- [5] Ghauri SK, Javaeed A, Chaudhry A, Khan AS, Mustafa KJ. Knowledge and attitudes of Pakistani intensive care unit nurses regarding oral care delivery to mechanically ventilated patients. *JPMA. The Journal of the Pakistan Medical Association*, 2020;70(7):1203-1208. doi: 10.5455/JPMA.5630.
- [6] Ibrahim AM, Al-Rafay SS, Tantawi HR. 1 Application of Care Bundle Approach for Preventing Device Associated Infections: A Training Program for Pediatric and Neonatal Nurses. *Medico-legal Update*, January-March 2021;21(1).
- [7] KP SV, CS S. Effectiveness of Video Assisted Teaching programme on knowledge regarding first aid management of foreign body aspiration among mothers of under-five children. *Asian Journal of Nursing Education and Research*, 2021;11(4): 459-465. doi: 10.52711/2349-2996.2021.00111
- [8] Mahmoud EA, EL-shafie E-L, E.-G. A-L, Abdel-Aziz MA. Effect of Educational Program for Nurses Performance Regarding Infection Control Precautions, toward patient on Mechanical Ventilation. *Assiut Scientific Nursing Journal*, 2020;8(20):94-104.
- [9] Ozan YD, Duman M. Nurses' Perceptions Regarding the Use of Technological Devices in Nursing Care Practices. *International Journal of Caring Sciences*, 2020;13(2): 901.
- [10] Sowan AK, Vera AG, Fonseca EI, Reed CC, Tarriela AF, Berndt AE. Nurse Competence on Physiologic Monitors Use: Toward Eliminating Alarm Fatigue in Intensive Care Units. *Open Medical Information Journal*. 2017 Apr 14;(11):1-11. doi: 10.2174/1874431101711010001.
- [11] Dipanjali R, Shivananda PM, Yashoda S. Effectiveness of an Educational Intervention on Knowledge and Practice of Staff Nurses on Prevention of Ventilator Associated Pneumonia among Neonates in Neonatal Intensive Care Unit. *International Journal of Caring Sciences*, 2020;13(2):1421.
- [12] Madhuvu A, Endacott R, Plummer V, Morphet J. Nurses' knowledge, experience and self-reported adherence to evidence-based guidelines for prevention of ventilator-associated events: A national online survey. *Intensive and Critical Care Nursing*, 2020;(59):102827.
- [13] Alnobani O, Zakaria N, Temsah MH, Jamal AA, Alkamel N, Tharkar S. Knowledge, Attitude, and Perception of Health Care Personnel Working in Intensive Care Units of Mass Gatherings Toward the Application of Telemedicine Robotic Remote-Presence Technology: A Cross-Sectional Multicenter Study. *Telemed J E Health*. 2021 Dec;27(12):1423-1432. doi: 10.1089/tmj.2020.0469.
- [14] Rhagnanan-Kramer V. *Critical Care Nurses' Perceptions of Safety Related to Using Complex Medical Devices in Daily Nursing Practice*. Nova Southeastern University. 2020.
- [15] Smith MW, Abarca Rondero D. Predicting electrocardiogram interpretation performance in Advanced Cardiovascular Life Support simulation: comparing knowledge tests and simulation performance among Mexican medical students. *PeerJ*. 2019 Mar 15;7:e6632. doi: 10.7717/peerj.6632.
- [16] Alja'afreh MA, Mosleh SM, Habashneh SS. Nurses' perception and attitudes towards oral care practices for mechanically ventilated patients. *Saudi Med J*. 2018 Apr;39(4):379-385. doi: 10.15537/smj.2018.4.21749.
- [17] Chen T-J, Chung Y-W, Chen P-Y, Hu SH, Chang C-C, Hsieh S-H, et al. Effects of daily sedation interruption in intensive care unit patients undergoing mechanical ventilation: A meta-analysis of randomized controlled trials. *International Journal of Nursing Practice*, 2021. //doi.org/10.1111/ijn.12948
- [18] Sujun Chen, Li Hua, Qianqian Jin, Hezhao Wang.

Correlation of ICU Nurses' Cognitive Level with Their Attitude and Behavior toward the Prevention of Ventilator-Associated Pneumonia, *Journal of Healthcare Engineering*, 2022, Article ID 8229812:2022;(7). doi.org/10.1155/2022/8229812

- [19] Aradhna, Uma D, Amoldeep S. Effectiveness of Nursing Care Bundle in Terms of Knowledge and Practices Regarding Care of Patients on Mechanical Ventilator among Nursing Personnel. 2021;14(22): *International Journal of Nursing Education*. doi.org/10.37506/ijone.v14i2.17990
- [20] Estrem, Bruce BA, RRT-NPS; Wall, Jill BSN, CRNI; Paitich, Lindsey BSN, RN; Maynard, Roy MD, FAAP The Ventilator-Dependent Child, *Home Healthcare Now*: March/April 2020;38(2):7579 [doi:10.1097/NHH.0000000000000852](https://doi.org/10.1097/NHH.0000000000000852)



Original Article

Frequency of Different Types of Urinary Incontinence and Their impact on Quality of Life of Pakistani Women

Sohail Hassan¹, Kiren Khurshid Malik², M. Adil Khurshid³, Athar Hameed Seikh⁴, Azfar Ali⁵ and Ammad Ahmad Siddiqui¹¹Department of Urology, Sahara Medical College, Narowal, Pakistan²Department of Obstetrics and Gynecology, Services Institute of Medical Sciences, Lahore, Pakistan³Department of Urology, CMH Medical College, Lahore, Pakistan⁴Department of Urology, Allama Iqbal Medical College, Lahore, Pakistan⁵Department of Urology, PGMI and AIMC, Lahore, Pakistan

ARTICLE INFO

Key Words:

Pelvic floor disorder, Urinary Incontinence, Women's health, Quality of life, Health promotion

How to Cite:

Hassan, S., Malik, K. K., Khurshid, M. A., Seikh, A. H., Ali, A., & Siddiqui, A. A. (2022). Frequency of Different Types of Urinary Incontinence and Their impact on Quality of Life of Pakistani Women: Different Types of Urinary Incontinence and Their impact on Quality of Life. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.190>

*Corresponding Author:

Sohail Hassan
Department of Urology, Sahara Medical College,
Narowal
drhassan_99@hotmail.comReceived Date: 13th Feb, 2022Acceptance Date: 27th May, 2022Published Date: 30th June, 2022

ABSTRACT

The International Continence Society (ICS) defines Incontinence of urine as involuntary loss of urine. **Objective:** To determine the frequencies of different types of incontinence of urine and their impact on quality of life of Pakistani women. **Method:** Descriptive observational study was conducted at outpatient department of five centers. Three validated questionnaires were used for quality-of-life assessment, International Consultation Incontinence Questionnaire Short Form (ICIQ-SF), Medical Outcome Study 36 items Short Form (SF-36) and King's Health Questionnaire (KHQ). **Result:** The study included 436 women. The most frequent type of incontinence of urine was mixed (n=281, 64.45%) followed by stress incontinence (n=129, 29.59%) and urge incontinence (n=26, 5.96%). The women suffering from mixed type of incontinence of urine had maximum effect on quality of life both general and specific. **Conclusions:** All types of incontinence of urine had an effect on quality of life but the mixed type had more impact.

INTRODUCTION

The International Continence Society (ICS) defines Incontinence of urine as "involuntary loss of urine". Incontinence of urine is classified into three types. SUI (Stress Urinary Incontinence) which is defined as involuntary loss of urine due to increased intra-abdominal pressure due to exertion. UUI (Urge Urinary Incontinence) is defined as loss of urine after a desire of urination is developed, and MUI (mixed Urinary Incontinence) when both these types are present. The management of urinary incontinence is always challenging. For the proper

evaluation and treatment of women who are suffering from incontinence of urine and to evaluate its effects on quality of life, a correct diagnosis is necessary [1,2]. Apart from this fact different studies show that about 12.4 % of women of younger age [3], post-menopausal and middle age women show 45 % [4] and among women of older age, 75 % are suffering from some kind of urinary incontinence [5]. Most of the women with incontinence of urine are psychologically stressed, depressed, emotionally disturbed and socially isolated [6]. Considering this, it is

recommended by the ICS (International Continence Society) to include quality of life assessment into clinical practices. Different questionnaires are being used to assess quality of life in the last decades by emergence of valid questionnaires for different pathologies [7]. There are different studies which are carried out in Pakistan about incontinence of urine and its adverse effects on quality of life of patients. But these studies are usually single centered with less number of patients [8]. The purpose of this study was to calculate frequencies of different types of incontinence of urine and their impact on quality of life of Pakistani women attending different centers by using three different validated questionnaires.

METHOD

This study is descriptive observational conducted at outpatient departments of Urology at Sughra Shafi Medical Complex Narowal, Gynae Unit III of SIMS Lahore, CMH Lahore, Jinnah Hospital Lahore and LGH Lahore. All centers deal with urogynaecology and tertiary care and referral centers. Quality of life assessment in incontinence of urine is routinely performed in these centers. All patients coming to these centers were included in the study. As recommended by ICS (International Continence society) detailed information was taken from the patient involving socio demographic, obstetric and gynecological data and urinary symptoms. A complete physical examination and relevant investigations were carried out to make a diagnosis and establish the types of incontinence of urine. Before starting any medicine, the assessment of quality of life was carried out by a valid questionnaire. Three different kinds of validated questionnaires used in this study, SF-36 (Medical Outcomes Study 36-items Short Form Health Survey) [9], KHQ (King's Health Questionnaire) [10] and ICIQ-SF (International Consultation Incontinence Questionnaire Short Form) [7]. Patients coming from first July 2019 to 31 January 2020 were inducted in the study at all centers. The women above 18 years of age who can give their consent were inducted in the study. Data was recorded on a Performa at outpatient department. The patients suffering with incontinence of urine were divided into three different groups according to their type. The SPSS version 20 was used for statistical analysis. Descriptive data was analyzed with relative and absolute frequencies. Total scores of each questionnaire were analyzed by using the median, 25th and 75th quartiles. For analysis of categorical data, the Chi-Square test was used. A p value less than or equal to 0.05 was considered as statistically significant.

RESULTS

A total of 436 patients with urinary incontinence who reported and consented in outpatient departments of both hospitals were included in the study. The most prevalent

urinary incontinence was MUI (N=281, 64.45%), after that SUI (N=129, 29.59%) and UUI (N=26, 5.96%). The range of age of the patients was from 18 to 67 years. The SUI was more in younger patients while UUI was more in older group. By considering the gynecological and obstetric history it was observed that the patients with multiple numbers of pregnancies and deliveries had more UUI and MUI. In post menopausal patients the UUI was more. For the general assessment of quality of life of patients, the questionnaire SF-36 was used with a score ranging from 0 to 100 (Figure 1). Out of eight domains of questionnaire five showed differences. Considering the perception of patient about General Health, Mental Health, Vitality, body aches and Physical Activity, patients who are suffering from MUI had worse scores as compared with other types ($p \leq 0.05$). By using ICIQ-SF questionnaire, the frequency of urinary incontinence was from once daily or once a week was 67.6% and 55.9% (Figure 2). The patients suffering from MUI showed that the complaint of urinary incontinence is between most of times in a day to every time in a day (75.2%, $p \leq 0.01$). While considering volume of loss of urine during incontinence, which was evaluated by ICIQ-SF, all patients of all groups reported that there was a little volume of urine was lost which showed that there was no significant difference between the volume of urine lost among these groups ($p \leq 0.05$) (Figure 2). Patients with MUI showed more negative effect on daily life and showed higher score in the total score as compared with SUI. By using KHQ for assessment of specific quality of life, there was difference in eight domains out of nine (Figure 3). The quality of life was worse as compared to SUI (both presented with same score). Only in the domain of measurement of severity of incontinence, all groups showed different results from each other and MUI showed worse results.

Variables	SUI, n = 129, 29.5%	UUI, n = 26, 5.9%	MUI, n = 281, 64.45%	P value
Age (Years)	45 (36.6-49.2)	66 (54.5-75.0)	52 (45.5-63.0)	0.01
Schooling in years	9 (5.0-12.0)	7.5 (3.0-12.0)	6 (3-10)	0.07
Family income Rs/Per month	10,000 (37000-4000)	13280 (42000-8000)	10765 (36000-7000)	0.34
Menopause	61	20	287	0.01
Co-morbidities	98	18	207	0.31
No. of day time urination	5 (4-8)	5 (4-10)	8 (5-10)	0.01
No. of night time urination	2 (1-2.7)	2 (1-3)	3 (2-4)	0.01

Table 1: Distribution of type of incontinence of urine in relation to socio-demographic characteristics

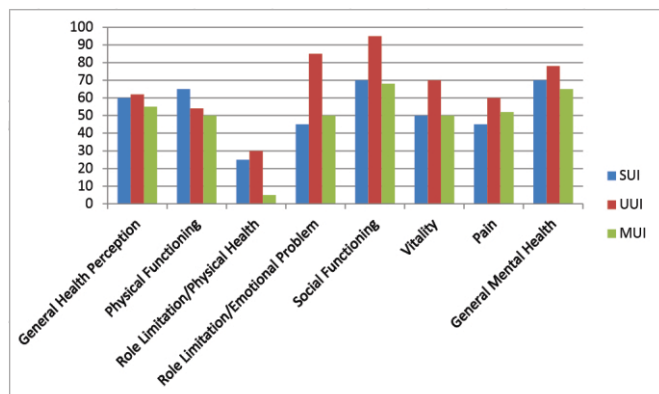


Figure 1: Median scores of the SF-36, among different types of urinary incontinence

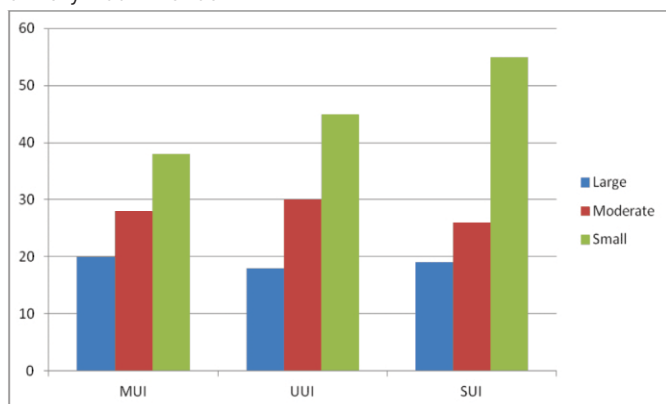


Figure 2: Amount of urinary losses among different types of UI using the ICIQ-SF

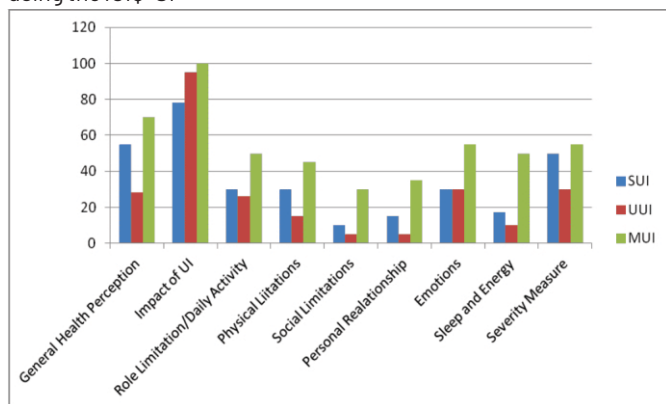


Figure 3: Median of scores of KHQ domains in different types of urinary incontinence

DISCUSSION

The gynecological-obstetric and socio demographic characteristics of all the participants are same as found in other studies of similar kind [11,12]. The women suffering with Mixed urinary incontinence are older than other types of urinary incontinence [13]. In a large survey conducted in Norway, among 27923 women, it was found that SUI was more common among young patients [14]. The relationship between factor due to an obstetric history and causation of stress urinary incontinence is quite clear [15]. As

mentioned in another study, 656 women suffering from incontinence of urine the association of obstetric history was less with UUI and MUI [16]. Some common diseases present in middle aged women have been related to Urge incontinence. A study based on larger population showed that Diabetes Mellitus is a risk factor and the patients suffering from urinary incontinence with Diabetes Mellitus have a reduced chance of urinary incontinence remission [16]. Some studies of urinary incontinence mentioned Systemic Arterial Hypertension and Diabetes Mellitus as important risk factor [7,12]. Considering the type of incontinence of urine, the mixed urinary incontinence was the most prevalent type as mentioned in some studies [12,15,17,18]. However, results from other studies showed that Stress urinary incontinence was more prevalent [13,19,20]. This difference in results may be due to characteristic differences of the patients included in study and the tools used for the diagnosis of incontinence of urine (Urodynamic study or Urinary complaints). However, in special units where the patients themselves approach for their symptoms, it seems that Mixed urinary incontinence is more prevalent [11,12,17]. There is scarce data in literature to assess the quality of life of patients by using different validated questionnaires. That is why the International Continence Society emphasizes on using specific questionnaire for the assessment of quality of life in patients suffering from urinary incontinence. However, both questionnaires used in this study not only allows the evaluation of mental health effects of incontinence of urine but also on general health of the patient [6]. Although it is difficult to compare the data, found in the literature, because they used different methods and questionnaires, but it is still possible to observe the impact of UI on quality of life, especially in social, mental, physical and sexual health [6,19]. In a study which deals with continence, EQ-5D (the EuroQoL-5 dimension) questionnaire was used. A significant association was found between incontinence of urine and different subscales of EQ-5D (Usual activity, Mobility, discomfort/pain and anxiety/depression) [3,22]. When another questionnaire, Beck Anxiety Inventory, was applied then it was observed that Stress urinary incontinence creates more anxiety as compared to patients with Urge incontinence and Mixed incontinence. Both of these had similar level of anxiety [19]. Another study stated, the association between severity of urinary incontinence and its type was found by using KHQ. It was found that patients suffering with MIU had 2.8 times more severe effect on quality of life of patient as compare to SIU [12]. The studies which used IIQ-7, also showed the similar results with more effect on quality of life of patient by mixed urinary incontinence [19]. Evaluation of different types of incontinence of urine by using ICIQ-SF is used in several

studies and it was observed that Mixed urinary incontinence had more effect on quality of life [6,13,21,22]. It is observed in an Arab study that patients with mixed urinary incontinence had more severe disease and had more impact on daily life [23]. In another large study comprising of 1,203 incontinent women, which was carried out in four European countries showed there is no significant change in quality of life of patients by the type of incontinence of urine. Women with higher volume of urine loss per day in several episodes of urinary incontinence had more negative effect on quality of health which was measured by the RQOL [24]. However, some studies had used other variables as quantity of loss, to show the effect of incontinence of urine rather than the different types of urinary incontinence [24,25].

CONCLUSION

It was concluded that Mixed urinary incontinence had the highest frequency. Regarding the assessment of Quality of, all women suffering with incontinence of urine, showed a negative impact on general as well as specific quality of life. However, the patients suffering from MIU showed worse results in all questionnaires used in the study.

REFERENCES

- [1] Abrams P, Cardozo L, Khoury S, Wein A. Incontinence. Bristol: ICUD; 2013.
- [2] Siddiqui NY, Levin PJ, Phadtare A, Pietrobon R, Ammarell N. Perceptions about female urinary incontinence: a systematic review. *Int Urogynecol J*. 2014;25(7):863-71. doi.org/10.1007/s00192-013-2276-7
- [3] Bardino M, Di Martino M, Ricci E, Parazzini F. Frequency and determinants of urinary incontinence in adolescent and young nulliparous women. *J Pediatr Adolesc Gynecol*. 2015;28(6):462-70. doi.org/10.1016/j.jpag.2015.01.003
- [4] Güvenç G, Kocaöz S, Kök G. Quality of life in climacteric Turkish women with urinary incontinence. *Int J Nurs Pract*. 2016;22(6):649-59. doi.org/10.1111/ijn.12495
- [5] Shamliyan T, Wyman J, Kane RL. Nonsurgical treatments for urinary incontinence in adult women: diagnosis and comparative effectiveness [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2012 [cited 2016 Aug 10]. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK92960/>
- [6] Seshan V, Muliira JK. Dimensions of the impact of urinary incontinence on quality of life of affected women: a review of the English literature. *Int J Urol Nurs*. 2014;8(2): 62-70. doi.org/10.1111/ijun.12034
- [7] Tamanini JTN, Dambros M, D'Ancona CAL, Palma PCR, Rodrigues Netto Júnior N. Validation of the "international consultation on incontinence questionnaire- short form"(ICIQ-SF) for Portuguese. *Rev Saúde Pública*. 2004;38(3):438-44. doi.org/10.1590/S0034-89102004000300015
- [8] Yaqub U, Habib M, Shaheen T. Frequency of Urinary Incontinence (Ui) And Its Associated Risk Factors in Pregnant Population. *Pakistan Armed Forces Medical Journal*, 2019;69(1), 117-22.
- [9] Ciconelli RM, Ferraz MB, Santos W, Meinão I, Quaresma MR. Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida SF-36 (Brasil SF-36). *Rev Bras Reumatol*. 1999;39(3):143-50.
- [10] Tamanini JTN, D'Ancona CAL, Botega NJ, Rodrigues Netto Junior N. Validação do "King's Health Questionnaire" para o português em mulheres com incontinência urinária. *Rev Saúde Pública*. 2003;37(2):203-11. doi.org/10.1590/S0034-89102003000200007
- [11] Karbage SAL, Santos ZMSA, Frota MA, Moura HJ, Vasconcelos CTM, Vasconcelos Neto JA, et al. Quality of life of Brazilian women with urinary incontinence and the impact on their sexual function. *Eur J Obstet Gynecol Reprod Biol*. 2016; 201:56-60. doi.org/10.1016/j.ejogrb.2016.03.025
- [12] Faria CA, Moraes JRD, Monnerat BRD, Verediano KA, Hawerth PAMM, Fonseca SC. Impacto do tipo de incontinência urinária sobre a qualidade de vida de usuárias do Sistema Único de Saúde no Sudeste do Brasil. *Rev Bras Ginecol Obstet*. 2015; 37(8):374-80. doi.org/10.1590/S0100-720320150005394
- [13] Minassian VA, Devore E, Hagan K, Grodstein F. Severity of urinary incontinence and effect on quality of life in women, by incontinence type. *Obstet Gynecol*. 2013;121(5):1083. doi.org/10.1097/AOG.0b013e31828ca761
- [14] Ebbesen MH, Hunskaar S, Rortveit G, Hannestad YS. Prevalence, incidence and remission of urinary incontinence in women: longitudinal data from the Norwegian HUNT study (EPINCONT). *BMC Urol*. 2013;13:27. DOI: 10.1186/1471-2490-13-27.
- [15] Tahtinen RM, Cartwright R, Tsuei JF, Aaltonen RL, Aokih Y, Cárdenas JL, et al. Long-term impact of mode of delivery on stress urinary incontinence and urgency urinary incontinence: a systematic review and meta-analysis. *Eur Urol*. 2016;70(1):148-58. doi.org/10.1016/j.eururo.2016.01.037
- [16] Singh U, Agarwal P, Verma ML, Dalela D, Singh N, Shankhwar P. Prevalence and risk factors of urinary incontinence in Indian women: a hospital-based survey. *Indian J Urol*. 2013;29(1):31-6. doi.org/10.4103/0970-1591.109981

- [17] Akkus Y, Pinar G. "Evaluation of the prevalence, type, severity, and risk factors of urinary incontinence and its impact on quality of life among women in Turkey." *Int Urogynecol J.* 2016;27(6):887-93.doi.org/10.1007/s00192-015-2904-5
- [18] Tannenbaum C, Agnew R, Benedetti A, Thomas D, van den Heuvel E. "Effectiveness of continence promotion for older women via community organisations: a cluster randomised trial." *BMJ Open.* 2013;3(12):e004135.doi.org/10.1136/bmjopen-2013-004135
- [19] Asoglu MR, Selcuk S, Cam C, Cogendez E, Karateke A. Effects of urinary incontinence subtypes on women's quality of life (including sexual life) and psychosocial state. *Eur J Obstet Gynecol Reprod Biol.* 2014;176:187-90. DOI: 10.1016/j.ejogrb.2014.02.008.doi.org/10.1016/j.ejogrb.2014.02.008
- [20] Herrmann V, Sessa D, De Grande RG, Ricceto CLZ, Morais SS, Castro EBD, et al. Associação entre o escore do International Consultation on Incontinence Questionnaire - Urinary Incontinence/Short Form e a avaliação urodinâmica em mulheres com incontinência urinária. *Rev Bras Ginecol Obstet.* 2013;35(1):16-20.doi.org/10.1590/S0100-72032013000100004
- [21] Asoglu MR, Selcuk S, Cam C, Cogendez E, Karateke A. Effects of urinary incontinence subtypes on women's quality of life (including sexual life) and psychosocial state. *Eur J Obstet Gynecol Reprod Biol.* 2014;176:18790. DOI:10.1016/j.ejogrb.2014.02.008.doi.org/10.1016/j.ejogrb.2014.02.008
- [22] Rebassa M, Taltavull JM, Gutiérrez C, Ripoll J, Esteva A, Miralles J, et al. Incontinencia urinaria en mujeres de Mallorca: prevalencia y calidad de vida. *Actas Urol Esp.* 2013;37(6):35461.doi.org/10.1016/j.acuro.2012.11.004
- [23] Ghafouri A, Alnaimi AR, Alhothi HM, Alroubil, Alrayashi M, Molhim NA, et al. Urinary incontinence in Qatar: a study of the prevalence, risk factors and impact on quality of life. *Arab J Urol.* 2014;12(4):269-74. doi.org/10.1016/j.aju.2014.08.002
- [24] Abrams P, Smith AP, Cotterill N. The impact of urinary incontinence on health-related quality of life (HRQoL) in a real-world population of women aged 45-60 years: results from a survey in France, Germany, the UK and the USA. *BJU Int.* 2015;115(1):143-52.doi.org/10.1111/bju.12852
- [25] Senra C, Pereira MG. Quality life in women with urinary incontinence. *Rev Assoc Med Bras.* 2015;61(2):178-83.doi.org/10.1590/1806-9282.61.02.178



Original Article

Evaluation of Breast Lesions Using Mammography

Mah Noor¹, Akash John¹, Abid Ali¹, Amna Yousaf¹, Khadija Bakhtawar¹¹Department of Allied Health Sciences, University Institute Of Radiological And Medical Imaging Sciences, The Univeristy of Chenab, Gujrat, Pakistan

ARTICLE INFO

Key Words:

Breast, Lesions, Cancer, Tumors, Mammography

How to Cite:

Mah Noor, ., John, A., Ali, A. ., Yousaf, A. ., & Bakhtawar, K. . (2022). Evaluation of Breast Lesions Using Mammography: Evaluation of Breast Lesions Using Mammography. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.545>
<https://doi.org/10.54393/pbmj.v5i6.545>

*Corresponding Author:

Mahnoor

Department of Allied Health Sciences, University Institute Of Radiological And Medical Imaging Sciences, The Univeristy of Chenab, Gujrat, Pakistan

Received Date: 12th June, 2022Acceptance Date: 26th June, 2022Published Date: 30th June, 2022

ABSTRACT

The second leading cause of death is breast cancer and annual mammograms have been found to incite the early identification of breast cancer. The diagnosis of cancer at initial stage is helpful in lowering the mortality rate. The most prevalent pathologies of breast cancer are swelling, cysts, and adenosis, and benign or malignant tumors. **Objective:** To evaluate Breast Lesions Using Mammography. **Method:** It was a cross-sectional study comprised of a sample size of 47 female patients, calculated via a convenient sampling approach by taking mean of three previous published studies. Women with age of 29 years and above were included in this study. The study was performed in Faisalabad, Pakistan from December 2021 to March 2022. The digital mammographic equipment was used in this study and data was entered and analyzed by SPSS version 20. **Results:** The majority 33(70.2%) patients were included in 30-49 years age group while least were 2(4.3%) in 70 and above. The ill-defined shape tumors were 18 (38.3%) and the the microlobulated shaped tumors were 1(2.1%). The tumors with well-defined margin were 17(36.2%) and tumors with ill-defined margin were 1(2.1%). The tumors without calcification were 31(66%) and the calcified tumors were 16(34%). The tumors with involvement of lymph nodes were 30(63.8) and tumors with single lymph node involved were 1(2.1%) **Conclusion:** A mammogram is necessary for determining the stage of breast cancer. A mammogram can be very useful to determine the location and shape of the lesion for demonstrating a lesion's radiographic features.

INTRODUCTION

Among American women, the second leading cause of death is breast cancer, after lung cancer [1]. Among women of United States, the most frequent type of cancer is breast cancer, excluding skin cancers [2]. One in every eight women is affected with breast cancer at some point in their lives (12%). The most common cause of cancer mortality is breast cancer in women [3]. Breast cancer mortality has been lowering as a result of early discovery, management, and postoperative treatment [5]. For breast cancer screening, mammography is the primary method [6]. It's widely available, well-tolerated, and reasonably priced [7,8]. Women aged 40 to 74 years old have shown an increased mortality risk in randomized controlled studies [9]. Mammography has been proven in several trials to be

especially advantageous for women over the age of 80 years [10,11]. Breast cancer was detected in one out of every seven women in 2007 [12]. Mammography can identify changes in the breast up to two years before symptoms occurrence, mammography is critical in the early identification of breast cancer [13]. The United State Department of Health and Human Services has issued new rules [14]. The Department of Health and Human Services (HHS) and the American College of Radiology (ACR) both suggest screening [15]. Beginning at the age of 40 years, women should have a mammogram every year [16]. Annual mammograms have been found to incite to early identification of breast cancers, when they are treatable and breast-conservation medicines are accessible [17].

The breast is a gland that causes perspiration and its major role is to breastfeed children [18]. Fortunately, with better treatment options, severe mastectomy (surgical excision) is rarely needed nowadays [19]. The breasts of a woman keeps a significant volume during pubescence, which can enlarge by one-third during lactation [20]. In breast, mammary gland is a gland that produces milk [21]. The breasts do not start to expand until pubescence, at which point the skin of the breasts extends to accommodate different forms and sizes [22]. Acinar cells, which are grouped in the lobules and connect with the outside through the lactiferous canals, undergo hypertrophy and activation, resulting in the production and secretion of milk [23]. Breast size increases as a result of stimulation by hormone during menstrual cycle, lactation and pregnancy, besides hormone therapy and obesity [24]. Early in fetal development, the breast is formed by an invagination of the ectoderm of the embryo's ventral region [25,26]. Despite this, some women retain remains of these atrophied structures, and their breasts are more or less complete from the axilla to the groin [27]. The inverted nipples, hypertrophy and gynecomastia in males are all possible anomalies [28]. Mastitis, abscesses, fat necrosis, benign mammary dysplasia, cysts, fibroadenoma and carcinoma are the most common diseases [29]. It's vital to receive a diagnosis as soon as feasible because of the frequency of changes [30]. This demands regular medical checks, as well as breast self-examination, and gynecological treatment regularly [31]. The study's goal was to find mammographic criteria to distinguish between breast lesions. This research helps the physician to compare mammographic masses (malignant or benign) with clinical breast complaints such as palpable lumps, localised pain, and suspicious nipple discharge. The correlation in ages, presence of calcification, margin, and appearance of lymph node enlargements were all used to detect malignant tumours.

METHODS

It was a cross-sectional study comprised of a sample size of 47 female patients after informed consent, calculated via a convenient sampling approach by taking mean of three previous published studies [8,11,32]. The research was performed in Faisalabad, Pakistan from December 2021 to March 2022. Women with age below 29 years were not included in this study. The digital mammography was employed in this study. Females with clinical breast complaints and abnormal mammograms were included in this research. Data were entered and analyzed by SPSS version 20.

RESULTS

Table 1 shows that the age is distributed into four groups.

maximum age frequency of 33(70.2%) is seen in 30-49 years and a minimum frequency of 2(4.3%) is seen in 70 & above years. Table 2 shows the maximum frequency of ill define shape 18 (38.3%) and the minimum frequency of microlobulated shape of 1(2.1%). Table 3 shows the maximum frequency of a well-defined margin of 17(36.2%) and show minimum frequency of an ill-defined margin of 1(2.1%). Table 4 shows the maximum frequency of calcification is absent at 31(66%) and shows the minimum frequency of present calcification at 16(34%). Table 5 shows the maximum frequency of absence of lymph node 30(63.8) and show minimum frequency of single lymph node of 1(2.1%)

Age of patient				
Valid	Frequency	Percent	Valid Percent	Cumulative Percent
<29	2	4.3	4.3	4.3
30-49	33	70.2	70.2	74.5
50-69	10	21.3	21.3	95.7
70 & above	2	4.3	4.3	100.0
Total	47	100.0	100.0	

Table 1: frequency distribution of patient's age

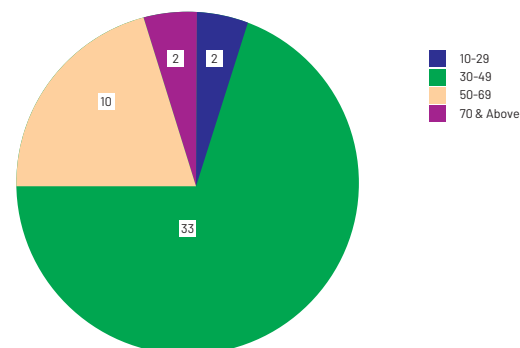


Figure 1: frequency distribution of patient's age

Shape of tumor				
Valid	Frequency	Percent	Valid Percent	Cumulative Percent
round	3	6.4	6.4	6.4
round & oval	2	4.3	4.3	10.6
ill defined	18	38.3	38.3	48.9
microlobulated	1	2.1	2.1	51.1
oval	13	27.7	27.7	78.7
speculated	1	2.1	2.1	80.9
tubal	2	4.3	4.3	85.1
well defined	7	14.9	14.9	100.0
Total	47	100.0	100.0	

Table 2: frequency distribution of tumor's shape

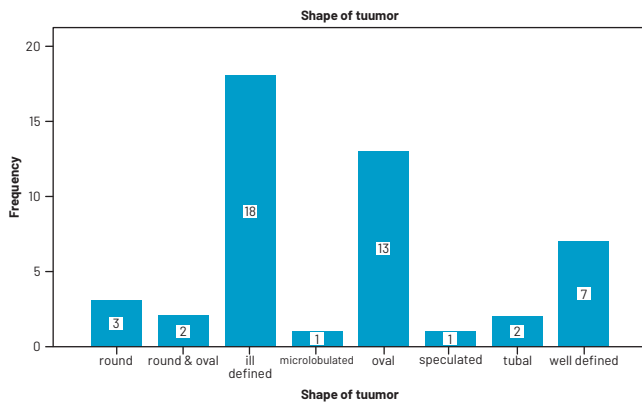


Figure 2: frequency distribution of tumor's shape

Margin of tumor				
Valid	Frequency	Percent	Valid Percent	Cumulative Percent
round	3	6.4	6.4	6.4
ill defined	1	2.1	2.1	8.5
irregular	1	2.1	2.1	10.6
lobulated	6	12.8	12.8	23.4
loculated	2	4.3	4.3	27.7
well-defined	17	36.2	36.2	63.8
obscured	2	4.3	4.3	68.1
oval	2	4.3	4.3	72.3
speculated	13	27.7	27.7	100.0
Total	47	100.0	100.0	

Table 3: frequency distribution of tumor's margin

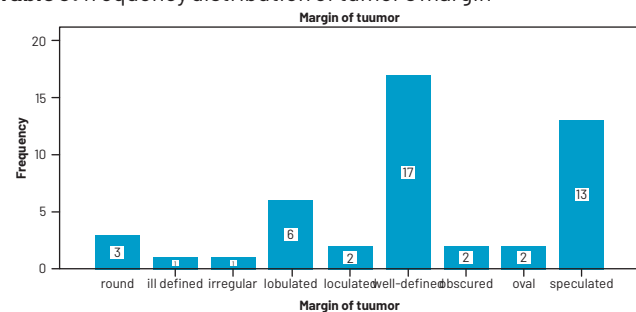


Figure 3: frequency distribution of tumor's margin

Calcification				
Valid	Frequency	Percent	Valid Percent	Cumulative Percent
present	16	34.0	34.0	34.0
absent	31	66.0	66.0	100.0
Total	47	100.0	100.0	

Table 4: frequency distribution of calcification

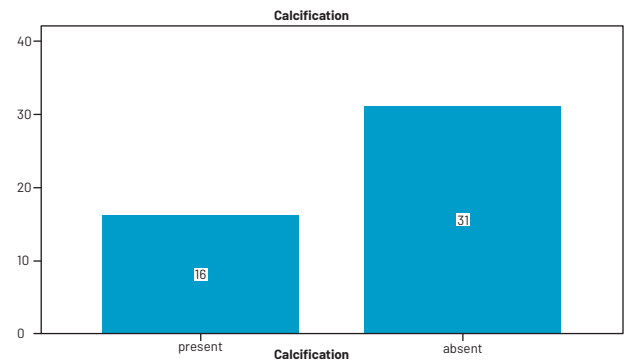


Figure 4: frequency distribution of calcification

Lymph nodes involvement				
Valid	Frequency	Percent	Valid Percent	Cumulative Percent
present	15	31.9	31.9	31.9
absent	30	63.8	63.8	95.7
single	1	2.1	2.1	97.91
multiple	1	2.1	2.1	100.0
Total	47	100.0	100.0	

Table 5: frequency distribution of lymph nodes involvement

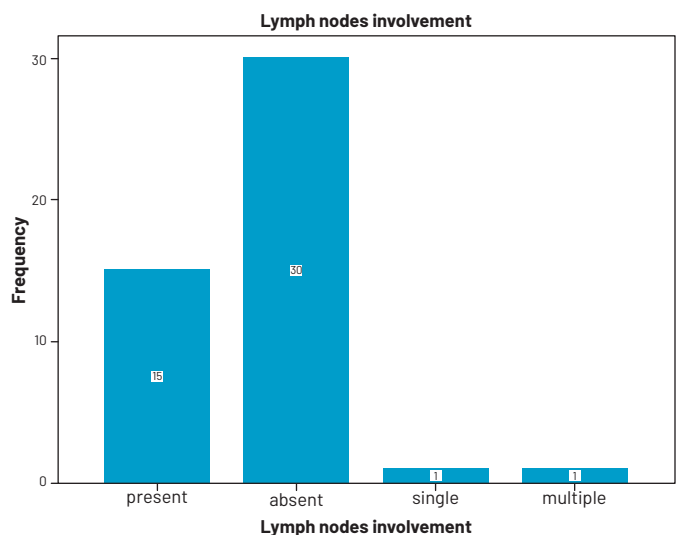


Figure 5: frequency distribution of lymph nodes involvement

DISCUSSION

One in every eight women affected by breast cancer. Breast cancer mortality has been lowering as a result of early discovery, management, and postoperative treatment. For breast cancer screening, mammography is the primary method. In the current study, the age was distributed into four groups. Maximum age frequency of 33(70.2%) is seen in 30-49 years and a minimum frequency of 2(4.3%) is seen in 70 & above years. Another previously published study by Eatizaz Abdelkareem Ahmed Alazhari published in 2017 has similar results that the most affected age group is (40-50) years. In the current study, the maximum frequency of an ill-defined shape was 18 (38.3%), and the minimum frequency of a microlobulated shape of 1(2.1%). Another

previously published study by Ali et.al., published in 2016 has similar results that the mean age is 50-52 years. In the current study the maximum frequency of a well-defined margin of 17(36.2%) and show minimum frequency of an ill-defined margin of 1(2.1%). Another previously published study by Salih et.al., published in 2015 has similar results that found that well defined margins were 16(25%) and speculated angulation were 13(20.3%). In the current study, the maximum frequency of calcification was absent at 31(66%) and showed the minimum frequency of present calcification at 16(34%). Another previously published study by Ali et.al., published in 2016 shows microcalcification 33%. In the current study, patients with absent lymph node were 30(63.8%), and single lymph node 1(2.1%). Another previously published study by Salih et.al., published in 2015 found the appearance lymph with majority of absent in 41(64.1%) and present in 20(31.2%).

CONCLUSION

Mammography is used to investigate breast disease such as lesions. A mammogram is necessary for determining the stage of breast cancer and is useful for demonstrating a lesion's radiographic features. The study found that the lesions were common in 30 to 49 years of age. The most frequent tumors diagnosed using mammography was ill-defined tumors in shape and calcifications were absent in most cases.

REFERENCES

- [1] Sung h, ferlay j, siegel rl, laversanne m, soerjomataram i, jemal a, et al. Global cancer statistics 2020: globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *Ca: a cancer journal for clinicians*. 2021;71(3):209-249.
- [2] Miller kd, fidler-benaoudia m, keegan th, hipp hs, jemal a, siegel rl. Cancer statistics for adolescents and young adults, 2020. *Ca: a cancer journal for clinicians*. 2020;70(6):443-459.
- [3] Wishart gc, azzato em, greenberg dc, rashbass j, kearins o, lawrence g, et al. Predict: a new uk prognostic model that predicts survival following surgery for invasive breast cancer. *Breast cancer research*. 2010;12(1):1-10.
- [4] Olfson m, gerhard t, huang c, crystal s, stroup ts. Premature mortality among adults with schizophrenia in the united states. *Jama psychiatry*. 2015;72(12):1172-1181.
- [5] Leong sp, shen z-z, liu t-j, agarwal g, tajima t, paik n-s, et al. Is breast cancer the same disease in asian and western countries? *World journal of surgery*. 2010;34(10):2308-2324.
- [6] Bleyer a, baines c, miller ab. Impact of screening mammography on breast cancer mortality. *International journal of cancer*. 2016;138(8):2003-12.
- [7] Kelly km, dean j, comulada ws, lee s-j. Breast cancer detection using automated whole breast ultrasound and mammography in radiographically dense breasts. *European radiology*. 2010;20(3):734-742.
- [8] Ali sbma. Study of breast disease using mammography: sudan university of science and technology; 2016.
- [9] Jacobs ij, menon u, ryan a, gentry-maharaja, burnell m, kalsi jk, et al. Ovarian cancer screening and mortality in the uk collaborative trial of ovarian cancer screening (ukctocs): a randomised controlled trial. *The lancet*. 2016;387(10022):945-956.
- [10] Lee ch, dershaw dd, kopans d, evans p, monsees b, monticciolo d, et al. Breast cancer screening with imaging: recommendations from the society of breast imaging and the acr on the use of mammography, breast mri, breast ultrasound, and other technologies for the detection of clinically occult breast cancer. *Journal of the american college of radiology*. 2010;7(1):18-27.
- [11] Salih mha. Characterization of breast tumors using mammography: sudan university of science and technology; 2015.
- [12] Liu l, rissling m, natarajan l, fiorentino l, mills pj, dimsdale je, et al. The longitudinal relationship between fatigue and sleep in breast cancer patients undergoing chemotherapy. *Sleep*. 2012;35(2):237-245.
- [13] Milosevic m, jankovic d, milenkovic a, stojanov d. Early diagnosis and detection of breast cancer. *Technology and health care*. 2018;26(4):729-759.
- [14] Health udo, services h. Us department of agriculture. 2015-2020 dietary guidelines for americans. December 2015. 2019.
- [15] Seung sk, larson da, galvin jm, mehta mp, potters l, schultz cj, et al. American college of radiology (acr) and american society for radiation oncology (astro) practice guideline for the performance of stereotactic radiosurgery (srs). *American journal of clinical oncology*. 2013;36(3):310.
- [16] Arleo ek, hendrick re, helvie ma, sickles ea. Comparison of recommendations for screening mammography using cisnet models. *Cancer*. 2017;123(19):3673-3680.
- [17] Schneble ej, graham lj, shupe mp, flynt fl, banks kp, kirkpatrick ad, et al. Current approaches and challenges in early detection of breast cancer recurrence. *Journal of cancer*. 2014;5(4):281.
- [18] Sabha bh, alzhairani f, almehdar ha, uversky vn,

- redwan em. Disorder in milk proteins: lactadherin multifunctionality and structure. *Current protein and peptide science*. 2018;19(10):983-997.
- [19] Mauermann e, ruppen w, bandschapp o. Different protocols used today to achieve total opioid-free general anesthesia without locoregional blocks. *Best practice & research clinical anaesthesiology*. 2017;31(4):533-545.
- [20] Pawłowski b, żelaźniewicz a. The evolution of perennially enlarged breasts in women: a critical review and a novel hypothesis. *Biological reviews*. 2021;96(6):2794-809.
- [21] Macias h, hinck l. Mammary gland development. *Wiley interdisciplinary reviews: developmental biology*. 2012;1(4):533-557.
- [22] Fuqua js. Treatment and outcomes of precocious puberty: an update. *The journal of clinical endocrinology & metabolism*. 2013;98(6):2198-2207.



Original Article

Safety and Efficacy of Ureterorenoscopy in the Management of Ureteric Stone During Pregnancy

Aftab Ahmed Channa¹, Sadia Khanam², Shumaila Ashfaq³, Nauman Ahmed⁴, Abdul Basit Niazi⁵ and Muhammad Zahid Ahmad⁶

¹Department of Urology, Islam Medical & Dental College, Sialkot, Pakistan

²Department of Obstetrics and Gynecology, Islam Medical & Dental College, Sialkot, Pakistan

³Department of Anesthesia, Islam Medical & Dental College, Sialkot, Pakistan

⁴Department of Urology, Government KOT Khuwaja Saeed Teaching Hospital, Lahore, Pakistan

⁵Department of Urology, Niazi Medical College Sargodha, Pakistan

⁶Department of Urology, King Edward Medical University (Pakistan) KEMU/Mayo Hospital, Lahore, Pakistan

ARTICLE INFO

Key Words:

Ureterorenoscopy, Clinical symptoms, Ureteral Calculi, pregnancy

How to Cite:

Ahmed Channa, A. ., Khanam, S. ., Ashfaq, S. ., Ahmed, N. ., Basit Niazi, A. ., & Zahid Ahmad, M. (2022). Safety And Efficacy of Ureterorenoscopy in The Management of Ureteric Stone During Pregnancy: Ureterorenoscopy in Management of Ureteric Stone During Pregnancy. *Pakistan BioMedical Journal*, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.592>

***Corresponding Author:**

Aftab Ahmed Channa
 Department of Urology, Islam Medical & Dental College, Sialkot, Pakistan
draftab.channa@gmail.com

Received Date: 15h June, 2022

Acceptance Date: 21st June, 2022

Published Date: 30th June, 2022

ABSTRACT

Ureterorenoscopy is a procedure to examine the urinary tract using an ureteroscope.

Objective: To identify the effectiveness of ureterorenoscopy for treatment of ureteric stones in pregnant women. **Methods:** A total of 33 pregnant women visited the Obstetric and Urology departments of hospital were included in the study. They had complaint of renal colic pain. Their demographic features, age, trimester and clinical features were noted during initial profile records. The statistical analysis using SPSS Version-21 was performed. **Results:** In this research 33 subjects presented with renal colic pain belonging to a gestation period of 8 weeks to 33 weeks. Ureterorenoscopy was performed on all patients (right side stone in 18, 13 with the left side, and 2 with bilateral). Hematuria was observed in 6 patients, nausea vomiting in 18 patients, the two were presented with acute urine retention, and one patient presented with oliguria due to bilateral ureteric obstruction. Stone was broken, and clearance was observed in 28 (85%) patients. In other 5 (15%) patients, stone was pushed back, and obstruction was relieved. **Conclusion:** Ureterorenoscopy is a definitive first-line Treatment. It is safe and effective in pregnancy with calculus obstructive uropathy.

INTRODUCTION

In the mid-1980s, kidney stones were treated using lithotripsy and percutaneous nephrolithotomy, while ureterorenoscopy was rarely carried out until the 1990s, now the ureteroscopes was being widely used for operating kidney and ureteral stones. Ureterorenoscopy is a process of performing endoscopy, passing it through the urethra, bladder to enter the upper urinary tract. The use of ureterorenoscopy has gained more popularity in recent

years. The advancements in procedures have made it a minimally invasive therapy with the least per-operative complications. According to various studies, the formation of stones in the bladder and urinary tract is highly frequent in pregnant women [1]. Patients presenting with urolithiasis during the first or second trimester normally have the complaint of renal colic pain, difficulty in urination, fever, tenderness, and hematuria. Some studies showed

left hydronephrosis >10mm to be one of the clinical symptoms that predict urolithiasis [2,3]. The most common clinical symptom of urolithiasis in pregnant women is pain on the side of the torso (also called flank pain), and in a study of 144 subjects, around 96.5% of cases reported it [8]. Other symptoms reported are hematuria, urinary retention, and other symptoms such as dysuria, nausea and vomiting [4,5]. However, traditional clinical signs can be less significant to base the diagnosis as back or flank pain, and hematuria can also result from the usual pregnancy changes [6]. In pregnant women, urolithiasis management needs detailed clinical assessment and considerate examination of imaging risks to the mother and fetus. As reported, around 0.026% to 0.531% of urinary calculi occurs during pregnancy and may be related to 40% of premature births. Due to the fetus's sensitivity and risks involved with radiation exposure, many scans test are entirely skipped in diagnosing the patient with renal colic pain. According to Lewis's study, such symptoms can lead to premature birth, abortion, or low-birth-weight infants [7,8]. Different methods are widely used to manage ureteric stones depending on the size of the stone and complexity, from ureterorenoscopy to laparoscopic ureterolithotomy extracorporeal shockwave lithotripsy (ESWL). Comparatively, the results of Ureterorenoscopy are reported to be 76.9%-100% accurate than other available treatments [9,10]. Therefore, an abdominal ultrasound examination is mostly chosen for pregnant patients and conclusive investigations are carried out in cases with abdominal pain and alleged renal colic. Around 5-15% in the world are affected by renal colic, with 50% having a repeat rate. Due to the high prevalence, Urinary stone disease is a significant liability in Pakistan healthcare departments [11].

METHODS

The study was conducted at Islam Medical and Dental College/ Islam Teaching Hospital, Sialkot from Jan 2016 to Dec 2019. A total of 33 pregnant women attended the Obstetric and Urology departments of hospital were included in the study. The sample size was calculated by taking the confidence interval as 95%, margin of error as 5%. Non-probability consecutive sampling was employed [12]. Clinical details, including checks for renal functioning, urine culture, ultrasound and consultation records of obstetricians were collected. To ensure safety of the fetus, no KUB, IVU, or CT scan was done on the patients. Inclusion Criteria: Patients with renal colic pain, Patients with ureteric calculi, Patients with hydronephrosis. Patients who didn't respond to oral antibiotics were referred for surgical interventions. Ureterorenoscopy was performed

as first-line treatment in all cases with semirigid ureteroscope and DJ stent placement. After induction of spinal anesthesia, Patients were laid in lithotomy position for surgery, the surgeon elevated the right side of patient to divert pressure on the uterus's inferior vena cava. Fetal heart sounds were monitored throughout the obstetrician's operation while ureterorenoscopy was performed using 6/7.5 for semirigid ureteroscope (Wolf) with a 4.2 × 4.6 Fr working channel and 7.3/8 with a 3.6 working channel. For emergencies of the ureteric orifice, balloon dilators were available. Renal ultrasound monitoring was done without fluoroscopy, and fragmentation of stones was done using pneumatic lithoclast, and Upper ureteric stones were confined in the dormia basket during disintegration. An introduction of a DJ stent was done at the close of the process in almost all the cases. Other post-operative care and fetal monitoring were advised for women showing symptoms of cramps and vaginal discharge. Patients were released according to the health of the fetus and the child.

RESULTS

Out of the 33 patients, all women were presented with renal colic pain. The age distribution is shown in the table below (table 1). The patients' mean age is calculated as 31 years (standard deviation: 5.71; range: 22-41 years). The most repeated age groups were 30-34 years with nine patients (27%) and 22-26 years and 38-41 years with seven patients (21%) each with the gestation period varying from 8 weeks (1st trimester) to 33 weeks (3rd trimester). The stone size ranged from 0.4cm to 1.2cm, with a mean size of 0.95 cm.

Demographics	Variables	Total Population	Clinical Symptoms	
			Variable	PL=33
	Mean Age ± SD	31±5.71	Stone Size-(cm)	
	Max	41	Mean Size ± SD	0.95± 0.307
	Min	22	Max	1.2
	Gender, No (%)	Females: 33 (100%)	Min	0.4

Table 1: Demographics of Patients and other clinical symptoms

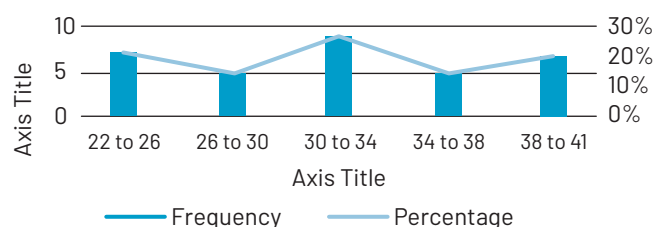


Figure 1: Age-Range of Ureteric Stones in Pregnant Women

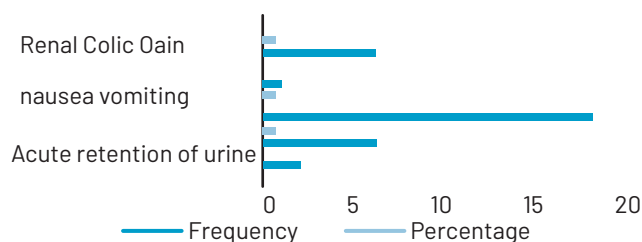


Figure 2: Clinical Symptoms of Patients with ureteric Calculi

Patients presenting during the first trimester were 4, and 2nd trimester was 17, and 12 patients were presented in 3rd trimester. Severe renal colic pain was observed in 6 patients (18%) and haematuria was presented in 6 patients (18%), nausea vomiting in 18 patients (55%), two were presented with acute retention of urine (6%), and one patient (3%) presented with oliguria due to bilateral ureteric obstruction.

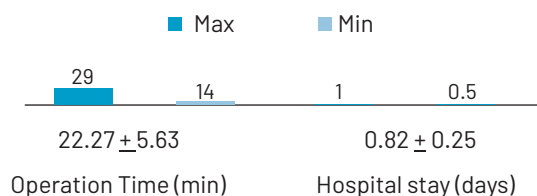


Figure 3: Details of Operation time of Patients The average time taken for the surgical procedure was 22.27 ± 5.63 min while the maximum time noted was 29 mins and 14 mins minimum in the treatment of all the 33 cases; however, the hospital stays varied from 1 day to 6 hours with an average time taken 9.84 hours and 0.82 (in days)

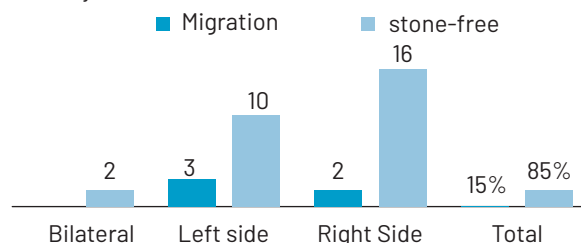


Figure 4: Post-operative Results of stone-clearance location wise

Amongst all the patients presented with renal colic pain, 18 presented with the right side, out of which 48% got stone cleared, and 6% had reported migration towards kidney. While 13 patients presented stones on the left side, 30% successful stone clearance and 9% migration, and lastly, 6% had a successful stone clearance on the bilateral side. Thus, overall stone was broken, and clearance was achieved in 28 patients (85%), and in five patients (15%), stones were pushed back and obstruction was relieved. However, no obstetric or urological complications were noted. Only temporary difficulty in urination and burning micturition in few cases were recorded.

DISCUSSION

According to studies, about 25 to 40% of pregnant patients

need intervention, thus raising the need to manage ureteric stones through ureterorenoscopy or other methods. Due to the risks and sensitivity of pregnancy and fetus involvement, ureteric stone removal has, by far, proven to be the safest and effective method. In a published study (2008), the meta-analysis conducted on 108 subjects, ureterorenoscopy treatments were considered safe and efficient [13]. Commonly the rate of stone clearance in pregnant women is higher approximately 80% of the cases are treated clinically. Furthermore, the witnesses' complication rates of URS are low as reported in studies of Semins and colleagues; out of 108 patients, 14 reports showed a complication rate of 8.3% is similar in results in contrast to non-pregnant women. Additionally, Ureterorenoscopy is also reported to be less costly a technique [14]. In our study, the patients' mean age is calculated as 31 years (standard deviation: 5.71; range: 22-41 years). While the most repeated age groups were 30-34 years (27%) each, however, the gestation period is varying from 8 weeks (1st trimester) to 33 weeks (3rd trimester). The comparative study reported 25.5 ± 4.6 years (range 16-41 years), and the gestation period of 9 to 36 weeks [15]. Semin and colleagues found a 67.9%, 63.4%, and 66.5% clearance rate in the upper, mid, and lower ureter [16]. While in our study amongst all the patients presented with renal colic pain, on the right, left, and bilateral side; an overall stone was broken, and clearance achieved in 28 patients (85%) and five patients (15%) stones were pushed back, and obstruction was relieved. However, no obstetric or urological complications were noted [17]. Only temporary difficulty in urination and burning micturition in few cases were recorded. Some other studies show the risk of premature birth and renal colic and its complications increase early birth risk [18-21]. In our study, the average time taken for the surgical procedure was 22.27 ± 5.63 min in the treatment of all the 33 cases; however, the hospital stays varied from 1 day to 6 hours. The stone size ranged from 0.4cm to 1.2cm, with a mean size of 0.95 cm. In similar works on 128 pregnant women suffered from acute renal colic/ ureteral calculi of Foshan Maternal and Child Health Hospital, the success rate was 83 to 96%. Abdel-Kader reported ureterorenoscopy conducted on 17 women with stone-free rate to be 100% [22,23].

CONCLUSION

Thus, we can define ureterorenoscopy as a preferred first-line treatment that is harmless and effective for treating obstructive ureteric stones during pregnancy.

REFERENCES

- [1] Korkes F, Rauen EC, Heilberg IP. Urolithiasis and pregnancy. *Brazilian Journal of Nephrology*. 2014 Jul;36:389-95 English, Portuguese. doi:

- 10.5935/0101-2800.20140055.
- [2] Drago JR, Rohner Jr TJ, Chez RA. Management of urinary calculi in pregnancy. *Urology*. 1982 Dec 1;20(6):578-81. doi: 10.1016/0090-4295(82)90302-8.
- [3] Fregonesi A, Dias FG, Saade RD, Dechaalani V, Reis LO. Challenges on percutaneous nephrolithotomy in pregnancy: Supine position approach through ultrasound guidance. *Urology Annals*. 2013 Jul;5(3):197-9. doi: 10.4103/0974-7796.115750.
- [4] Abdel-Kader MS, Tamam AA, Elderwy AA, Gad M, El-Gamal MA, Kurkar A, et al. Management of symptomatic ureteral calculi during pregnancy: Experience of 23 cases. *Urology annals*. 2013 Oct;5(4):241-4. doi: 10.4103/0974-7796.120294.
- [5] Lewis DF, Robichaux AG 3rd, Jaekle RK, Marcum NG, Stedman CM. Urolithiasis in pregnancy. Diagnosis, management and pregnancy outcome. *International Journal of Reproductive Medicine* 2003 Jan;48(1):28-32. doi.org/10.1097/01.OGX.0000074323.48257.83
- [6] Abdel-Gawad M, Kadasne R, Anjekar C, Elsobky E. Value of Color Doppler ultrasound, kub and urinalysis in diagnosis of renal colic due to ureteral stones. *official journal of the Brazilian Society of Urology* 2014 Jul-Aug;40(4):513-9. doi: 10.1590/S1677-5538.IBJU.2014.04.10.
- [7] N'gamba M, Lebdaï S, Hasting C, Panayotopoulos P, Ammi M, Sentilhes L, et al. Acute renal colic during pregnancy: management and predictive factors. *The Canadian Journal of Urology*. 2015 Apr 1;22(2):7732-8.
- [8] Andreoiu M, MacMahon R. Renal colic in pregnancy: lithiasis or physiological hydronephrosis?. *Urology*. 2009 Oct 1;74(4):757-61. doi: 10.1016/j.urology.2009.03.054.
- [9] Korkes F, Gomes SA, Heilberg IP. Diagnóstico e tratamento de litíase ureteral. *Brazilian Journal of Nephrology* 2009 Aug 24;31(1):55-61.
- [10] Butler EL, Cox SM, Eberts EG, Cunningham FG. Symptomatic nephrolithiasis complicating pregnancy. *Obstetrics and gynecology*. 2000 Nov;96(5 Pt 1):753-6. doi: 10.1016/s0029-7844(00)01017-6.
- [11] Moe OW. Kidney stones: pathophysiology and medical management. *Lancet*. 2006 Jan 28;367(9507):333-44. doi: 10.1016/S0140-6736(06)68071-9.
- [12] Tipu SA, Malik HA, Mohhayuddin N, Sultan G, Hussain M, Hashmi A, et al. Treatment of ureteric calculi-use of Holmium: YAG laser lithotripsy versus pneumatic lithoclast. *JPMA*. 2007 Sep;57:440-3.
- [13] Soomro MI, Shaikh NA, Jokhio AH. Ureterolithotripsy With Semi-Rigid Ureteroscope: An Early Experience With 100 Cases. *Journal Of Surgery Pakistan*. 2007 Jul;12(3):98.
- [14] Charalambous S, Fotas A, Rizk DE. Urolithiasis in pregnancy. *International Urogynecology Journal Pelvic Floor Dysfunction*. 2009 Sep;20(9):1133-6. doi: 10.1007/s00192-009-0920-z.
- [15] Semins MJ, Trock BJ, Matlaga BR. The safety of ureteroscopy during pregnancy: a systematic review and meta-analysis. *The Journal of urology*. 2009 Jan;181(1):139-43. doi: 10.1016/j.juro.2008.09.029.
- [16] Wymer K, Plunkett BA, Park S. Urolithiasis in pregnancy: a cost-effectiveness analysis of ureteroscopic management vs ureteral stenting. *American Journal of Obstetrics and Gynecology* 2015 Nov;213(5): 691.e1-8. doi: 10.1016/j.ajog.2015.07.024.
- [17] White W, Klein F. Five-year clinical experience with the Dornier Delta lithotripter. *Urology*. 2006 Jul;68(1):28-32. doi: 10.1016/j.urology.2006.01.031
- [18] Johnson EB, Krambeck AE, White WM, Hyams E, Beddies J, Marien T, et al. Obstetric complications of ureteroscopy during pregnancy. *The Journal of urology* 2012 Jul;188(1):151-4. doi: 10.1016/j.juro.2012.02.2566.
- [19] Nawaz A, Wazir BG, Orakzai AN. Early Experience of Pneumatic Lithoclast for The Management of Ureteric Stones at Peshawar. *Journal of Ayub Medical College, Abbottabad: JAMC*. 2016 Jul 1;28(3):542-4.
- [20] Kamran T, Zaheer K, Akhtar MS. Pneumatic lithotripsy for the management of ureteric calculi. *Journal of the College of Physicians and Surgeons—Pakistan: JCPSP*. 2003 Feb 1;13(2):101-3.
- [21] Manan A, Muhammad A, Asad S, Arshad M, Riaz T. Efficacy of pneumatic lithoclast in the management of ureteric calculi.
- [22] Nawaz A, Wazir BG, Orakzai AN. Early Experience Of Pneumatic Lithoclast For The Management Of Ureteric Stones At Peshawar. *Journal of Ayub Medical College, Abbottabad: JAMC*. 2016 Jul 1;28(3):542-4.
- [23] Khan AA, Hussain SA, Khan NU, Kamran Majeed SM, Sulaiman M. Safety and efficacy of ureteroscopic pneumatic lithotripsy. *Journal of College of Physicians and Surgeons Pakistan* 2011 Oct 1;21(10):616-9.



Original Article

Assessment of Knowledge About Breast Cancer Screening Among Female Faculty of University of Lahore

Saira Farhat¹ Tallat Anwar Faridi² Sajid Hameed² Khalid Mehmood³ Muhammad Azzam Khan⁴¹Central park medical college, Pakistan²The university institute of public health ,Faculty of allied health sciences The university of Lahore. , Pakistan³District Health Authority Bahawalpur, Pakistan⁴Department of Rehabilitation Sciences, Faculty of Allied health Sciences the University of Lahore, Pakistan

ARTICLE INFO

Key Words:

Breast Cancer Screening, Knowledge, BSE, CBE, Mammography

How to Cite:

Farhat, S. ., Anwar Faridi, T. ., Hameed, S. ., Mehmood, K. ., & Azzam Khan, M. . (2022). Assessment of Knowledge About Breast Cancer Screening Among Female Faculty of University of Lahore: Assessment of Knowledge About Breast Cancer Screening Among Female Faculty of University of Lahore. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.544>

***Corresponding Author:**

Saira Farhat
 Central park medical college, Lahore, Pakistan
drsairafarhat@gmail.com

Received Date: 11th June, 2022Acceptance Date: 20th June, 2022Published Date: 30th June, 2022

ABSTRACT

Carcinoma of breast is now the most frequent of all cancers, both in male and female malignancies. It is also the fifth leading cause of death from all types of malignancies, and the first among those tumors that kill women. **Objective:** To assess the knowledge about breast cancer screening among female faculty of University of Lahore, Pakistan. **Methods:** This was a cross-sectional descriptive research that used a non-probability purposive sampling technique. After getting permission from the participants, data from 356 female faculty members at the University of Lahore was obtained. SPSS version 22 was used to evaluate and enter the data. **Results:** The findings suggested that female faculty members had a moderate understanding of cancer screening. Even though majority of the participants were aware that mammography is a fundamental and conventional technique for breast cancer screening, they were unaware of when to begin and how frequently it should be done. Respondents also knew what breast self-examination (BSE) and clinical breast examination (CBE) were, but they didn't know when they should begin or how often they should be conducted. **Conclusions:** In summary, female academic staff at the University of Lahore have a moderate level of knowledge. It is suggested that breast cancer screening methods be made more widely known and educated about through frequent conferences and seminars highlighting the proper age and time for starting BSE, CBE, and Mammography, as well as the need of doing these procedures on a regular basis.

INTRODUCTION

Cancer can be defined as the unchecked and aberrant proliferation of cells, which results in mortality as these malignant cells spread throughout the body [1]. Carcinoma of breast has a wide range of characteristics, including differences across tumors from different persons (inter-tumor variance) and alterations between cancer cells [2-4]. Breast cancer is currently the most common of all cancers, including both male and female malignancies. It is also the fifth leading cause of mortality among all types of malignancies, and the top among those tumors that kill women. Asia has the highest breast carcinoma incidence and mortality rates, at 45.4 percent and 50.5 percent,

correspondingly. Cancer of breast has the highest incidence of all malignancies in both males and females in Pakistan, according to WHO. [5,6]. It is also predicted that one out of every nine women may develop breast cancer, with the incidence being 2.5 times greater in Asia than in adjacent nations such as India and Iran. [7]. According to a systematic study undertaken by the American Cancer Society, lower mortality in breast cancer is directly connected to the length of follow-up, and mammography screening can also lead to enhanced life expectancy. Other studies have revealed that the stage at the time of diagnosis might predict survival odds; the earlier the

diagnosis, the better the chances of survival. Furthermore, early identification and detection, particularly with mammograms, may reduce the incidence of advanced breast cancer (stage II B) [8-11]. As a result, screening is critical for illness prevention, early detection, and treatment. Breast self-examination, clinical breast examination, and mammography are all screening modalities. Breast self-examination and clinical breast inspection are no longer advised by the American Cancer Society (ACS), but they are still used in developing nations. The justification for this is because these are non-invasive, non-expensive techniques that don't require any special apparatus and can be done in the privacy of one's own home [12, 13]. Many research have shown that there is a knowledge and awareness gap when it comes to breast cancer and its screening procedures. Among Pakistan, many studies have been conducted to investigate breast cancer awareness and knowledge in various populations of Pakistani females. Khalid A et al., did a research in Lahore in 2018. Only 34% of the recruited girls had known of breast self-examination, 30% had known of clinical breast examination, and 29.5 percent had known of mammography, according to the study's findings. Our research population's awareness of breast cancer, its risk factors, signs and symptoms, and early identification procedures was generally lacking [14]. In a rural part of Lahore, another KAP research on breast self-examination was done. For statistics, 135 rural Lahore women were surveyed. According to the data, 19.3% of people surveyed knew about breast self-examination, 28.9% knew about breast cancer, and only 24.4 percent knew about breast self-examination, while 35.6 percent knew that only physicians may check the breast. The period between breast self-examinations was known by 34.1 percent of research participants, but not by 46 percent. The findings indicated that in rural Lahore, women of reproductive age lack knowledge, attitudes, and behaviours [15]. In 2020, the KAP research was undertaken to determine the frequency of breast self-examination within Pakistani women. There were 385 women in the research, with an average age of 30.09 +/- 7.09 years. Overall, 259 individuals indicated they had accurate information, 123 people said they had suitable actions, and 187 people said they had favorable attitudes regarding breast self-examination. But unfortunately, it was discovered that there was a lack of popular knowledge regarding breast self-examination [16]. In Tehran, Iran, a study was designed to assess BSE knowledge, attitudes, and behaviours among females over the age of 20. 40.57 percent of the participants knew something about breast cancer, and 23.03 percent knew something about BSE. While 47.86 percent of the participants were positive, only 11.6 percent of them practiced BSE on a monthly basis.

According to the findings, the participants in this study had inappropriate BSE understanding, attitudes, and behaviours [17]. In the year 2020, Sachdeva S et al., published a KAP research on BSE in Indian women. A total of 1000 women aged 30 or older from all around India took part in this study. 54.4 percent, 15.1 percent, 21.3 percent, and 9.2 percent of the respondents came from Northern, Southern, Western, and Eastern India, respectively. The cumulative KAP score was 70 out of a potential 110, as per the data. Out of a maximum of 30, 52, and 28, the scores for the knowledge, attitude, and practices categories were 22.0 (5.0), 36.0 (7.0), and 13.0 (8.0), accordingly. [18]. The study had been carried out on the female faculty members to know their level of knowledge on breast screening. The assessment of knowledge on breast cancer screening among female faculty members had importance in context that teachers are associated with the students and they can play an important part in educating their students about breast cancer screening methods. So, first, there is need to assess their level of knowledge. Assessing how much people know about breast cancer screening and how they do it would assist not just to raise awareness about it, but also to identify the need for ongoing health education initiatives to enhance people's understanding of the illness and routine screening procedures.

METHODS

It is a descriptive cross sectional study conducted at University of Lahore, Lahore, Pakistan including 356 participants. The study duration was nine months. After reviewing literature questionnaire had been formed. The validity of research instruments were determined by consulting the educational experts by researchers, the reliability of instrument was evaluated by use of pilot testing. Pilot testing was done on 30 participants who were not a part of study and reliability was determined through Cronbach Alpha which was 0.78. There were total 38 questions related to knowledge about breast cancer and breast cancer screening methods. One point is given for a correct answer and zero for an incorrect or no answer. Knowledge had a maximum score of 38 (100%) and a lowest value of 0 (0 percent). The knowledge level was graded as "poor" for scores ranging from 0 to 49%, "moderate" for scores ranging from 50 to 79%, and "high" for scores ranging from 80 to 100% [19,20]. Data were collected after approval from Ethical Review Board of University of Lahore. Data were analyzed by utilizing SPSS version 25.0. Categorical data were presented as frequency distribution tables. Chi-Square was used to determine the association of knowledge level and sociodemographic variables. P value of less than or equal to 0.05 ($P \leq 0.05$) was taken as significant.

RESULTS

The total number of participants were three hundred and fifty six. Among them 175 (49.2%) participants were between the age of 24 to 30 years while 181 (50.8%) were above the age of 30 years up to 47 years. Out of them 159 (44.7%) females were unmarried, and 197 (55.3%) were married. Most of the participants have M.Phil. / PhD degree i.e. 239 (67.1%) and 101 (28.4%) hold Masters/Graduation degree, the remaining participants 16 (4.5%) have Professional/Technical qualification. And most of the respondents i.e. 258 (72.5%) were lecturers and senior lecturers while 78 (21.9%) of them were assistant professors, however 20 (5.6%) of the respondents did not reply to this question. Out of total 93(26.1%) were from diet and nutrition sciences department, and there were 73 (20.5%) were from pharmacy department and 55 (15.4%) belonged to nursing department and 45 (12.6%) were from physical therapy department, while 36 (10.1%), 30 (8.4%) belonged to medical lab technology and health professional technologies respectively, on the other hand only 13 (3.7%) and 7 (2.0%) female faculty members participated from public health and from radiological and imaging technology respectively. Remaining 4 (1.1%) participants did not respond to this question. Results showed that all of the respondents, 356 (100%) have heard of breast cancer. Most common source of information 271 (76.1%) regarding breast cancer was Media (TV, Radio, Internet etc.) followed by books 251 (70.5%), hospital or any health care person 215 (60.4%), conferences/seminars 188 (52.8%), friends or family members 175 (49.2%), lecture 143 (40.2%). All the faculty members 347 (97.5%) knew that breast cancer is one of the most common cancer among females, only 9 (2.5%) had no knowledge. 260 (73.0%) of respondents thought that only females are effected by breast cancer or they don't know about this, while 96 (27.0%) gave correct answer to this question. Majority of the female faculty members 332 (93.3%) answered that breast cancer cannot be transmitted from one person to another person, while 24 (6.7%) participants did not give correct answer or don't know about this. According to this table that 258 (72.5%) female faculty members women below 30 years of age can get breast cancer while 98 (27.5%) don't think or don't know about this. Most commonly mentioned signs and symptoms of breast cancer were lump in breast 334 (93.8%), pain in breast 288 (80.9%), lump under the armpit 270 (75.8%) and change in size, shape or color of breast 255 (71.6%). On the other hand, 220 (61.8%), 187 (52.5%), 177 (49.7%), 173 (48.6%) participants responded nipple discharge, weight loss, dimpling of breast and ulceration of breast as the signs and symptoms of breast cancer respectively. Positive family history of breast cancer was identified as a main risk factor by 327 (91.9%) of

participants. Other commonly identified risk factors by female faculty members were increasing age 236 (66.3%), obesity 216 (60.7%), and never having breastfed a child 207 (58.1%). On the other hand less commonly considered risk factors were early menarche 162 (45.5%), smoking 154 (43.3%), late menopause 147 (41.3%), first child above 30 years of age 136 (38.2%) and 55 (15.4%) of participants considered large breasts as a risk factor of breast cancer. 166 (46.6%) female faculty members knew about the stage of breast cancer which can be cured, while 190 (53.4%) had no knowledge about it. 320 (89.9%) female faculty members knew that early detection of breast cancer increases the chances of survival, while 36 (10.1%) did not have knowledge about this. Among all of the respondents mostly, i.e. 293 (82.3%) of them knew that mammography is one of the screening methods of breast cancer, while 271 (76.1%) and 231 (64.9%) of them considered BSE and CBE as screening methods respectively. Regarding breast self-examination shows that majority of the respondents 293 (82.3%) do not know about the best time to do BSE. Similarly most of the respondents 233 (65.4%) also do not know how often BSE should be done, and more than half of the respondents 183 (51.4%) do not know the age at which BSE should be started. However, many participants 245 (68.8%) knew that BSE should be done by whom. Regarding clinical breast examination (CBE) shows that majority of the respondents 250 (70.2%) do not know how often CBE should be done. Similarly, most of the respondents 240 (67.4%) also do not know at what age CBE should be started and 214 (60.1%) do not know the method of CBE. However, many participants knew that who will perform CBE. All most all of the respondents 333 (93.5%) knew that mammography is the basic and standard screening procedure and 300 (84.3%) knew that very small lump can be detected by mammogram. On the other hand, small number of participants 154 (43.3%) knew about starting age of mammography similarly, less participants 131 (36.8%) knew that how often mammography should be performed. Level of knowledge of the participants according to the correct responses given by participants. Results shows that 68% of the participants were having moderate level of knowledge while 21.6% of the participants had low level of knowledge and only 10.4% of the participants had high level of knowledge. (Table 1) There is a borderline association between "Age" of the respondent and level of knowledge as p-value = 0.05. (Table 2)

Level of Knowledge categories	Age Categories		Total	Chi-Sq	p-value
	24 – 30 Years	30.5 to 47 Years			
"Low" 0 – 49%	44	33	77	6.106	0.05
	25.1%	18.2%	21.6%		
"Moderate" 50 – 79%	119	123	242		
	68.0%	68.0%	68.0%		
"High" 80 – 100%	12	25	37		
	6.9%	13.8%	10.4%		
Total	175	181	356		
	100.0%	100.0%	100.0%		

Table 1: Cross tab of Age with level of knowledge Significant association between the "Designation" of the respondent and knowledge level of respondents was found as P-value is 0.019. (Table 2)

Level of Knowledge categories	Age Categories		Total	Chi-Sq	p-value
	24 – 30 Years	30.5 to 47 Years			
"Low" 0 – 49%	52	18	70	7.892	0.019
	20.2%	23.1%	20.8%		
"Moderate" 50 – 79%	186	46	232		
	72.1%	59.0%	69.0%		
"High" 80 – 100%	20	141	34		
	7.8%	7.9%	10.1%		
Total	258	78	336		
	100.0%	100.0%	100.0%		

Table 2: Cross Tab of Designation with level of knowledge Highly significant association between "Marital Status" "Education Level" and "Department" of the respondents and Level of Knowledge as P-values are 0.001, 0.001, 0.0001 respectively, (Table 3, 4, 5).

Level of Knowledge categories	Age Categories		Total	Chi-Sq	p-value
	24 – 30 Years	30.5 to 47 Years			
"Low" 0 – 49%	36	41	77	13.58	0.001
	22.6%	20.8%	21.6%		
"Moderate" 50 – 79%	117	125	242		
	73.6%	63.5%	68.0%		
"High" 80 – 100%	6	31	37		
	3.8%	15.7%	10.4%		
Total	159	197	356		
	100.0%	100.0%	100.0%		

Table 3: Cross Tab Marital Status with level of knowledge

Level of Knowledge categories	Age Categories		Professional/ Technical	Total	Chi-Sq	p-value
	Graduation - Masters	M.Phil. - PhD.				
"Low" 0 – 49%	18	55	42	77	30.783	< 0.001
	17.8%	23.0%	5.0%	21.6%		
"Moderate" 50 – 79%	59	174	95	24		
	58.4%	72.8%	6.3%	268.0%		
"High" 80 – 100%	242	10	31	37		
	3.8%	4.2%	8.8%	10.4%		
Total	101	239	16	356		
	100.0%	100.0%	100.0%	100.0%		

Table 4: Cross Tab Educational Level with level of knowledge

Level of Knowledge categories	Age Categories								Total	Chi-Sq	p-value
	Diet and Nutrition sciences	Health Professional Technology	Medical Lab. technology	Nursing	Pharmacy	Physical Therapy	Public Health	Radiological and Imaging technology			
"Low" 0 – 49%	16	12	52	0	21	23	0	0	77	214.69	<0.0001
	17.8%	0.0%	5.0%	0.0%	28.8%	51.1%	0.0%	0.0%	21.8%		
"Moderate" 50 – 79%	59	248	277	213	51	22	13	7	238		
	58.4%	0.0%	5.0%	8.2%	69.9%	48.9%	100.0%	100.0%	67.6%		
"High" 80 – 100%	242	0	0	34	1	0	0	0	37		
	3.8%	0.0%	0.0%	61.8%	1.4%	0.0%	0.0%	0.0%	10.5%		
Total	101	30	36	55	73	45	131	7	352		
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%		

Table 5: Cross Tab of Department with level of knowledge

DISCUSSION

The average age of the female faculty members in our study was 31.56+/-4.7 years, whereas the average ages of academics in previous studies were 36.27+/-7 years, 39.02+/-8.7 years, and 44.79+/-7.6 years [21-23]. In this survey, all 356 participants (100%) had heard of breast cancer, and the most prevalent source of knowledge was the media (TV, radio, Internet) with 271 (76.1%), followed by books with 251 percent (70.5 percent). During medical school, the most often cited information source was books and literature, according to a study of physicians and nurses in Punjab and Sindh. [24]. Breast cancer was the most frequent female malignancy, according to almost all of the responders (347, or 97.5 percent). While according to another study cancer of breast is the most frequent malignancy among Pakistani women, according to the findings of a Punjab study of medical and non-medical students. 73 percent of non-medical students and 80 percent of medical students understood this [25]. Positive family history of breast cancer was indicated as a key risk factor by 327 (91.9%) of participants when it came to breast cancer risk factors. Likewise, surveys done in Karachi in 2019 and Ghana in 2019 found that 270 (70.9%) and 236 (83.9%) of participants

consider family history to be a major risk factor, respectively, and also another research performed on community pharmacists discovered that 81.8 percent of pharmacists consider family history to be a main indicator of risk [26,27,28]. As per our research, the most often stated signs and symptoms of breast cancer were a lump in the breast (334%), discomfort in the breast (288%), a lump beneath the armpit (270%), and a change in the size, shape, or colour of the breast (255%). (71.6 percent). While a survey of pharmacists found that the majority of respondents thought that pain is the most prominent sign of breast cancer (70.3%), and that nipple discharge and skin edema are common manifestations (54.3%). [28]. Mammography is one of the screening procedures for breast cancer, according to 293 (82.3%) of the respondents, whereas BSE and CBE are regarded screening methods by 271 (76.1%) and 231 (64.9%) of the respondents, respectively. Breast self-examination (60.5%), mammography (42.5%), and ultrasound (40.5%), according to a research done in China, were the most often utilized procedures for disease identification (41.4 percent). Similar research in Ethiopia found that self-breast inspection was recognized by 88.9% of women who knew about breast cancer screening, with 61.8 percent clinical breast examination, 40.9 percent mammography, 17.3 percent ultrasound, and 2.2 percent biopsy being the most common. [29,30]. The results suggest that 68 percent of the participants had a moderate level of knowledge, 21.6 percent had a poor level of knowledge, and just 10.4 percent of the subjects had a high level of knowledge. When compared to the findings of a research conducted on Walailak University female employees, 35 percent had strong understanding of breast cancer screening, 7.6 percent had acceptable knowledge, and 7.4 percent had poor knowledge. [31]. Another research was undertaken in Iraq in 2021, with 51.2

percent of the people demonstrating a satisfactory level of understanding [32]. Surprisingly, according to the results of an Egyptian rural women's study, only 46.9% of the participants possessed a moderate or high level of knowledge [33]. I furthermore, a survey of female employees at Mosul University in Iraq found that 57.3 percent of them had a low or inadequate level of expertise [34]. When it comes to breast self-examination, the percentage of the participants (293 or 82.3%) had no idea when is the optimum time to conduct it. Likewise, the number of respondents (233, or 65.4%) had no idea how often BSE should be done, and more than half of the respondents (183, or 51.4%), have no idea when BSE should be begun. Conversely, many participants (245, or 68.8%) were aware of who should do BSE. In a research of Debre Berhan University female students, 143 (35.8%) of those who participated knew how to do BSE. Furthermore, three out of ten people (30.5%) were aware of when BSE should be performed [35]. The most of the 250 respondents (70.2 percent) do not know how often they should get a clinical breast examination (CBE). Similarly, the majority of participants, 240 (67.4%), do not know when CBE should begin and 214 (60.1%) do not know how CBE should be conducted. Many participants, on the other hand, were aware of who would be performing the CBE. In a study of female tertiary health care workers, it was discovered that the majority of survey participants had no idea how CBE is performed, with 30 (18.8%) believing it is performed using ultrasound, 47 (29.4%) believing it is performed using a mammography machine, and another 35 believing it is performed using a mammography machine (21.9 percent). Another research conducted at Riyadh Hospital found that just 26.6 percent of people are aware that CBE should be done once a year [36]. In our analysis, 333 (93.5%) of the respondents recognized that mammography is a fundamental

and standard screening technique, and 300 (84.3%) of the respondents knew that mammography may detect extremely tiny lumps. On the other hand, only 154 (43.3%) of participants were aware of the beginning age for mammography, and only 131 (36.8%) were aware of how often mammography should be conducted. The findings are comparable to those of a study of tertiary health care personnel, which found that 86.3 percent of them were aware that it may be used as a technique for early diagnosis of diseases. Additionally, 41.9 percent of respondents recognized that mammography should begin at the age of 40, and 40.0 percent of respondents knew that mammography should be done on an annual basis [37].

CONCLUSION

Finally, while the majority of the participants were aware that mammography is a fundamental and standard method for breast cancer screening, the majority were unaware of the age at which mammography should be initiated or how frequently it should be conducted. Similarly, they were aware of CBE and BSE but did not know when they should be begun or when they should be conducted. Age and amount of knowledge had a borderline association, while marital status, level of education, designation, and department were all very significantly associated with level of knowledge.

REFERENCES

- [1] Mandal A, Islam NK, Scott J, Okafor B, Mandal PK. African Americans and Cancer: A Minority Health Advocacy. *Journal of Bioprocessing and Biotechnology*. 2014; 4(7):1-3. doi:10.4172/2155-9821.1000e117
- [2] Smalley M, Ashworth A. Stem cells and breast cancer: a field in transit. *Nature Reviews Cancer*. 2003 Nov; 3:832-44. doi: 10.1038/nrc1212
- [3] Clarke RB, Anderson E, Howell A, Potten CS. Regulation of human breast epithelial stem cells. *Cell Proliferation*. 2003 Oct; 3:45-58. doi: 10.1046/j.1365-2184.36.s.1.5.x
- [4] Dontu G, Al-Hajj M, Abdallah WM, Clarke MF, Wicha MS. Stem cells in normal breast development and breast cancer. *Cell Proliferation*. 200 Oct; 36:59-72. doi: 10.1046/j.1365-2184.36.s.1.6.x
- [5] American Cancer Society. *Cancer Facts & Figures 2019*. Atlanta: American Cancer Society, Inc.; 2019 Jan.
- [6] World Health Organization. *Breast Cancer Fact Sheets*. [Last accessed on: July 31, 2021]. Retrieved from: <https://gco.iarc.fr/to-day/data/factsheets/cancers/20-Breast-fact-sheet.pdf>.
- [7] World Health Organization. *Cancer Country Profile*. [Last accessed on: July 12, 2021]. Retrieved from: <https://gco.iarc.fr/today/data/factsheets/populations/586-pakistan-fact-sheets.pdf>.
- [8] American Cancer Society. *Breast cancer facts & figures 2019-2020*. American Cancer Society. 2019 Jul: 1-44.
- [9] Myers ER, Moorman P, Gierisch JM, Havrilesky LJ, Grimm LJ, Ghatge S, et al. Benefits and harms of breast cancer screening: a systematic review. *JAMA*. 2015 Oct; 314(15):1615-34. doi:10.1001/jama.2015.13183
- [10] Oeffinger KC, Fontham ET, Etzioni R, Herzig A, Michaelson JS, Shih YC, et al. Breast cancer screening for women at average risk: 2015 guideline update from the American Cancer Society. *JAMA*. 2015 Oct; 314(15):1599-614. doi:10.1001/jama.2015.12783
- [11] Nelson HD, Cantor A, Humphrey L, Fu R, Pappas M, et al. *Screening for breast cancer: A systematic review to update the 2009 U.S. Preventive Services Task Force Recommendation*. Rockville (MD): Agency for Healthcare Research and Quality (US). Report No: 14-05201-EF-1, 2016.
- [12] Bambidele O, Ali N, Papadopoulos C,

- Randhawa G. Exploring factors contributing to low uptake of the NHS Breast Cancer Screening Program among Black African women in the UK. *Diversity and Equality in Health and Care*. 2017;14(4):212-19.
- [13] Adami HO, Hunter DJ, Laggiou P, Mucci L, eds. *Cancer Epidemiology*. 3rd ed. New York: OxfordUniversityPress;2016.doi.10.1093/acprof:oso/9780195311174.001.0001
- [14] Khalid A, Hassnain S, Gakhar H, Khalid B, Zulfiqar F, Wahaj A. Breast cancer among young girls: a KAP study conducted in Lahore. *International Journal of Scientific Report*.2018Jun;4(6):16671.doi:10.18203/issn.2454-2156.IntJSciRep20182206
- [15] Batool T, Sarwar H, Afzal M, Gilani SA. Knowledge, Attitude and Practices of Women towards Breast Self- Examination in Rural Area of Lahore, Pakistan. *Annals of Punjab Medical College*. 2018 Jun;12(2):158-61. DOI: 10.29054/apmc/2018.137
- [16] Ali A, Jameel N, Baig NN, SM ZH, SI AJ, Younus M.. Assessment of knowledge, attitude and practice regarding breast self-examination among females in Karachi. *The Journal of the Pakistan Medical Association*. 2020Nov;70:198589.doi:10.5455/JPMA.25836
- [17] Paknejad H. Knowledge, attitude and practices of breast self-examination among over 20 year females in Tehran. *Razi Journal of Medical Sciences*. 2019 Feb; 25(11):34-41.
- [18] Sachdeva S, Mangalesh S, Dudani S. Knowledge, Attitude and Practices of Breast Self-Examination amongst Indian Women: A Pan-India Study. *Asian Pac J Cancer Care*. 2021May;6(2):14147.doi10.31557/APJCC.2021.6.2.141-147
- [19] Parsa P, Kandiah M, Zulkefli NM, Rahman HA. Knowledge and behavior regarding breast cancer screening among female teachers in Selangor, Malaysia. *Asian Pacific journal of cancer prevention*. 2008;9(2):221-8.
- [20] Lamport L, Andre T. AIDS knowledge and sexual responsibility. *Youth and Society*. 1993Sep;25(1):3861.doi.10.1177/0044118X93025001003
- [21] Eldessouki R, Mabrouk S, Eid S. Assessment of Knowledge on Breast cancer risk factors and the practice of breast self-examination among college educated female administrative employees in Fayoum University. *Fayoum University Medical Journal*. 2019 Jun; 3(1):29-41. doi: 10.21608/FUMJ.2019.60385
- [22] Salman AA. Breast Cancer: Knowledge, Attitudes and Practices of Female Secondary Schoolteachers and Students in Samarra City. *Iraqi Journal of Cancer and Medical Genetics*. 2015;8(1):52-9.
- [23] Kaur M, Gupta NL, Kaur S, Thakur S. A study to assess the Knowledge, Attitude and Practices Regarding Breast Cancer among Government School Teachers of Ambala Cantt, District Ambala, Haryana. *International Journal of Current Research*. 2020;12(10):1420818.doi.10.24941/ijcr.39861.10.2020
- [24] Jamil A, Kouser S, Zarreen A, Saeed S, Anwar KB. Awareness and Practice of Breast Self-Examination among Doctors and Nurses in Punjab and Sindh. *JSOGP*. 2015;5(3):161-66.
- [25] Noreen M, Murad S, Furqan M, Sultan A, Bloodsworth P. Knowledge and awareness about breast cancer and its early symptoms among medical and nonmedical students of Southern Punjab, Pakistan. *Pakistan. Asian Pacific Journal of Cancer Prevention*. 2015 Mar;16(3):97984.doi:10.7314/apjcp.2015.16.3.979
- [26] Rasoolm S, Iqbal M, Siddiqui A, Ahsan R, Mukhtar S. Knowledge, Attitude, Practice towards Breast Cancer and Breast Self-examination among Female Undergraduate Students in Karachi, Pakistan. *JAMMR*. 2019; 29(9):1-11. doi: 10.9734/ jammr/2019 /v29i9

- 30126
- [27] Osei-Afriyie S, Addae AK, Oppong S, Amu H, Ampofo E, Breast cancer awareness, risk factors and screening practices among future health professionals in Ghana: A cross-sectional study. *PLoS ONE*. 2021 Jun; 16(6):1-17. doi:10.1371/journal.pone.0253373
- [28] Ayoub NM, Nuseira KQ, Othman AK, Abu Alkishik S. Knowledge, attitudes and barriers towards breast cancer health education among community pharmacists. *Journal of Pharmaceutical Health Services Research*. 2016 Sep; 7:189-98. doi:10.1111/jphs.12140
- [29] Dinegde NG, Xuying L. Awareness of Breast Cancer among Female Care Givers in Tertiary Cancer Hospital, China. *Asian Pacific Journal of Cancer Prevention*. 2017; 18(7):1977-83. doi: 10.22034/APJCP.2017.18.7.1977
- [30] Abeje S, Seme A, Tibelt A. Factors associated with breast cancer screening awareness and practices of women in Addis Ababa, Ethiopia. *BMC Women's Health*. 2019 Dec; 19(1):4-11. doi:10.1186/s12905-018-0695-9.
- [31] Kotepui M, Piwkhram D, Chupeerach C, Duangmano S. Knowledge, attitudes and practice of breast cancer screening among female personnel of Walailak University. *Health Expectations*. 2015 Dec; 18:3069-78. doi:10.1111/hex.12292
- [32] Yahyaa BT. Woman's Knowledge about Breast Cancer in Al-Ramadi City, Iraq. *Annals of R.S.C.B*. 2020;25(5):4901-10.
- [33] Hassan EE, Seedhom AE, Mahfouz EM. Awareness about Breast Cancer and Its Screening among Rural Egyptian Women, Minia District: a Population-Based Study. *Asian Pacific Journal of Cancer Prevention*. 2017; 18(6):1623-28. doi: 10.22034/APJCP.2017.18.6.1623
- [34] Al-Qazaz HK, Yahya NA, Ibrahim DK. Knowledge, awareness, and practice of breast self-examination among females in Mosul city Iraq. *Journal of Cancer Research and Therapeutics*. 2020 Oct; 16:1376-81. doi: 10.4103/jcrt.JCRT_736_19.
- [35] Birhane K, Alemayehu M, Anawte B, Gebremariyam G, Daniel R. Practices of Breast Self-Examination and Associated Factors among Female Debre Berhan University Students. *International Journal of Breast Cancer*. 2017 May: 8026297. doi: 10.1155/2017/8026297
- [36] Binhussien BF, Ghoraba M. Awareness of breast cancer screening and risk factors among Saudi females at family medicine department in security forces hospital, Riyadh. *Journal of Family Medicine and Primary Care*. 2018 Nov; 7:1283-7. doi:10.4103/jfmpc.jfmpc_286_18
- [37] Heena H, Durrani S, Riaz M, Al-Fayyad I, Tabasim R, Parvez G, et al. Knowledge, attitudes, and practices related to breast cancer screening among female health care professionals: a cross sectional study. *BMC Women's Health*. 2019 Dec; 19(1):122-32. doi:10.1186/s12905-019-0819-x



Original Article

To Determine the Outcomes of Transurethral Nephroscope For the Treatment of Large Vesical Stone With Using Pneumatic Lithoclast

Aftab Ahmed Channa^{1*}, Muhammad Asif², Nauman Ahmed³, Shumaila Ashfaq⁴, Muhammad Zahid Ahmad² and Abdul Basit Niazi⁵

¹Department of Urology, Islam Medical & Dental College, Sialkot, Pakistan

²Department of Urology, Department of Urology Unit II, KEMU/ Mayo Hospital Lahore, Pakistan

³Department of Urology, Government Kot Khawaja Saeed Teaching Hospital, Lahore, Pakistan

⁴Department of Anaesthesia, Islam Medical & Dental College, Sialkot, Pakistan

⁵Department of Urology, Niazi Medical College, Sargodha, Pakistan

ARTICLE INFO

Key Words:

Pneumatic lithoclast, Bladder stone, transurethral nephroscope, complications

How to Cite:

Ahmed Channa, A. ., Asif, M. ., Ahmed, N. ., Ashfaq, S. ., Zahid Ahmad, M. ., & Basit Niazi, A. . (2022). To determine the outcomes of transurethral nephroscope for the treatment of large vesical stone with using pneumatic lithoclast. Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.593>

*Corresponding Author:

Aftab Ahmed Channa
 Department of Urology, Islam Medical & Dental College, Sialkot
draftab.channa@gmail.com

Submitted: 12th June,

Accepted: 28th June,

Published 30th June

ABSTRACT

Objective: To study the determine the outcomes of transurethral nephroscope for the treatment of vesical stones using pneumatic lithoclast **Methods:** The detailed study was conducted in Department of Urology, Islam Medical & Dental College/ Islam teaching/Central hospital Sialkot, from March 2019-March 2020. A total of 25 males and 5 females with vesical stones greater then 4 cm that was fragmented using the through transurethral use of a nephroscope via 26F amplatz sheath were enrolled. History from medical cards was obtained and physical examinations, lab tests, urine culture and ultrasonography of urinary tract were conducted. Then the X-Ray KUB film for stone clearance was used. The mean age, operation time, presenting symptoms, complications and the post operative status of the stone clearane was calculated and conducted analysis using SPSS version 21 **Results:** The mean age \pm SD was noted to be 48.79 \pm 12.499 years and male to female percentage being 89% to 11%. The mean stone size was 4.53 \pm 0.38 cm and mean operation time was 48.79 \pm 8.73 minutes. Thirty-one patients (31%) developed retention of urine and straining during micturition in (17%), dribbling of urine (15%), hematuria (10%), frequent urination (10%) and abdominal pain was reported in 15% patients. Ninety-six (96%) patients achieved the stone-free status and had no complications while only 1 patient had an intravesical bleeding. **Conclusions:** The treatment of large stone using a nephroscope via a transurethral amplatz sheath is an effective procedure and quick too. The Amplatz sheath helps in pneumatic lithotripsy is indeed an effective and safe procedure to be carry out in patients with large bladder stones.

INTRODUCTION

Incidents of bladder stones has been recorded since old times in medical texts back in Egyptiam mummies and doing surgeries of bladder has been the most earliest of choosen form of surgery [1]. Commonly bladder stones are found in underdeveloped or poorly resourced areas and about 12% of stone in adults are urinary tract stones [2]. New and new methods have been developed from open cystolithotomy to endourologicaal treatments from optical cystolitholapaxy, cystoscopic or percutaneous

cystolithotripsy and extracorporeal shock wave lithotripsy [3]. The most common symptoms of bladder stones are changes in urine color, hematuria, frequent urination, pain while males are found more than females being affected with vesical calculi [4-13]. Presently techniques like transurethral lithoclast for the removal of stones in the bladder has been most commonly utilized by surgeons. Its observed that transurethral nephroscope is faster and effeicient for larger stones [5-16]. Ultimately the many

tehncique of stone clearance aim to fragment the stone and make an easy passage with nominal morbidity and complications to the patient. In our study we will be assessing the outcomes of the transurethral using nephroscope for lрге bladder stones.

METHODS

The comprehensive work was carried out in Department of Urology, Islam Medical & Dental College/ Islam Teaching Hospital and Islam cental Hospital Sialkot from 1st April 2019 to March 31st 2020, 25 males and 5 females presenting with vesical stones greater then 4 cm of age above 30 and less than 75 years were included. Medical history was talem from medical cards and conducted physical examinations, lab tests and urine culture and ultrasonagraphy of urinary tract. Then KUB film was used post operatively for stone clearance. We noted the mean age, operation time, presenting symptoms and complications and the post operative status of the stone and conducted our analysis using SPSS version 21. Exclusion Criteria was past history of pelvic radiotherapy, abdominal surgery, distressed with hydronephrosis, severe renal problems and bladder tumors. The gender, mean age, operation time, stone size and presenting symptoms prior to surgery of the patients was recorded and also the resulting complications and stone-free status by periodical followups and analyzed the data using SPSS Version 21.

RESULTS

Out of the overall population the mean age ± SD was noted to be 48.79±12.499 years and with maximum and minimum age being 75 and 30. However it was mostly male dominated with male to female percentage being 89 to 11%. The mean stone size was 4.53±0.38 cm and mean operation time was 48.79±8.73 minutes (Table 1).

	Variable	Total Population
Demographics	Mean Age ± SD	48.79±12.499
	Max	75
	Min	30
	Male : Female(%)	89% :11%
Operation Statistics	Stone Size-(cm)	4.53±0.38
	Operation time (minutes)	48.79±8.73

Table 1: Demographics & Operation Statistics of Patients

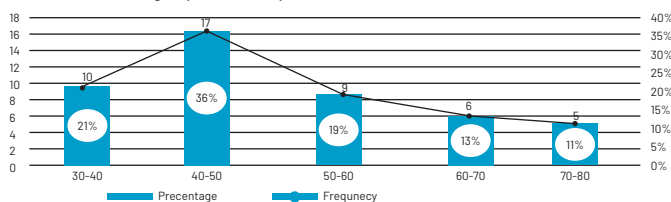


Figure 1: Peak Age Group in bladder Calculi Patients
Amongst the patients most patients fell in the 40-50 age - range about 36% followed by 21% in 30-40 years and 19% in

50-60 and 13% in 60-70 and 11% 70-80 years' age group. (Figure 1).

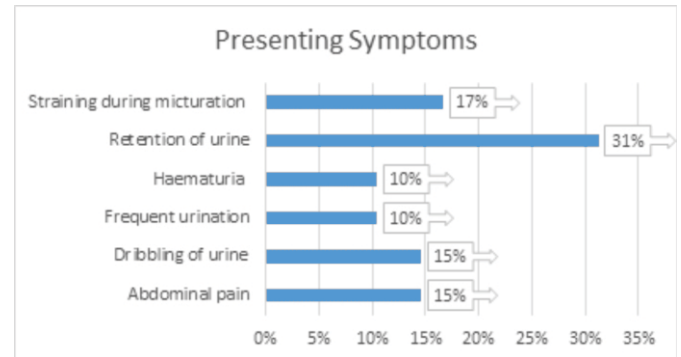


Figure 2: Presenting Symptoms of Patients
The most frequent symptoms were retention of urine observed in 31% of patients while most patients shared the lower urinary tract symptoms (LUTS) with straining during micturition in 17% while dribbling of urine in 15%, haematuria in 10% and frequent urination in 10% while 15% patients presented with abdominal pain.



Figure 3: Post-Operative Status
Largely 46 (96%) patients achieved the stone-free status and had no complication while only 1(2%) patient had an intravesical bleeding (Figure 3). However no complication lasted for long.

DISCUSSION

Vesical stones usually affect men and according to a study and amount to about 5% of urinary stones. Mainly occurring due to bladder obstruction, infection or foreign bodies invasion [5,6]. Considering the development in this modality, many methods have been used to manage the stones in the bladder for instance Open cystolithotomy, extracorporeal shockwave lithotripsy, transurethral cystolithotripsy and percutaneous suprapubic systolithotripsy however it highly depends on the surgeon and patients physical and medical history of presentation and test as to which method to be used. Yet transurethral nephroscope is the common method used worldwide as it allowed other devices like laser and pneumatic lithotripter for fragmentation and we have used pneumatic in our study [7,8]. In our research of 30 subjects consisting of primarily males, i.e 89% male and 11% females (min 30 and maximum 75 years) with the mean(SD) age of 48.79±12.499 years while Abdul Mannan and his fellows reported 80% males and 20% females with a mean age of 55 years (minium age 18 and maximum 73 years) [9,10]. The mean (SD) stone size was

4.53±0.38 cm in our study while Ahmet et al. reported a mean age of 49.58 ± 9.50 years and stone size of 4.34 ± 0.78cm [7]. Similar local study of 146 patients showed a mean age of 40.1 years and stone size of 2.7 cm [11,12]. Most of the patients fell in the age bracket of 40-50 years and similar findings were reported by with age of patients falling between 11 to 70 years. In our study the average time taken for fragmentation was 48.79 minutes while Rai et al. [9] took 58 minutes. As such no particular aetiology can be associated for bladder calculi as supported by Okeke and his fellows in their study too [10,14]. Most patients achieved the stone-free status about 96% and had no complication while only 1 patient had an intravesical bleeding while shaikh and friends reported urethral in 7.5% and bladder bleeding 6% and only 3.5% had incidents of infection [15,16]. Ahmed Rasheed showed a stone did not break in 3.3%, 2.69% had partial fragmentation making a 84% stone free status while in our study stone free status was 96% [17,18]. Similarly Msihra and colleagues conducted their research using transurethral lithotripsy and reported no complications in all patients proving nephroscopy to be more effective [19,20]. However we also showed that large fragments of stones can be prevented various entries to the urethra and the damage to the tract is also minimum [21,22].

CONCLUSIONS

Thus we conclude that vesical stone removal using nephroscope transurethraly is safe and effective and only minor complications were witnessed in our data and can be safely performed.

REFERENCES

- [1] Kusumi K, Becknell B, Schwaderer A. Trends in pediatric urolithiasis: patient characteristics, associated diagnosis, and financial burden. *Pediatric Nephrol.* 2015;30:805-10.
- [2] Kirakoya B, Kabore M, Pare AK, Abubakar BM. Giant bladder stone in a patient with tumor of the bladder: a rare co-morbidity. *J West Afr Coll Surg.* 2018 Jul-Sep;8(3):114-120.
- [3] Ghanshyam S, Ashok A, Lamichhane N, Belokar WK. Transurethral use of nephroscope in the management of bladder stone. *Journal of College of Medical Sciences-Nepal.* 2014 Jan 14; 9(1);14-18. doi: 10.3126/jcmsn.v9i1.9668.
- [4] Vidhyarthi AK, Hameed T, Lal R, Kumar A, Sahni S, Mendoza N. Giant Bladder Calculus in an Adult- A Persistent Problem in the Developing World: A Case Report. *Clin Pract Cases Emerg Med.* 2020 Nov;4(4):544-547. doi: 10.5811/cpcem.2020.7.47653.
- [5] Gupta R, Gupta S, Das RK, Basu S, Agrawal V. Comparative study of a new technique using nephroscope and resectoscope sheath and the percutaneous cystolithotripsy for the treatment of bladder calculus. *Cent European J Urol.* 2017;70(4):400-404. doi: 10.5173/ceju.2017.1379.
- [6] Mannan A, Anwar S, Zaheer K, Arshad M, Shah A. Transurethral cystolithotripsy for large vesical calculi. *Esculapio J Services Inst Med Sci Jan-Mar* 2013; 9(1): 1-3.
- [7] TunçOzdemir A, Koyuncu H, Altınova S, Asil E, Isgoren E and Gurdal M. Comparison of Transurethral use of Nephroscope with Cystoscope in Transurethral Cystolithotripsy Sistolitotripside Transüretal Nefroskop Kullaniminin Sistoskop ile Karşılaştırılması. 2014 journal of clinical and analytical medicine. Available online at <http://www.jcam.com.tr/files/KATD-1248.pdf>
- [8] Shaikh J, Khalid S, Siddiq A, Mithani S, Saulat S and Sharif I. Use of Amplatz sheath in percutaneous nephroclithotomy and effect of its various sizes: Randomized Controlled Trial. *Pak J Med Dentistry* July-Sept 2020,9(3): 37-41.
- [9] Rai RS, Patrule K, Rai R, Gupta E, Kayastha A, Sawhney S. Lithoclast® Master in Intracorporeal Lithotripsy during Percutaneous Nephrolithotomy : Our Experience. *Med J Armed Forces India.* 2008 Jul;64(3):232-3. doi: 10.1016/S0377-1237(08)80100-1.
- [10] Okeke C & Obi A. Giant bladder calculus in a male patient with chronic alcoholic liver disease. *International Journal of Case Reports and Images.* doi:10.105348/100996Z010J2019CR.
- [11] Shaikh AR, Shaikh GH, Shaikh AH, Shaikh AH, Shaikh NA. Endoscopic Treatment of vesical calculi in children. *Rawal Med J Jan-June* 2010;35(1): 15-8.
- [12] Shaikh AR, Shaikh NA, Soomro AA, Shaikh AH, Iqbal M and Malik M. Experience of upper urinary tract stones with Dornier Mpl 9000 lithotriper. *Pak J Med Res* Oct 2010;49(4): 127-30.
- [13] Hasan O, Ellis A, Powers R, Vidal P. Vesical megalithiasis. *Urology Case Reports.* 2019 Mar;23:41-43. doi: 10.1016/j.eucr.2018.11.012.
- [14] Mishra DK, Bhatt S, Mukhilesh R, Somani BK, Agrawal MS. Mini-percutaneous cystolithotripsy (mPCCL) versus transurethral cystolithotripsy (TUC) in pre-school children: Prospective comparative non-randomized outcomes over 8 years. *J Pediatr Urol.* 2020 Dec;16(6):782.e1-782.e6. doi: 10.1016/j.jpuro.2020.09.021.
- [15] Ali AI, Fathelbab TK, Abdelhamid AM, Elbadry M, Alshara L, Anwar AZ, Galal EM, Tawfiek ER. Transurethral Pneumatic Cystolithotripsy: A Novel Approach. *J Endourol.* 2016 Jun;30(6):671-3. doi: 10.1089/end.2015.0862.

- [16] Channa AA, Akhtar SMH, Cheema NA, Anwer A, Nauman F, Cheema ZQ. "Efficacy and safety of pneumatic lithotripsy in pediatric vesical stone". *Rawal Med J.* 2020; 45(3): 728-30.
- [17] Ali L, Ali S, Shafieullah ON. Role of pneumatic lithotripsy in paediatric bladder stone: I will not cut upon stone. *Khyber Medical University Journal.* 2014 Apr 20;6(2):1-6.
- [18] Masood A, Khan IZ, Farouk K, Nisar H, Ijaz R, Ishtiaq S, Taimur M. Endoscopic management of bladder calculi in paediatric male patients: An experience with 57 patients. *Isra Med J.* 2019;11(3):167-70.
- [19] Ali L, Orakzai N. E146 Role of pneumatic lithotripsy by using ureterscope in paediatric bladder stones: I will not cut upon stone. *European Urology Supplements.* 2011;7(10):505.
- [20] Faizan M, Gurmani MA, Siddiqui AA, Choudhary QA, Anjum Z. A comparison between transurethral cystolithoclasty and vesicolithotomy in pediatric male patients. *Journal of University Medical & Dental College.* 2020 Mar 18;11(1):31-8.
- [21] Arzoz M, Ibarz L, Roca J, Edo S, Valverde I, Buisan O, Ruiz-Dominguez J, Bayona S. Relationship between chronic stress and calcium oxalate stone: Differences between first time (FS) and recurrent stone (RS) formers. *European Urology-Supplements.* 2011 Jan 1;10(7):504-.
- [22] Ali L, Ali S, Hussain SA, Haider F, Ali S. Role of spiritual sentiments in improving the compliance of water intake in patients with urolithiasis. *Journal of Religion and Health.* 2018 Feb;57(1):26-32.



Original Article

Efficacy of Indigenous Microbes for Removal of Oil Contaminated Soil by Producing Biosurfactant

Humaira Niamat^{*}, Aisha Waheed Qureshi¹, Uzma Rafi¹, Zunaira Khaliq¹ and Syeda Shazia Bokhari¹¹Department of Biology, Lahore Garrison University, Lahore, Pakistan

ARTICLE INFO

Key Words:

Biosurfactants, Blood Hemolytic Assay, Foaming Activity, Emulsification Assay, Oil Spreading Technique

How to Cite:

Niamat, H., Aisha Waheed Qureshi, Uzma Zeeshan Rafi, Zunaira Khaliq, & Syeda Shazia Bokhari. (2022). Efficacy Of Indigenous Microbes for Removal of Oil Contaminated Soil by Producing Biosurfactant: Efficacy of Indigenous Microbes for Removal of Oil Contaminated Soil by Producing Biosurfactant. *Pakistan Bio Medical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.542>

*Corresponding Author:

Humaira Niamat
Department of Biology, Lahore Garrison University,
Lahore, Pakistan
humairaniamat@lgu.edu.pkReceived Date: 14th June, 2022Acceptance Date: 21st June, 2022Published Date: 30th June, 2022

ABSTRACT

Bacteria with ability to produce biosurfactants have potential applications in environmental protection. They are surface active chemicals that can lower the surface tension between two liquids or a solid and a liquid. Microorganisms of several types manufacture them. **Objective:** To isolate, optimize, screen, and describe bacteria that produce biosurfactants from petroleum-contaminated soil. **Methods:** Isolates were named as ZMS1 and ZMS2, which were gram positive rods with mucoid colonies and off white or colorless appearance, respectively. The isolation was carried out using initial screening methods including blood hemolytic assay, foaming activity, emulsification assay and oil spreading technique in kerosene supplemented media at culture conditions of pH7 and temperature 37°C. **Results:** The results of these different tests showed the production of biosurfactant by bacteria. Stain removal efficiency of bacterial supernatant considered as a biosurfactant, was also tested following previously described method. Both isolates, ZMS1 and ZMS2 were producing biosurfactants with the capacity remove stains of blood and tea. Furthermore, to get the biosurfactant production using cheaper carbon source, potato peel extract and molasses extract were used as a carbon source in synthetic medium for the growth of ZMS1 and ZMS2. Despite the fact that the isolates produced biosurfactant, they were not purified or eluted. However, both the isolates ZMS1 and ZMS2 shown their significance in several biotechnological and industrial domains. **Conclusions:** Present study will be helpful in future and these microbes can be utilized for the remediation of oil polluted soil, which in turn can be proven in the improvement of soil fertility.

INTRODUCTION

Biosurfactants are surface-active, degradable organic chemicals of biological origin that have recently been utilized in numerous sectors [1]. Because of its industrial and therapeutic applications, bio surfactants have attracted a lot of attention in recent years [2]. The more specificity, easy preparation lower toxicity and widespread applicability of biosurfactants make it more pertinent. These compounds can also be used as emulsifiers, moistening agents, foaming agents, dispersing agents, detergents, and beneficial food items in a wide range of industries, including organic chemicals, petrochemicals, pharmaceuticals, beverages and foods, petroleum, biological control and management, and so on [3, 4].

Biosurfactants' pharmacological and immunological applications were further addressed by Cameotra and Makkar (2004). Biosurfactant fermentation nutrients have lately been available in a wide variety of agronomic, industrial byproducts, and material residues [5, 6]. So, there is potential for future microbial surfactants, which will rely heavily on the usage of abundant and inexpensive substrates, which can significantly enhance production [7-10]. The oils and fats are most commonly utilized in the food business, which generates a lot of frying oil waste. The problem of frying oil waste disposal is a major issue, which explains the growing interest in utilizing frying oil waste for microbial transformation [4]. Because of their beneficial

effects, Biosurfactants produced by extremophilic bacteria i.e. halophilic and thermophilic bacteria gained much more attention for the isolation and characterization purposes [11-13]. Bio surfactants are the compounds of chemical origin. One of the established classes is glycolipids formed by *Rhodococcus erythropolis* that create the mono, di and trisaccharides that is used in oil spill clean-up process [14]. Another class of biosurfactants is Sphorolipids with many environments applications and is produced by *Candida bombicola* [15]. *Pseudomonas aeruginosa* produced another class of biosurfactants named Rhamolipids which have applications in bioremediation of oil contaminated sites [16]. However, phospholipids biosurfactants are reported to have applications in environmental management [17]. Biosurfactants have been useful in reducing the surface and interfacial tension [18]. Due to the production of biosurfactants, hydrocarbon degradation in the presence of microorganisms is enhanced [19]. Biosurfactant-producing microorganisms exist in nature and can be found in both water and soil. Moreover, these microorganisms also inhabit extreme environments such as extreme temperature and salinity [20]. Salinity and pH 4-10 can alter the action and solubility of biosurfactants [21]. Hydrocarbons are also produced by living cells in the form of natural oils and fats [22]. Scientists discovered that the oceans are not covered in an oily coating, which indicates that oil-degrading bacteria are active. Many bacteria have been found to feed exclusively on oil-degrading microorganisms [23]. As a result, biosurfactants are crucial in the bioremediation of hydrocarbon-polluted environments. In the biodegradation of hydrocarbons, biodegradative enzymes play a crucial role [24]. Numerous biosurfactants have also been demonstrated to have antimicrobial activity against bacteria, fungus, algae, and viruses. Biosurfactants have numerous advantages over their chemically manufactured equivalents. The presence of biosurfactant-producing bacteria is strongly influenced by the environment in which they dwell [25]. The current study aims to assess the potential of bacterial isolates from petroleum-polluted soil for biosurfactant synthesis for use in several biotechnological domains.

METHODS

Isolation of bacteria:

Petroleum contaminated soil was collected from Lahore and was used as a source of bacterial isolation. 10-fold dilution of soil sample was made and 10 µl of it was spread on nutrient agar plate enriched with 0.1% crude oil. Plates were then incubated at 37°C for 24 hours. After 24 hours, bacterial colonies were observed, of which selected colonies were streaked for purification.

Morphological and biochemical characterization of bacterial isolates:

Bacterial smear was prepared and then stained with gram stain. The color and shape of the stained cells were then observed under light microscope. For the biochemical characterization, different biochemical tests i.e. catalase test, citrate test, urease test, methyl red test, nitrate test and indole test and starch hydrolysis test were performed [26].

Screening of biosurfactant producing bacteria:

For the screening of biosurfactant producing bacteria, following tests were performed:

a) Biosurfactant screening:

The LB Broth medium was prepared with the addition of kerosene oil. The bacteria were inoculated and incubated for 24 hours at 37°C. The growth was measured at 600nm after incubation. The supernatant was utilized to determine biosurfactant after the culture was harvested at 2000 rpm for 5 minutes.

b) Oil spreading Assay:

A thin layer of kerosene oil was applied to the surface of the Petri plate. Then, on top of the oil layer, a 10µl bacterial culture was gently deposited. The presence of biosurfactant is shown by the clear zone. Oil displacement activity is another name for this. To measure the displaced diameter of oil, different inoculum sizes (5 µl, 10 µl, 25 µl, 50 µl, 100 µl and 200 µl) can be utilized.

c) Emulsification assay:

It was calculated using the E24 emulsification index. In 1mL of cell-free supernatant, 2 mL of kerosene oil was added and vortexed for 5 minutes. After 24 hours, the emulsification activity was measured and computed using the formula:

$$E24 = (\text{Total height of the emulsion layer} / \text{height of the aqueous layer}) \times 100$$

d) Foaming Activity:

In each flask, 100 ml of nutrient broth medium was prepared and inoculated with isolated bacteria. The flasks were then incubated for 72 hours at 37°C in a shaking incubator at 200 rpm. Foaming activity is divided into three categories: foam stability, foam height, and foam shape.

Blood Hemolysis Test:

The bacterial colony was streaked onto the agar plate using blood agar medium (including Peptone 5.0g/L, Beef extract 3.0g/L, Sodium chloride 3.0g/L, Agar 15.0g/L, Sterile defibrinated blood 10 ml). It was then incubated at 37°C for 24 hours. Blood hemolysis was measured as clear zones.

e) Stain removal efficiency test: [27]

10 mL supernatant was added to four beakers for stain removal to measure biosurfactant efficiency. The sterile bandage was divided into four equal parts. For 20 minutes,

two of these pieces were stained with tea and the other two with blood. The stained pieces were then air dried before being placed in the appropriate beaker and incubated for 24 hours at 37°C. By rinsing cloth pieces with sterile water after 24 hours, the stain removal efficacy of biosurfactant was measured.

Biosurfactant Optimization Through the Use of Different Carbon Sources [28]

For the production of biosurfactants, Agro-industrial wastes i.e. molasses obtained from sugarcane and potato peel extracts (prepared by boiling method) were used.

Optimization of bio surfactant by using kerosene oil, potato peels extracts and molasses as carbon source.

Sterilized minimal medium (containing Glucose 40g/L, NH_4HPO_4 0.39g/L, Na_2HPO_4 5.67g/L, KH_2PO_4 4.08g/L, $\text{FeSO}_4 \cdot 7\text{H}_2\text{O}$ 0.015g/L, $\text{MnSO}_4 \cdot \text{H}_2\text{O}$ 0.002g/L, $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$ g/L, $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ 0.001g/L, Agar 15g/L; pH: 6.8–6.9) was prepared and syringe filtered kerosene oil, potato peel extract and molasses were added into it. Colonies were streaked and cultured at 37°C for 24 hours. The data were recorded after incubation.

Hydrophobicity assay:

Bacterial strains were cultured in L broth for 24 hours at 37 degrees Celsius. Following a 15-minute centrifugation at 5000 xg, the pellets were washed twice with phosphate buffer saline, and the optical densities of the bacteria were determined at 540 nm and adjusted to $A_{540}=1.0$. For 30 seconds, 1 ml of bacterial solution was vortexed vigorously with 1 ml of each hydrocarbon (Xylene, chloroform, and toluene). The optical density of the aqueous phase was measured again after phase separation and compared to the initial value. The hydrophobicity was estimated using the equation below, as described in the protocol.

$$\text{Hydrophobicity} = \frac{(A_{540} \text{ initial} - A_{540} \text{ aqueous phase})}{A_{540} \text{ initial}} \times 100 = \%$$

RESULTS

Isolation of bacteria:

The two bacterial isolates were found in oil-contaminated soil. ZMS1 and ZMS2 were assigned to the isolates. These isolates were characterized using Bergey's manual of systematic Bacteriology's cultural, morphological, and biochemical characteristics.

(a) Cultural Characteristics:

ZMS1 colonies were round, mucoid, with a smooth surface and irregular edges, whereas ZMS2 colonies were round, dry, flat, and concave. ZMS1 and ZMS2 colonies were white and colorless, respectively.

(b) Morphological and biochemical characterization:

Gram staining was used to determine the morphological characteristics of the isolates, and it was discovered that

both isolates were Gram positive and rod-shaped bacteria. Different biochemical tests were used to select the strains for biochemical characterization.

Biosurfactant Screening, Production and Optimization With Different Carbon Sources

The isolated strains were tested for biosurfactant synthesis.

(a) Blood Hemolytic Assay:

Both bacterial strains tested negative for hemolysis when carbon was provided via kerosene, indicating that no zones had formed. Bacterial strains are tested for hemolytic activity using potato peel extracts showed negative results for both strains. While both bacterial strains using molasses also showed negative hemolytic activity.

(b) Emulsification Assay:

Carbon source	Bacterial Strain	Emulsified layer (cm)	Total liquid layer (cm)	E24 (%)
Kerosene oil	ZMS 1	1.00±0.057735	1.8 ±0.2848	55.5±6.799591
	ZMS 2	0.8±0.173205	1.9±0.21798	42.10±6.334386
Potato peel extract	ZMS1	1.1±0.145297	1.3±0.120185	84.6±3.48441
	ZMS2	0.6±0.202757	1.4±0.173205	42.8±4.801851
Molasses	ZMS1	1.0±0.11547	1.8±0.152753	55.4±5.512511
	ZMS2	0.4±0.088192	1.7 ±0.218581	23.5±2.107922

Table 1: Results of Emulsification Assay using medium containing different carbon sources

(c) Foaming Activity of bacterial strains using different carbon sources:

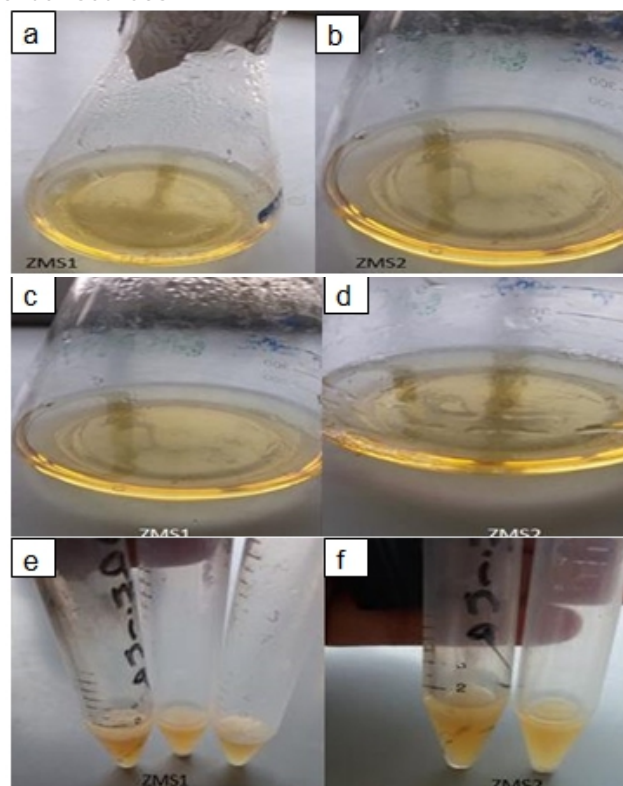


Figure 1: (a & b) Foaming activity of bacterial strains using kerosene as a Carbon source. ZMS1 strain showed visible foaming

activity as compared to that of ZMS2 strain. (c & d) Bacterial strains using potato peel extract as carbon source. ZMS1 strain showed visible foaming activity as compared to that of ZMS2 strain. (e & f) Bacterial strains using molasses as a carbon source. ZMS2 strain showed more visible foaming activity as compared to ZMS1 strain

(c) Oil spreading technique:

When medium was supplemented with potato peel extract, molasses and kerosene oil, the ZMS1 strain showed the maximum diameter of clear zone of about 3.3, 3.1 and 3.0 cm respectively, while ZMS2 strain showed the maximum diameter of about 3.2, 3.3 and 3.3 respectively showing the positive results.

Quantity of cell free culture broth	Diameter of zone (potato peels)	Diameter of zone (molasses)	Diameter of zone (kerosene oil)
5 µl	1.0±0.120185	1.1±0.057735	1.2±0.152753
10 µl	1.8±0.128295	1.0±0.24037	1.6± 0.290593
25 µl	1.9±0.128295	2.1±0.088192	2.0±0.088192
50 µl	2.3±0.120185	2.9±0.185592	2.2±0.24801
100 µl	3.0±0.24037	3.0±0.2848	2.7±0.208167
200 µl	3.3±0.11547	3.1± 0.2848	3.0±0.057735

Table 2: Results of oil spreading assay for strain ZMS1

Quantity of cell free culture broth	Diameter of zone (potato peels)	Diameter of zone (molasses)	Diameter of zone (kerosene oil)
5 µl	1.6±0.176383	1.0±0.260342	1.5±0.11547
10 µl	2.00±0.152753	1.6±0.145297	1.9±0.260342
25 µl	2.2±0.120185	2.2±0.057735	2.1±0.057735
50 µl	2.9±0.260342	2.9±0.264575	2.2±0.152753
100 µl	3.1±0.145297	3.0±0.145297	3.0±0.145297
200 µl	3.2±0.208167	3.3±0.173205	3.3±0.202759

Table 3: Results of oil spreading assay for strain ZMS2

Optimization of biosurfactant producing bacteria by using potato peels & molasses as carbon source:

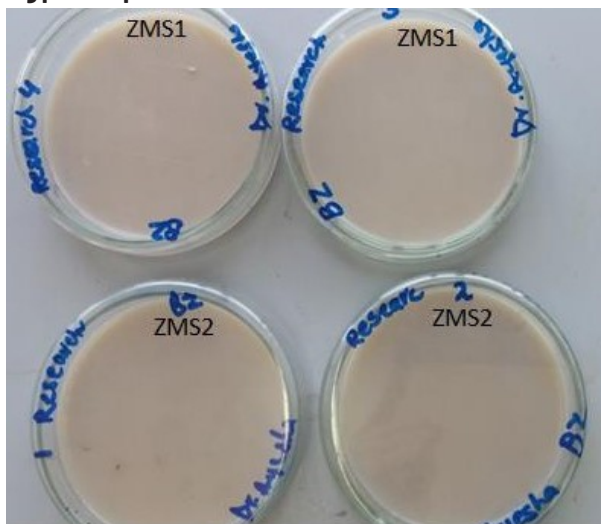


Figure 2: Results of bacterial strains by using molasses as carbon source

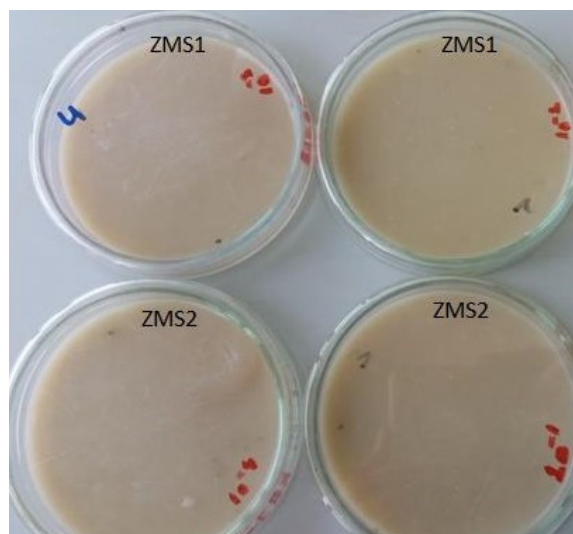


Figure 3: Results of bacterial strains by using potato peels as carbon source

Biosurfactant efficiency:

Both ZMS1 and ZMS2 strains showed positive results because stains of blood and tea disappeared after incubation of 72 hours.

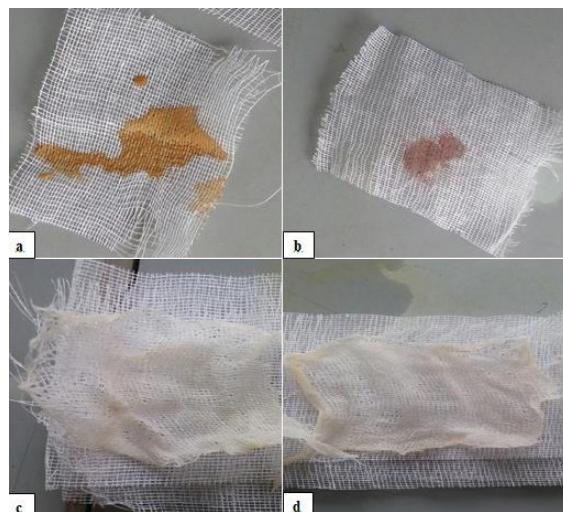


Figure 4: (a) Piece of bandage stained with tea. (b) Piece of bandage stained with blood. (c & d) Pieces of bandage after testing stain removal efficiency test.

Hydrophobicity assay:

Medium supplemented with hydrocarbons	Hydrophobicity % of ZMS1 strain	Hydrophobicity % of ZMS2 strain	Hydrophobicity % of ZMS1 strain	Hydrophobicity % of ZMS2 strain	Hydrophobicity % of ZMS1 strain	Hydrophobicity % of ZMS2 strain
Medium containing kerosene oil treated with chloroform	13.3 %	20.6 %	19.1 %	13.9 %	22.2 %	21.0 %
Medium containing kerosene oil treated with xylene	.33.3 %	.36.5 %	.31.0 %	.39.7 %	.33.1 %	.38.1 %
Medium containing kerosene oil treated with toluene	.46 %	53 %	.54.7 %	.56.9 %	.55.5 %	.57 %

Table 4: Results of Hydrophobicity assay of ZMS1 and ZMS2 strain (Using Kerosene Oil, potato peel extract and Molasses)

DISCUSSION

The two bacterial strains were isolated and were named as ZMS1 and ZMS2. Both strains are Gram positive and have a rod and circular form, respectively. Both strains were evaluated for hemolytic activity, which some authors believe is suggestive of biosurfactant synthesis and can be used as a quick way to screen bacteria [29]. Biosurfactant generating microorganisms are regarded as a generous gift of nature due to their large-scale productivity, selectivity, performance under harsh conditions, potential uses in environmental protection, and diversity. The need for bioremediation in our environment has gradually increased interest in these bacteria [30]. Many studies described various strategies for screening biosurfactant generating microorganisms. Some prior studies described only two or three strategies, whereas numerous reports discussed six to eight ways for screening purposes. The most frequent procedures are the hemolytic assay, the emulsification assay, and the oil spreading technique. Oil spreading technique and drop collapse assay are two more reliable procedures for screening a large number of samples. These procedures only require a little amount of biosurfactant solution, about 5–10 µl. The order of relevant methods for screening biosurfactant production includes oil spreading technique, emulsification assay, foaming activity, and drop collapse test, according to the findings of this study. Using kerosene oil as the sole carbon source, biosurfactant-producing bacterial strains were identified and screened from oil-contaminated soil. In 2012, Ghayyomi Jazeh and colleagues discovered 160 biosurfactant-producing bacteria in oil-contaminated soil, resulting in the discovery of 160 strains capable of creating biosurfactant. In this study, the oil spreading method, blood hemolysis test, foaming activity, and emulsification assay were used to look for bacteria that produce biosurfactants, and both bacterial strains ZMS1 and ZMS2 showed positive oil spreading technique. The emulsifying activity of strain ZMS1 was 55.2%, while it was 42.10% in strain ZMS2. The two categories of biosurfactants are low-molecular-mass molecules, which efficiently lower surface and interfacial tensions, and high-molecular-mass polymers, which are more effective as emulsion stabilising agents. Microbial growth and survival in the environment are dependent on biosurfactants. *Bacillus subtilis*, for example, requires surfactin production to form fruiting bodies [31]. Both strains indicated the negative hemolysis test because no zone formation observed. And the foaming stability in ZMS2 is higher than ZMS1. Several studies focused on high emulsifying abilities [32, 33]. Present study showed the significance of microbes isolated from oil spills and their ability to produce the biosurfactants. It is also useful for bioremediation of oil polluted soil.

CONCLUSIONS

It is concluded that the bacterial strains isolated from polluted soil were found to be capable of producing biosurfactants with varying responses to fabric stain removal and hydrophobicity. These strains can be used in the field to help bioremediate polluted soil and improve soil fertility.

REFERENCES

- [1] Samadi N, Abadian N, Akhavan A, Fazeli MR, Tahzibi A, Jamalifar H. Biosurfactant production by the strain isolated from contaminated soil. *J. Biol. Sci.* 2007 7(7):1266-1269
- [2] Banat IM. Biosurfactants production and possible uses in microbial enhanced oil recovery and oil pollution remediation: a review. *Bioresource technology.* 1995 Oct 51(1):112 [https://doi.org/10.1016/0960-8524\(94\)00101-6](https://doi.org/10.1016/0960-8524(94)00101-6)
- [3] Perfumo A, Smyth T, Marchant R, Banat I. Production and roles of biosurfactants and bioemulsifiers in accessing hydrophobic substrates. In *Handbook of hydrocarbon and lipid microbiology.* 2010 1501-1512 DOI 10.1007/978-3-540-77587-4_103
- [4] Vedaraman N, Venkatesh N. Production of surfactin by *Bacillus subtilis* MTCC 2423 from waste frying oils. *Brazilian Journal of Chemical Engineering.* 2011 Jun 28(2):175-180 <https://doi.org/10.1590/S0104-66322011000200001>
- [5] Da Silva GP, Mack M, Contiero J. Glycerol: a promising and abundant carbon source for industrial microbiology. *Biotechnology advances.* 2009 Feb 27(1):30-39 <https://doi.org/10.1016/j.biotechadv.2008.07.006>
- [6] Savarino P, Montoneri E, Biasizzo M, Quagliotto P, Viscardi G, Boffa V. Upgrading biomass wastes in chemical technology. Humic acid-like matter isolated from compost as chemical auxiliary for textile dyeing. *Journal of Chemical Technology & Biotechnology: International Research in Process, Environmental & Clean Technology.* 2007 Sep 82(10):939-948 <https://doi.org/10.1002/jctb.1767>
- [7] Makkar RS, Cameotra SS, Banat IM. Advances in utilization of renewable substrates for biosurfactant production. *AMB express.* 2011 Mar 1(1):5
- [8] Mukherjee S, Das P, Sen R. Towards commercial production of microbial surfactants. *TRENDS in Biotechnology.* 2006 Nov 24(11):509-515 <https://doi.org/10.1016/j.tibtech.2006.09.005>
- [9] Mukherjee S, Das P, Sivapathasekaran C, Sen R. Enhanced production of biosurfactant by a marine bacterium on statistical screening of nutritional parameters. *Biochemical Engineering Journal.* 2008

- Dec42(3):254260 <https://doi.org/10.1016/j.bej.2008.07.003>
- [10] Mutalik SR, Vaidya BK, Joshi RM, Desai KM, Nene SN. Use of response surface optimization for the production of biosurfactant from *Rhodococcus* spp. MTCC 2574. *Bioresource Technology* 2008 Nov 99(16):7875-7880 <https://doi.org/10.1016/j.biortech.2008.02.027>
- [11] Joshi S, Bharucha C, Jha S, Yadav S, Nerurkar A, Desai AJ. Biosurfactant production using molasses and whey under thermophilic conditions. *Bioresource technology*. 2008 Jan 99(1):195-199
- [12] Kumar AS, Mody K, Jha B. Evaluation of biosurfactant/bioemulsifier production by a marine bacterium. *Bulletin of environmental contamination and toxicology*. 2007 Oct 79(6):617-621
- [13] Mnif S, Chamkha M, Sayadi S. Isolation and characterization of *Halomonas* sp. strain C2SS100, a hydrocarbon-degrading bacterium under hypersaline conditions. *Journal of Applied Microbiology*. 2009 Aug 107(3):785-794
- [14] Peng F, Liu Z, Wang L, Shao Z. An oil-degrading bacterium: *Rhodococcus erythropolis* strain 3C-9 and its biosurfactants. *Journal of applied microbiology*. 2007 Jan 102(6):1603-1611 <https://doi.org/10.1111/j.1365-2672.2006.03267.x>
- [15] Daverey A, Pakshirajan K. Kinetics of growth and enhanced sphorolipids production by *Candida bombicola* using a low-cost fermentative medium. *Applied biochemistry and biotechnology*. 2010 Oct 160(7):2090-2101
- [16] Chen SY, Lu WB, Wei YH, Chen WM, Chang JS. Improved production of biosurfactant with newly isolated *Pseudomonas aeruginosa* S2. *Biotechnology progress*. 2007 Sep 23(3):661-666 <https://doi.org/10.1021/bp0700152>
- [17] Wiącek AE, Adryńczyk E. Interfacial properties of phosphatidylcholine-based dispersed systems. *Industrial & Engineering Chemistry Research*. 2015 Jun 54(25):6489-6496 <https://doi.org/10.1021/acs.iecr.5b01429>
- [18] Pacheco GJ, Ciapina EMP, Gomes EDB, Pereira Junior N. Biosurfactant production by *Rhodococcus erythropolis* and its application to oil removal. *Brazilian Journal of Microbiology*. 2010 Mar 41(3):685-693 <https://doi.org/10.1590/S1517-83822010000300019>
- [19] Ferradji FZ, Mnif S, Badis A, Rebbani S, Fodil D, Eddouaouda K, Sayadi S. Naphthalene and crude oil degradation by biosurfactant producing *Streptomyces* spp. isolated from Mitidja plain soil (North of Algeria). *International Biodeterioration & Biodegradation*. 2014 Jan 86:300-308 <https://doi.org/10.1016/j.ibiod.2013.10.003>
- [20] Chirwa EMN, Bezza FA. Petroleum hydrocarbon spills in the environment and abundance of microbial community capable of biosurfactant production. *J Pet Environ Biotechnol*. 2015 6(237):2 DOI: 10.4172/2157-7463.1000237
- [21] Al-Bahry SN, Al-Wahaibi YM, Elshafie AE, Al-Bemani AS, Joshi SJ, Al-Makhmari HS, Al-Sulaimani HS. Biosurfactant production by *Bacillus subtilis* B20 using date molasses and its possible application in enhanced oil recovery. *International Biodeterioration & Biodegradation*. 2013 Jul 81:141-146 <https://doi.org/10.1016/j.ibiod.2012.01.006>
- [22] De Lorenzo V. Blueprint of an oil-eating bacterium. *Nature biotechnology*. 2006 Aug 24(8):952-953
- [23] Yakimov MM, Giuliano L, Gentile G, Crisafi E, Chernikova TN, Abraham WR, Golyshin PN. *Oleispira antarctica* gen. nov., sp. nov., a novel hydrocarbonoclastic marine bacterium isolated from Antarctic coastal sea water. *International journal of systematic and evolutionary microbiology*. 2003 May 53(3):779-785 <https://doi.org/10.1099/ijs.0.02366-0>
- [24] Yong YC, Zhong JJ. Recent advances in biodegradation in China: New microorganisms and pathways, biodegradation engineering, and bioenergy from pollutant biodegradation. *Process Biochemistry*. 2010 Dec 45(12):1937-1943 <https://doi.org/10.1016/j.procbio.2010.04.009>
- [25] De Rienzo MD, Kamalanathan ID, Martin PJ. Comparative study of the production of rhamnolipid biosurfactants by *B. thailandensis* E264 and *P. aeruginosa* ATCC 9027 using foam fractionation. *Process Biochemistry*. 2016 Jul 51(7):820-827
- [26] Cappuccino J.G, Sherman N. *Microbiology: a laboratory manual* (6th ed) pearson. 2002.
- [27] Sajna KV, Sukumaran RK, Gottumukkala LD, Jayamurthy H, Dhar KS, Pandey A. Studies on structural and physical characteristics of a novel exopolysaccharide from *Pseudozyma* sp. NII 08165. *International Journal of Biological Macromolecules*. 2013 Aug 59:84-89 <https://doi.org/10.1016/j.ijbiomac.2013.04.025>
- [28] Nitschke M, Ferraz C, Pastore GM. Selection of microorganisms for biosurfactant production using agroindustrial wastes. *Brazilian Journal of Microbiology*. 2004 June 35(1-2):81-85 <https://doi.org/10.1590/S1517-83822004000100013>
- [29] Banat IM. Biosurfactants production and possible uses in microbial enhanced oil recovery and oil pollution remediation: a review. *Bioresource technology*. 1995 Oct 51(1):1-12 <https://doi.org/10.1016/j.biortech.1995.09.001>

1016/0960-8524(94)00101-6

- [30] Kaya A, Lobanov AV, Gerashchenko MV, Koren A, Fomenko DE, Koc A, Gladyshev VN. Thiol peroxidase deficiency leads to increased mutational load and decreased fitness in *Saccharomyces cerevisiae*. *Genetics*. 2014 Aug 198(3):905-917 <https://doi.org/10.1534/genetics.114.169243>
- [31] Rosenberg E, Ron EZ. High-and low-molecular-mass microbial surfactants. *Applied microbiology and biotechnology*. 1999 Aug 52(2):154-162
- [32] Bicca FC, Fleck LC, Ayub M. AZ. 1999. Production of biosurfactant by hydrocarbon degrading *Rhodococcus ruber* and *Rhodococcus erythropolis*. *Revista de Microbiologia*. 1999 Jul 30(3):231-236 <https://doi.org/10.1590/S0001-37141999000300008>
- [33] Bodour AA, Guerrero-Barajas C, Jiorle BV, Malcomson ME, Paul AK, Somogyi A, Maier RM. Structure and characterization of flavolipids, a novel class of biosurfactants produced by *Flavobacterium* sp. strain MTN11. *Applied and environmental microbiology*. 2004 Jan 70(1):114-120 <https://doi.org/10.1128/AEM.70.1.114-120.2004>



Original Article

The Antithrombotic Potential of Bioactive Peptides Induced by Buffalo Milk Probiotic Cheddar Cheese

Muhammad Anees Ur Rehman^{1*}, Khurram Ashfaq², Tehreem Ashfaq³, Muhammad Abuzar Ghaffari², Nasir Ali², Fatima Kazmi² and Nayab Sohail²¹Ruth Pfau College of Nutrition Sciences, Lahore Medical & Dental College, Lahore, Pakistan²Lahore Pharmacy College, Lahore Medical & Dental College, Lahore, Pakistan³Madinah Teaching Hospital, Faisalabad, Pakistan

ARTICLE INFO

Key Words:

Probiotics, Cheddar cheese, Ripening, Anti-thrombic, Functional Foods

How to Cite:

Anees Ur Rehman, M. ., Ashfaq, K. ., Ashfaq, T. ., Abuzar Ghaffari, M. ., Ali, N. ., Kazmi, F. ., & Sohail, N. . (2022). The Antithrombotic Potential of Bioactive Peptides Induced by Buffalo Milk Probiotic Cheddar Cheese. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.486>

*Corresponding Author:

Muhammad Anees Ur Rehman
Ruth Pfau College of Nutrition Sciences,
Lahore Medical & Dental College, Lahore, Pakistan
Anees.haraj@yahoo.comReceived Date: 25th May, 2022Acceptance Date: 15th June, 2022Published Date: 30th June, 2022

ABSTRACT

Cheddar cheese undergoes significant changes resulting in numerous microbiological and biochemical processes called glycolysis, lipolysis, and proteolysis, accountable for a unique texture, aroma, appearance, and taste. Specific bioactive peptides developed during these biochemical reactions impart health benefits. Addition of probiotics boots the development of bioactive peptides in foods. **Objective:** The current research investigated the therapeutic potential of water-soluble peptides (WSPs) extracts from buffalo milk probiotic Cheddar cheese regarding anti-thrombic facets. **Methods:** The appropriateness of Buffalo milk for Cheddar manufacturing was assessed by analysing its pH, acidity, fat, protein, and total solids content. Two batches of Cheddar cheese were produced, one having a mixture of Probiotic microorganisms and commercially available mesophilic cheese starter and the second containing only commercially available cheese starters. Both of the cheese batches were analysed for their physicochemical properties. Water-soluble extract of Cheddar cheese samples was analysed for anti-thrombic effects after two-month intervals during ripening. **Results:** Three concentrations of WSE of buffalo milk cheddar cheese were used to assess the antithrombotic effect during 60, 120, and 180 days of ripening at 4°C. Antithrombotic activity increased with the ripening period for both control and probiotic cheddar cheese samples **Conclusion:** A significantly increased effect of antithrombotic activity was observed by Probiotic adjunct on control cheddar cheese.

INTRODUCTION

Due to growing public awareness of diet and health in recent years, there has been a tremendous rise in the market for functional foods. Probiotic strains are used to prepare various foods, including yogurt, cheese, ice cream, dried yogurt (frozen), and fruit juices. Foods containing live probiotic bacteria are linked to several health advantages, such as the treatment of lactose intolerance, diarrhoea, cancer, high blood pressure, and immune system diseases [1]. At the time of intake, the probiotics must be viable within the recommended range in the food product. During processing and storage conditions of particular food items,

probiotic strains' viability must be considered. The number of viable probiotic strains for better health benefits must not be less than 10^9 CFU/100 gram or ml. In Japan, probiotic meals are suggested to include a minimum of 10^7 cells per 100g or ml [2]. In dairy products, the growth and survival of probiotic strains are supported. Yogurt and fermented milk are the best options for probiotic delivery during processing and storage conditions. The viability of probiotics in probiotic yogurt may be affected by factors such as low pH, the need for aerobic processing and packaging, hydrogen peroxide, and inhibiting compounds.

The factors affecting the viability of probiotic strains could be overcome by selecting suitable probiotic strains [3]. Cheese has a higher pH, solid consistency, and fat than freshly fermented dairy foods like yogurt. Cheese is the best dairy food for effective probiotic delivery [4]. It provides a protective environment to probiotic bacteria during their passage through the gastrointestinal tract. The buffering capacity of cheese is higher as compared to that of yogurt. Compared to cow milk, essential and non-essential fatty acids, casein proteins, vitamins, peptides, and other bioactive substances are abundant in buffalo milk. Buffalo milk is characterized by more conjugated linoleic acid, medium-chain fatty acids, total protein, retinol, and tocopherol. Certain kinds of gangliosides are only found in the milk of buffaloes [5]. The Buffalo milk differs from cows, goats, camels, and humans in that it has higher fat levels, total solids, proteins, lactose, and ash. It has been established that buffalo's milk is the best raw material for making dairy goods. Due to the composition of buffalo milk, yogurt and cheese are inherently thick. When making cheese or yogurt, no additional milk protein or other gelling agents are needed for buffalo milk. For this reason, buffalo milk is preferred by milk processors [6]. Buffalo cheese is recognized for its distinctive flavor, characteristic texture, and juicy consistency. Buffalo milk mozzarella cheese is treated as a premium product. Buffalo milk is exceptional for creating various dairy products because of its improved churning ability and increased heat stability [7]. There are numerous ways for encrypted bioactive peptides to emerge from precursor proteins like proteolysis, during the processing of milk and enzymatic hydrolysis by digestive enzymes, or a combination of two or more conditions. Milk protein release bioactive peptides in the digestive tract by digestive enzymes such as pepsin and pancreatic enzymes like trypsin, chymotrypsin, carboxyl, and aminopeptidases [8]. Bioactive peptides are released as a result of a number of structural and chemical changes that take place during food processing. By creating more inter- or intra-molecular connections, alkalizing and heating food can prevent it from hydrolyzing. Proteolytic starter cultures are utilized in the dairy sector to produce bioactive peptides [9]. The sequencing and makeup of the amino acids in a peptide determine its action. Opioid, antithrombotic, antihypertensive, immunomodulatory, anti-oxidative, antibacterial, anti-cancer, mineral reserve, and growth-inducing properties are among milk-derived bioactive peptides [10]. Bioactive peptides produced from milk may manifest their activity after absorption in the gastrointestinal system or throughout the body. The bioavailability of bioactive peptides should always be taken into account in vivo. The antithrombotic efficacy of buffalo

milk probiotic cheese was investigated in this study after ripening for 0, 60, 120, and 180 days at 4°C.

METHODS

Probiotic Cheddar cheese manufacturing

Buffalo milk was purchased from the local dairy farm. Milk was analysed for pH, fat, acidity, SNF, and protein. Control and probiotic cheddar cheese were manufactured using Murtaza *et al.*, [11] with some modifications. Typical mesophilic starter culture was used to prepare the control sample; *Lactobacillus acidophilus* and distinct mesophilic starter cultures were used as probiotic strains while manufacturing probiotic cheddar cheese. The cheese samples were hermetically packed and stored for ripening at 4°C for 180 days.

Analysis of probiotic cheddar cheese

The control and probiotic cheddar cheese samples were analysed for pH, fat, protein, and acidity after 60, 120, and 180 days of ripening [12].

Extraction of bioactive peptides from control and probiotic cheddar cheese

Cheddar cheese samples were mixed with distilled water and homogenized to prepare the slurry. The pH of the cheese slurry was adjusted to 4.6 by adding 0.1 M HCl. The samples were heated in the water bath at 40°C for 60 minutes, followed by centrifugation at 4000 rpm for 30 minutes. The temperature during centrifugation was adjusted to 4°C. After centrifugation, the supernatant was filtered out using Whatman filter no 40. The supernatant was further used for antithrombotic activities [13].

Antithrombotic Activity Assay

Prasad *et al.* studied the anti-thrombolytic action of peptides [14]. He selected twenty healthy volunteers for the said study. Selected subjects had their venous blood extracted. The blood was incubated at 37°C for 45 minutes in pre-weighed sterile microcentrifuge tubes. Clots occur as a result of incubation. Serum was extracted. Each tube's clot weight was estimated by weighing it again. (wt. of clot = clot weight including tube weight - empty tube weight). Clot-containing tubes were labelled correctly. The tubes were filled with Streptokinase (100 µl) and manifold dilutions in sterile distilled water. Distilled water was added as a negative thrombolytic control in one of the clot-containing tubes. At 90 minutes of incubation at 37°C, clot lysis was seen. After incubation, the tubes were weighed again by draining the acquired fluid. Clot lysis % was defined as the difference in weight before and after clot lysis.

Statistical analysis

The resulting data were statistically analysed using ANOVA in Minitab, and Tukey's test was utilized for multiple comparisons ($\alpha = 0.05$) between means. The findings were presented as mean values with standard error (SE)

RESULTS

Milk composition

Milk samples were analysed for compositional assays to assure their suitability for Cheddar cheese production. The physicochemical composition of milk for Cheddar cheese production is described in table 1. Buffalo milk is concluded to be the best milk source for the preparation of various dairy products, including cheese, by several findings.

Component	Composition (%)
Fat	5.54
Protein	3.92
pH	6.78
Acidity	0.13
SNF	38.54
Moisture	85.83

Table 1: Physicochemical composition of milk for Cheddar cheese

Cheddar Cheese composition:

Produced Control and probiotic cheddar cheese samples were analysed for their fat, protein, pH, and acidity during 60, 120, and 180 days of ripening at 4°C (Table 2). Overall a non-significant relation was observed between fat and protein assays of control and probiotic cheddar cheese samples. The pH of control and probiotic cheddar cheese samples decreased with an increase in ripening time. The lowest pH was observed in control and probiotic cheddar cheese during 180 days of ripening. The results indicate that the addition of probiotic adjunct did not significantly affect the composition of cheddar cheese.

Component (%)	Control			Probiotic Cheddar cheese			
	Ripening (days)	60	120	180	60	120	180
Fat		30.52±0.66	30.72±0.81	30.98±0.54	30.82±0.46	31.72±0.52	32.12±0.32
Protein		26.88±0.22	26.92±0.34	27.12±0.22	27.12±0.28	27.82±0.29	28.18±0.26
pH		5.15±0.02	5.01±0.12	4.91±0.06	5.14±0.02	5.00±0.12	4.89±0.06
Acidity		0.90±0.01	0.93±0.01	0.96±0.01	0.91±0.01	0.92±0.01	0.95±0.01
Moisture		38.74±0.14	37.43±0.12	36.22±0.16	37.88±0.11	37.12±0.13	36.11±0.13

Table 2: Composition percentage of control and probiotic cheddar cheese

Antithrombotic activity of control and probiotic cheddar cheese samples:

Thrombosis situations emerge in the human body due to an imbalance in hemostatic systems that results in the formation of a clot (thrombus) in arteries, veins, or the heart chamber. Aside from platelet attachment, dissemination and aggressiveness on the extracellular matrix contribute to thrombus formation. For control sample anti-thrombotic activity was recorded as 4.8 ± 0.34 (%), 16.0 ± 0.31 (%) and 38.2 ± 0.96 (%) at 60, 120 and 180 days of ripening respectively (Table 3). A highly significant increase in anti-thrombotic activity was observed with an increase in the ripening period for both control and probiotic Cheddar cheese adjuncts. Bioactivities of control and probiotic Cheddar cheese for anti-thrombotic activity were estimated using three different concentration levels

(250 µg/mL, 500 µg/mL, and 750 µg/mL) of water-soluble extracts. The maximum anti-oxidant activity was observed at 750 µg/mL concentration of WSE of peptides. Recorded values for anti-thrombotic activity at concentration level 750 µg/mL of WEPs extract is 8.1 ± 0.19 (%), 18.5 ± 0.27 (%) and 42.3 ± 0.66 (%) respectively. The table describes the interaction of WSPs extract and storage level. In current exploration, control and probiotic Cheddar cheese displayed a steady increase in anti-thrombotic activity as the ripening proceeds.

Samples	Level	Storage (days)			Means
		60	120	180	
Control	250 µg/mL	3.6±0.11	15.3±0.74	36.7±0.94	18.5±4.86
	500 µg/mL	5.0±0.20	16.3±0.38	38.0±2.15	19.8±4.88
	750 µg/mL	5.9±0.17	16.4±0.27	39.9±1.73	20.8±5.05
La	250 µg/mL	5.7±0.16	17.8±0.64	40.2±2.69	21.2±5.11
	500 µg/mL	7.1±0.25	18.2±0.27	40.1±0.58	21.8±4.85
	750 µg/mL	7.9±0.12	18.4±0.48	42.1±2.01	22.8±5.10

Table 3: Effect of cheese samples, storage and concentration level on anti-thrombotic activity (%) of WSE of probiotic cheddar cheese

DISCUSSION

Some variations in calcium contents of milk were reported in this assay. These changes are associated with feed, season, and lactation stages. Murtaza et al. [11] observed the variations in calcium contents and other minerals in the milk of Mediterranean buffaloes throughout the year due to these factors. The most critical factor during dairy product manufacturing is milk pH. Protein conformation, enzymatic activity, and milk acid dissociation are associated with milk pH. Various research works support milk pH in this study. The results of this study for moisture analysis of control and probiotic cheddar cheese during 180 days of ripening are in line with Moller et al. [15]. The present results show no direct effect on cheese moisture contents by adding probiotic adjuncts, which confirms the findings of Gardiner et al. [16]. The results of this study for fat analysis of control and probiotic cheddar cheese during 180 days of ripening are close to the effects of Ong et al. [17]. Fat is retained within the cheese matrix in buffalo milk. Milk fat undergoes enzymatic hydrolysis during ripening by lipase and esterase (lipolytic) and oxidative changes. During ripening, fat is hydrolyzed into free fatty acids, mono and diglycerides, and glycerol [18]. In cheese, probiotic bacteria contain proteolytic systems, which contribute to the release of small peptides and free amino acids. The addition of probiotic bacteria Lb has observed an increased rate of proteolysis. *paracasei*, or *Lb. Acidophilus* in Cheddar cheese, especially in forming low molecular mass peptides and free amino acids [19]. But the net quantity of nitrogenous components within the cheese matrix remains almost the same. However, a minute change in fat might be observed by reduced moisture contents [20]. The

results of this study for pH analysis of control and probiotic cheddar cheese during 180 days of ripening are compatible with the findings of Papetti and Carelli [21] that the pH of cheese varies within limits of 5.12 to 5.58 depending upon various factors. Ong *et al.*, in their study on probiotic Cheddar cheese, found pH in the range of 5.1 to 5.4 for different probiotic adjuncts. He also concluded that the nature of starter cultures (either probiotic or non-probiotic) does not significantly affect the pH of the product. These results are in line with the present study. Most lactose contents (about 98%) are drained off, and the whey. The rest of the lactose contents (0.8 to 1.8 %) remain present till the end of cheese manufacturing. In the early ripening stage, cheese's pH is decreased due to the residual lactose contents. Salting is another factor for the drop in pH. Starter lactic acid bacteria also participate in a decrease in pH. Reduced pH may affect the mineral content and growth of non-starter lactic acid bacteria in Cheddar cheese [22]. Furthermore, defects in platelet function may add to the complications of thrombotic events, ultimately connected to cardiovascular disease [23]. In the present study, a highly significant ($p < 0.01$) effect on % age of anti-thrombic activity of bioactive peptides was observed in the ripening stage, the concentration of WSE (a water-soluble extract) of bioactive peptide and cheese samples (control and probiotic adjuncts). A significant ($p < 0.01$) trend was observed in probiotic species' interactive effect with ripening days. The rapid evolving gene and post-translational modifications are also related to considerable variations in the primary sequences of α and β caseins. The water-soluble crude extracts of cheeses that contain major peptides formed during ripening may act synergistically to exert several physiological roles, including anti-thrombic activity [24]. It is an exciting fact that functional similarities exist between milk (κ casein) clotting and blood clotting (fibrinogen) [25]. The peptides casoplatelins derived from κ casein fractions showed anti-thrombic activity by inhibiting fibrinogen binding platelets. The caseino glycopeptidase (CGP) from bovine, caprine, and ovine sources has been demonstrated to inhibit thrombic formation [26]. Like the present findings, Qian *et al.* [5] found the anti-thrombic effect of sheep κ casein fraction in a dose-dependent manner. The present study is also supported by Sharma *et al.* [27], who revealed the dose-dependent anti-thrombic effect of bovine GMP..

CONCLUSION

The acidity of control and probiotic cheddar cheese increased with an increase in ripening. A significant difference in anti-thrombic activities was observed for probiotic Cheddar cheese and control Cheddar cheese. The percentage of clot lysis increased with the concentration of water-soluble peptides extracted from

both control and probiotic Cheddar cheese. The maximum anti-thrombic activity was observed in water-soluble peptides extracts at 180 days of ripening.

REFERENCES

- [1] Tholstrup Y. Dairy products and cardiovascular disease. *Curr. Opin. Lipidol.* 2006,17 (1):1-10. doi: 10.1097/01.MOL.0000199813.08602.58.
- [2] Kumar A and Kumar D. Development of anti-oxidant rich fruit supplemented probiotic yogurts using free and microencapsulated *Lactobacillus rhamnosus* culture. *J. Food Sci. Technol.* 2016, 53 (1): 667-675. doi: 10.1007/s13197-015-1997-7.
- [3] Ulpathakumbura CP, Ranadheera CS, Senaviratne ND, Jayawardene LPINP, Prasanna PHP and Vidanarachchi JK. Effect of biopreservatives on microbial, physico-chemical and sensory properties of Cheddar cheese. *Food Biosci.* 2016, 13: 21-25. doi: 10.1016/j.fbio.2015.12.003.
- [4] Cotter PD and Hill C. Surviving the Acid Test: Responses of Gram-Positive Bacteria to Low pH. *Microbiol. Mol. Biol. Rev. Sept.* 2003, 67(3): 429-453. doi: 10.1128/membr.67.3.429-453.2003.
- [5] ACGWMM-MAR-BMR-L. Bergillos-Meca T. In vitro evaluation of the fermentation properties and potential probiotic activity of *Lactobacillus plantarum* C4 in batch culture systems. *Food Sci Technol*, 2015, 60: 420-426.
- [6] Leghari A, Shahid S, Farid M, ... M. S.-L. S., and undefined 2021. Beneficial aspects of probiotics, strain selection criteria and microencapsulation using natural biopolymers to enhance gastric survival: A review. *researchgate.net*, Accessed: Feb. 11, 2021. [Online]. Available: https://www.researchgate.net/profile/Ali_Ahmad_Leghari/publication/348606260_Beneficial_aspects_of_probiotics_strain_selection_criteria_and_microencapsulation_using_natural_biopolymers_to_enhance_gastric_survival_A_review/links/60071a84299bf14088aa4499/Beneficial-aspects-of-probiotics-strain-selection-criteria-and-microencapsulation-using-natural-biopolymers-to-enhance-gastric-survival-A-review.pdf
- [7] Mumtaz S, Rehman SU, Huma N, Jamil A and Nawaz H. Xylooligosaccharide enriched yoghurt: Physicochemical and sensory evaluation. *Pakistan J. Nutr.*, 2008, 7(4): 566-569. doi: 10.3923/pjn.2008.566.569.
- [8] Rehman MAU, Sultan W and Ajmal M. Effect of Probiotic Strains on Sensory Attributes of Buffalo Milk Cheddar Cheese. *J. Food Nutr. Res.* 2021,9(9):492-498. doi: 10.12691/jfnr-9-9-6.
- [9] Cavera VL, Arthur TD, Kashtanov D and Chikindas ML.

- Bacteriocins and their position in the next wave of conventional antibiotics," *International Journal of Antimicrobial Agents*, Feb. 23, 2015, 46(5): 494-501, Elsevier B.V. doi: 10.1016/j.ijantimicag.2015.07.011.
- [10] Romero V, Borneo R, Passalacqua N and Aguirre A. Biodegradable films obtained from triticale (x Triticosecale Wittmack) flour activated with natamycin for cheese packaging. *Food Packag. Shelf Life*, Dec. 2016, 10:54-59, , doi: 10.1016/j.fpsl.2016.09.003.
- [11] Murtaza MA, Rehman MAU, Hafiz I, Ameer K and Celik OF. Effects of probiotic adjuncts on physicochemical properties, organic acids content, and proteolysis in cheese prepared from buffalo milk. *J. Food Process. 2022, Preserv.* 46(3):1-11. doi: 10.1111/jfpp.16385.
- [12] Chammem N, Issaoui M, De Almeida AID and Delgado AM. Food Crises and Food Safety Incidents in European Union, United States, and Maghreb Area: Current Risk Communication Strategies and New Approaches. *Journal of AOAC International*, Jul. 01, 2018, 101(4): 923-938, doi: 10.5740/jaoacint.17-0446.
- [13] Wu N, Xu W, Liu K, Xia Y and Shuangquan. Angiotensin-converting enzyme inhibitory peptides from *Lactobacillus delbrueckii* QS306 fermented milk. *J. Dairy Sci.*, 2019, 102(7): 5913-5921. doi: 10.3168/jds.2018-15901.
- [14] Pessione E and Cirrincione S. Bioactive molecules released in food by lactic acid bacteria: Encrypted peptides and biogenic amines. *Frontiers in Microbiology*, Frontiers Research Foundation, 2016, 7 :1-19. doi: 10.3389/fmicb.2016.00876.
- [15] Von Mollendorff JW, Todorov SW and Dicks LMT. Factors affecting the adsorption of bacteriocins to *Lactobacillus sakei* and *Enterococcus* sp. *Appl. Biochem. Biotechnol.*, Aug. 2007, 142(2): 209-220. doi: 10.1007/s12010-007-0024-5.
- [16] Evans MR et al. An outbreak of *Salmonella typhimurium* DT170 associated with kebab meat and yoghurt relish. *Epidemiol. Infect.* 1999, 122: 377-383.
- [17] Ong L and Shah NP. Probiotic Cheddar cheese: Influence of ripening temperatures on survival of probiotic microorganisms, cheese composition and organic acid profiles. *LWT - Food Sci. Technol.*, 2009, 42(7): 1260-1268. doi: 10.1016/j.lwt.2009.01.011.
- [18] Farkye NY and Fox PF. Objective indices of cheese ripening. *Trends Food Sci. Technol.* 1990, 1: 37-40. Costabel LM, Bergamini C, Vaudagna SR, Cuatrin AL, Audero G and Hynes E. Effect of high-pressure treatment on hard cheese proteolysis. 2016, 1992: 4220-4232. doi: 10.3168/jds.2015-9907.
- [20] Rehman MAU, Murtaza MA, Hafiz I, Shabbir MA, Arshad M. Antihypertensive and Anti-Oxidant impact of Probiotic cultures in Cheddar cheese. *J. Biol. Regul. Homeost. Agents*, 2019, 33(4): 1013-1018.
- [21] Cruz AG et al. Survival analysis methodology to predict the shelf-life of probiotic flavored yogurt. *Food Res. Int.*, Jun 2010, 43(5): 1444-1448. doi: 10.1016/j.foodres.2010.04.028.
- [22] O. Markey et al., "Consumer acceptance of dairy products with a saturated fatty acid-reduced, monounsaturated fatty acid-enriched content. *J. Dairy Sci.* 2017, 100 (10) 10:7953-7966, 2017, doi: 10.3168/jds.2016-12057.
- [23] Divya JB, Varsha KK and Nampoothiri KM. Newly isolated lactic acid bacteria with probiotic features for potential application in food industry," in *Applied Biochemistry and Biotechnology*, Jul. 2012, 167 (5): 1314-1324. doi: 10.1007/s12010-012-9561-7.
- [24] Anusha R and Bindhu OS. Bioactive Peptides from Milk in Milk Proteins - From Structure to Biological Properties and Health Aspects, *InTech*, 2016. doi: 10.5772/62993.
- [25] Song Y, Li TY, Van Dam RM, Manson JAE and Hu FB. Magnesium intake and plasma concentrations of markers of systemic inflammation and endothelial dysfunction in women. *Am. J. Clin. Nutr.* Apr 2007, 85(4):1068-1074. doi: 10.1093/AJCN/85.4.1068.
- [26] Kanatani MOKSK. Isolation and characterization of acidocin A and cloning of the bacteriocin gene from *Lactobacillus acidophilus*," *Appl Env. Microbiol*, 1995, 61: 1061-1067.
- [27] Kamboj SS and Sharma B. Comparative Analysis of Antigiardial Potential of Heat Inactivated and Probiotic Protein of Probiotic *Lactobacillus rhamnosus* G.G. in Murine Giardiasis," *Probiotics Antimicrob. Proteins*, Mar. 2020, 12(1): 271-279. doi:10.1007/s12602-018-9506-8.



Original Article

The Effects of High Intensity Exercise to Exhaustion on the Concentrations of Endostatin and VEGF in Plasma.

Inayat Shah¹, Tasleem Arif², Amber³ and Imdad Ali³¹Institute of Basic Medical Sciences (IBMS), Khyber Medical University, Peshawar.²The University of Haripur³Sarhad University of Science & Information Technology (SUIT), Peshawar

ARTICLE INFO

Key Words:

High Intensity, Exercise, Healthy, Volunteer, VEGF, Plasma

How to Cite:

Inayat Shah, Arif, T., Amber, ., & Ali, I. . (2022). The Effects of High Intensity Exercise to Exhaustion on the Concentrations of Endostatin and VEGF in Plasma: Effects of Exercise on Endostatin and VEGF concentrations. *Pakistan BioMedical Journal*, 5(6), 329–335. <https://doi.org/10.54393/pbmj.v5i6.590>

*Corresponding Author:

Tasleem Arif
The University of Haripur
tasleem.arif@uoh.edu.pkReceived Date: 5th June, 2022Acceptance Date: 19th June, 2022Published Date: 30th June, 2022

ABSTRACT

Endostatin and Vascular Endothelial Growth Factor (VEGF) are important markers driving the angiogenic switch. It is clear that short periods of moderate to high intensity exercise significantly increase the concentration of endostatin and VEGF in plasma. **Objective:** To investigate concentration of circulatory endostatin in plasma and impact of different intensities of exercise encompassing from low to maximum on distribution of endostatin and VEGF concentrations in plasma. **Methods:** Eight healthy male volunteers were recruited through advertisements and personal contacts, after assessing their fitness through two pre-participation health screening questionnaires, PAR-Q and ACSM Health Fitness Facility pre-participation health screening questionnaire for performing maximal exercise to volitional exhaustion. All the volunteers attend the lab on 2 consecutive days. The blood was centrifuged at 1000 RPM for 15 minutes for endostatin and VEGF and at 3000 RPM for 15 minutes for lipid profiles and insulin. Samples were analysed for endostatin and VEGF concentrations using Quantikin[®] ELISA kit of the R&D systems, while Insulin was measured using ELISA kit (Merckodia, Uppsala Sweden). **Results:** The basal endostatin concentration remained consistent and higher intensity of exercise significantly increased the endostatin concentration for up to 2 hours. Exercise also influenced VEGF concentration transiently and only at 30 minutes' interval increase in VEGF was statistically significant. **Conclusion:** It is worth noting that those participants who showed an immediate decrease in VEGF after exercise, later on exhibited a concentration higher than basal.

INTRODUCTION

Endostatin and Vascular Endothelial Growth Factor (VEGF) are important markers driving the angiogenic switch. An imbalance of which can lead to atherosclerosis. It is clear that short periods of moderate to high intensity exercise significantly increase the concentration of endostatin and VEGF in plasma [1]. These changes are different at different intensities of exercise. However, the changes were observed for 1 hour only without a return to baseline. The possibility of later changes in VEGF or endostatin concentration could not be ruled out completely, as significant changes in endostatin and VEGF concentrations up to 6 hours after exercise has been reported [2]. Moreover, it was thought that factors important in development of atherosclerosis and endothelial functions such as; body fat composition,

fasting lipid profile, fasting blood glucose concentration and insulin sensitivity should be explored to determine any possible association with endostatin and VEGF. Endostatin is a part of collagen in the basement membrane. It is in close proximity to the endothelium and other vascular structures. It is known that internal milieu strongly influences the endothelium and other vascular structure's functions. For example, an increase in body fat is associated with activation of renin angiotensin aldosterone system (RAAS), and subsequent increases in angiotensin II affects the vascular stiffness [3]. Moreover, increase in body fat increases the risk type 2 diabetes [4] which in turn increases the risk of atherosclerosis [5]. Similarly, insulin resistance is associated with endothelial dysfunction and impaired vascular relaxation which in turn

contributes to atherosclerosis and other cardiovascular events [6]. In addition, deranged lipid profile and hyperglycaemias are important determinants of endothelial dysfunction derived health problems, including atherosclerosis and peripheral vascular diseases [7].

Thus, the possibility of an association of endostatin with these metabolic factors could not be ruled out. Therefore, experiment was designed to look for the influence of high intensity exercise on endostatin and VEGF concentration in plasma for a longer duration (24 hours) after exercise and to investigate their correlation with other factors involved directly or indirectly in the pathogenesis and development of atherosclerosis.

METHODS

The Research Ethics Committee of the College of Medical, Veterinary and Life Sciences, University of Glasgow, granted the approval for this study. Eight healthy male volunteers were recruited through advertisements and personal contacts, after assessing their fitness through two pre-participation health screening questionnaires, PAR-Q and ACSM Health Fitness Facility pre-participation health screening questionnaire [8] for performing maximal exercise to volitional exhaustion. Different characteristics of all participants with mean \pm SD are illustrated. Ht; Height in m, Wt; Weight in kg, BMI; Body mass index, SBP; Systolic blood pressure, DBP; Diastolic blood pressure, WC; Waist circumference, HC; Hip circumference, W:H ratio; Waist to hip circumference ratio. All the volunteers attend the lab on 2 consecutive days. The total duration of their stay, was 6 to 7 hours on the first day and about 30 minutes on the second day. On initial visit, the participants were requested to visit the lab in fasted. After signing consent forms, their height, weight, blood pressure, heart rate, waist and hip circumference were measured and body fat percentages were estimated using air displacement plethysmography in a Bod Pod. The fasting blood glucose concentrations of the participants were determined using glucometer (Accu-Chek Aviva, Mannheim, Germany). After rest 3 blood samples of 5 ml were taken, one each for endostatin, VEGF and fasting blood lipid profile and insulin concentration. The participants were then given isotonic drinking solution to restore some energy. The participants performed maximal exercise test on the treadmill using the modified Taylor protocol [9]. During the test, maximal oxygen uptake of the participant was measured with breath by breath analyser (Medical Graphics Corporation, Borngasse, Germany). The test was completed by all the volunteers and they were encouraged to make a maximum effort. The effort was considered maximum, if most of the following criteria were observed, as per ACSM guidelines [8]: Achieved heart rate during the test was in the range of age predicted maximum

heart rate \pm 10 bpm. A respiratory exchange ratio of more than 1.10. A post exercise lactate concentration of 8 mmol. A plateau in oxygen consumption (VO_2) or failure in oxygen uptake by $150\text{ml}\cdot\text{min}^{-1}$, beside increase in work rate, as shown in the figure 6-1 from the data of one participant. A rating of >17 on Borg scale of perceived exertion. At the end of the test all the participants walked slowly for 5 minutes till the heart rate dropped to 120 bpm. Blood was taken by a finger prick at 0, 3, and 5 minutes at the end of running to measure the lactate concentrations. The participants then relaxed in a quiet room and more blood samples were taken at 10, 30, 60, 120, and 240 minutes after the exercise. During this time, they watched movies or videos as per choice, while sitting on a chair. They were given biscuits and isotonic drinks during this time. After the final blood sample, cannula was removed and a full meal was served. They were asked to attend the lab on next day for a 24-hour sample. On day 2 the participants attended the lab for two blood samples, one each for VEGF and endostatin.

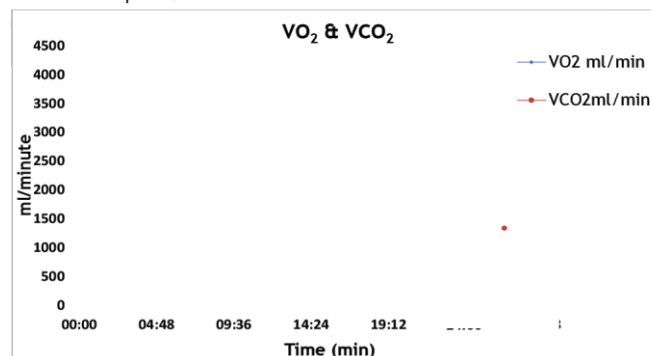


Figure 1: Breath by breath oxygen consumption and carbon dioxide production.

Show oxygen consumption (VO_2) and carbon dioxide production (VCO_2) from one of the participant during exercise. The initial 3 minutes are the resting period and the maximum effort was noticed at 22 minutes. The dotted line on the horizontal axis shows the maximum effort period during which the plateau in oxygen consumption can be seen. The blood was centrifuged at 1000 RPM for 15 minutes for endostatin and VEGF and at 3000 RPM for 15 minutes for lipid profiles and insulin. Plasma was separated into 3 aliquots each for endostatin, VEGF and lipid profile into 1ml Eppendorf tube using disposable plastic pipettes (Wilford Ind. Nottingham, UK). Samples were analysed for endostatin and VEGF concentrations using QuantikinR ELISA kit of the R&D systems, while Insulin was measured using ELISA kit (MercoDia, Uppsala Sweden). Plasma glucose, total and high density lipoprotein, triglyceride and non-esterified fatty acid (NEFA) were determined using commercially available enzymatic kits. Friedewald equation was used for the determination of low density lipoprotein (LDL), as follow

[10]; LDL mmol l⁻¹ = (Total cholesterol – HDL cholesterol) – (TG / 2.2) Insulin resistance was determined using the QUICKI equation as follow; QUICKI = 1/ (log G0 + log I0). Where G0 is the fasting blood glucose concentration in mg/dl, I0 is the fasting insulin concentration in Mu/l. SPSS version 17.0 and Minitab version 16.0 were used for the statistical analyses. The normalities of all variables were determined and where necessary log transformations were carried out. Summary statistics were carried out for data and presented as mean ± SD. ANOVA with repeated measures was used for checking the difference between the mean in pre and post exercise blood samples. Correlations between endostatin, VEGF and other variables were determined using person correlation. Box plot were produced to graphically present the data, where necessary.

RESULTS

Anthropometric data and are physical characteristics of the participants shown in the Table 1 below.

S. no	Age (Yrs.)	Ht. (m)	Wt. (kg)	BMI (kg/m ²)	SBP (mmhg)	DBP (mmhg)	WC (cm)	HC (cm)	W:H ratio
1	34	1.68	75.1	26.6	112	76	79	93	0.85
2	25	1.85	69.9	20.4	116	76	80	99	0.81
3	36	1.61	61.3	23.6	123	76	75	79	0.95
4	27	1.82	72.2	21.8	123	82	88	99	0.89
5	30	1.91	70.1	19.2	118	81	74	95	0.78
6	34	1.71	67.2	22.9	130	80	83	99	0.84
7	22	1.75	69.7	22.8	118	62	81	96	0.84
8	40	1.80	88.9	27.4	126	76	85	94	0.90
Mean	31±	1.77	71.8±	23.1	121	76	81	94	0.86
±SD	6.1	±0.1	7.9	±2.8	±6	±6	±5	±7	±0.05

Table 1: Anthropometric and physical Characteristics of the participants

All the volunteers performed exercise without any complications. The mean duration for the test was 17.04 ± 2.6 minutes (ranging 12 to 19 minutes) during which the participants covered a mean distance of 2.1 ± 0.34 Km. All the participants run at fixed speed of 8 km/hr with a mean maximum gradient of 11 ± 2%. The mean maximum heart rate achieved during the test was 191 ± 10 bpm which increased by 167% from the mean basal heart rate of 72 bpm (p < 0.001). A mean increase of 38 ml/kg/min in oxygen consumption (VO₂) was observed with the maximum oxygen consumption (VO₂max) of 42 ml/kg/min achieved during the test (P < 0.001). Mean lactate concentration post exercise was 7.4 mmol (ranging 5.4 to 9.8 mmol). The individual values and mean ± standard deviations of the parameters of exercise are given in Table below 2.

S. no	BHR	Max HR	Duration	distance	Max Grad	BVO ₂	Vo ₂ Max	RER	RR
1	68	180	12.04	1.45	7.5	3.3	33	1.20	62
2	71	194	19.25	2.40	12.5	4.3	45	1.44	48
3	68	184	18.04	2.20	10.0	4.8	44	1.29	39
4	70	210	18.16	2.25	12.5	4.3	39	1.59	49
5	82	184	19.10	2.38	12.5	3.9	45	1.17	35
6	82	194	15.07	1.84	10.0	4.8	39	1.23	48
7	76	196	19.28	2.43	12.5	5.4	47	1.34	47
8	63	184	15.44	1.93	10.0	4.0	44	1.30	41
Mean	72	191	17.04	2.1±	11±	4.3±	42±	1.3±	46
±SD	±9	±10	±2.6	0.34	1.9	0.6	5	0.6	±8

Table 2: Different parameters of exercise at base levels and during exercise

The individual values for components of exercise and mean ± standard deviation are shown. These indicate a maximal effort by all participants according to ACSM guidelines. BHR; Basal heart rate (beats per minute), Max HR; Maximum heart rate, Max Grad; Maximum gradient (%), BVO₂; Resting oxygen consumption (ml/kg/min), VO₂Max; Maximum oxygen consumption (ml/kg/min), RER; Respiratory exchange ratio, RR; Respiratory rate (breaths per minutes). Mean concentrations of endostatin in plasma before and after exercise are shown in figure 2. It is clear, that single bout of short period of high intensity exercise increased the mean endostatin concentration as confirmed by ANOVA with Bonferroni corrections (P < 0.001). The mean values were: 126 ± 16, 139 ± 15, 132 ± 12, 129 ± 12, 120 ± 23 and 107 ± 15 ng/ml respectively, at 10 minutes, 30 minutes, 1 hour, 2 hours, 4 hours and 24 hours after the exercise. These changes correspond to increases of 21% (P = 0.003), 34% (P < 0.001), 27% (P < 0.001), 24% (P = 0.001), 15% (P = 0.07), and 3% (P = 0.883) compared to resting endostatin concentration. The changes at points 1-4 i.e. up to 2 hours post exercise were statistically significant. The highest increase was observed at 30-minute interval after the exercise as shown in Figure 2.

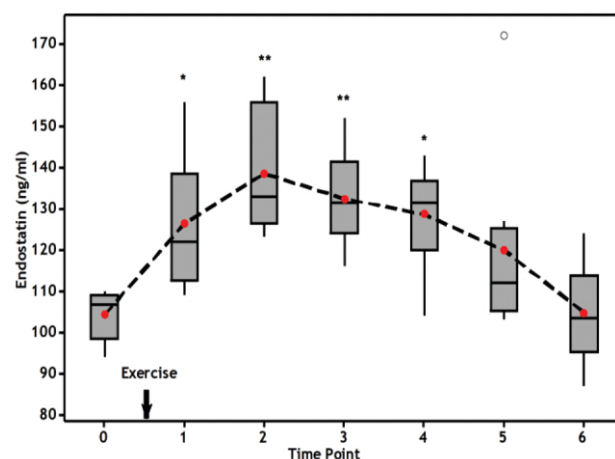


Figure 2: Endostatin concentration before and different intervals after maximal exercise

Endostatin concentration before and different intervals after exercise (0 = before exercise, 1= 10 minutes, 2 = 30 minutes, 3 = 1 hour, 4 = 2 hours, 5 = 4 hours and 6 = 24 hours after exercise). Significant changes in mean endostatin concentrations were observed after exercise at 10 minutes, 30 minutes, 1 hour and 2 hour intervals. (*= P value <0.05 between basal and time point, ** = P value <0.001 between basal and time point). Clear circle represent outlier. The effect of exercise on VEGF concentration was also investigated. The mean VEGF concentrations were: 102 ± 46 , 115 ± 35 , 109 ± 40 , 113 ± 38 , 108 ± 53 and 99 ± 23 pg/ml at 10 minutes, 30 minutes, 1hour, 2 hours, 4 hours and 24 hours respectively, after the exercise. These changes are equal to 12% (P=0.43), 26% (P=0.04), 19% (P=0.32), 24% (P=0.067), 19% (P=0.077) and 9% (P=0.36), respectively. The increase in VEGF concentration was only significant at 30-minute interval (P = 0.04). The VEGF concentration remained higher than basal at all-time points up to 24 hours after exercise, as shown in Figure 3.

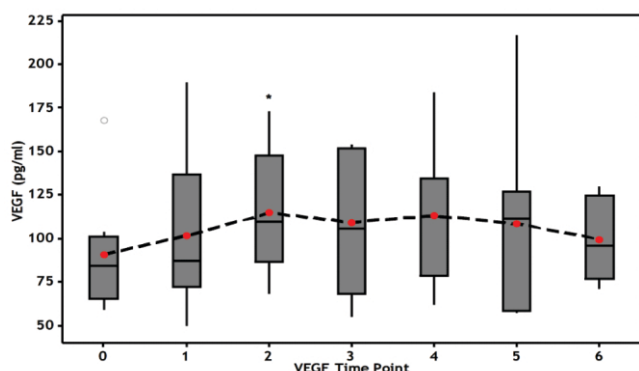


Figure 3: VEGF concentrations before and different intervals after maximal exercise test

Figure shows the VEGF concentrations before and at different time points after exercise (0 = before exercise, 1= 10 minutes, 2 = 30 minutes, 3 = 1 hour, 4 = 2 hours, 5 = 4 hours and 6 = 24 hours after exercise). The significant change in VEGF concentration was only observed at 30 minutes after exercise (P=0.04). Clear circle shows outlier in basal VEGF. Correlations of changes in endostatin and VEGF with anthropometric lipid profile and exercise parameters. Finally, the changes in endostatin and VEGF concentrations were extensively correlated with anthropometric parameters (age, weight, height etc) lipid profile (Cholesterol, TG, LDL, HDL) and exercise parameters (maximal heart rate, RER, VO₂ max etc.), however, no significant correlations of statistical importance were observed.

DISCUSSION

This study was aimed to determine the effect of maximal intensity exercise to volitional exhaustion (VO₂max) on plasma concentration of endostatin and VEGF in young

healthy participants. Additional aims include the correlation of basal endostatin and VEGF with anthropometric, physical and metabolic characteristics of the individuals. Moreover, the effects of changes in endostatin concentration on the respective changes in VEGF were also aimed. This study provided more conclusive results in terms of effect of exercise on endostatin concentration. The change in endostatin concentration was clear and more pronounced [1]. Moreover, this study also verified the results in the previous studies i.e. the basal endostatin concentration remained consistent and higher intensity of exercise significantly increase the endostatin concentration for up to 2 hours. Additionally, no correlations of statistical significance between anthropometric characteristics including body fat percentages and metabolic parameters including fasting lipid profile, fasting blood glucose and insulin with endostatin and VEGF were observed. Exercise also influenced VEGF concentration transiently and only at 30-minute interval increase in VEGF was statistically significant. The participants showed the increase in VEGF concentration at different time points after exercise. Due to this variation in person to person response after exercise, quantification of VEGF is difficult. However, it is worth noting that even those participants who showed an immediate decrease in VEGF after exercise, later on exhibited a concentration higher than basal. High intensity exercise showed significant increase in endostatin. Although the endostatin concentration after exercise in plasma was higher than basal, up to 4 hours but significantly high concentrations were observed up to 2 hours. The results in this study confirm the previous results, when the volunteers exercised at 70% and 80% predicted maximum heart rate. Moreover, these results are also consistent with previous published studies carried out by many researchers [2;11; 12; 13; 14]. It seems that short bouts of relatively high intensity exercise increase the endostatin concentration transiently for duration up to 2 hours. The extent of change in endostatin concentration was, however, different and can be attributed to the difference in mode, intensity and physical characteristics of the participants. Gu and his colleagues has reported a significant increase up to 6 hours after exercise [2]. Physical fitness seems to affect the degree of increase in endostatin concentration after exercising [13]. This also implies that many other reasons, such as easy fatigability, presences of co-morbid conditions and age of the participants could cause the difference in the extent of changes. This could be true as one study reported increase in endostatin concentration only in healthy and young individuals and not in old age individuals [14]. However, our results can be compared with study done by Suhr, who also

found significant increase lasting for two hours after exercise [11]. The effects of long term physical activity on the basal endostatin concentration are contradictory. Sponder and his colleagues reported significantly high basal endostatin concentration in athlete males and females compared to their controls. It was assumed, that high basal endostatin concentration is due to the regular physical training of the athletes [13]. In contrast, decrease in basal endostatin concentration after 6 months of regular physical training in 50 – 60 years old individuals [15], as well as in long and short track elite runners have been reported [16]. The mechanism behind these differences is not clear and needs further studies. The other aim of the study was to correlate the basal endostatin concentration with anthropometric and metabolic parameters of the participants. Good metabolic profile indicates healthy endothelial status and well-being of the individual. It was hypothesised, that they might affect basal endostatin concentration, as well as the change in it after exercise. No correlations of significant importance were observed either with the basal endostatin concentration or the change in it at any time point after the exercise. To the author's knowledge this is a complete novel finding. It is interesting due to the fact that deranged lipid profile, glucose intolerance or insulin insufficiency play important roles in early endothelial events leading to atherosclerosis. Despite endostatin being present in blood and basement membrane, did not show any interactions with these parameters. However, sample size is small to appreciate any such associations and study with a bigger sample size will be required to draw solid conclusion. Finally, no correlation of statistical significance was observed between endostatin concentration and anthropometric measurements. The exercise intensity in this series of experiments was higher than used previously. The duration of near maximal exercise was shorter and the use of breath by breath measurement allowed the gas exchange to be monitored in real time. Different features of exercise showed no statistically significant correlations with the changes in endostatin concentrations, at different time points after the exercise. These results are different from Gu who reported a strong linear correlation between change in exercise and peak oxygen consumption [2]. In author's opinion, the results in our study are more reliable because the values for the peak oxygen consumption, in Gu's study, were estimated by calculation rather than measured. Moreover, Gu's findings could not be confirmed in later studies [12; 13]. It was observed consistently that moderate to high intensity exercise increase the endostatin concentration without direct correlations with any exercise feature. From this it can be assumed, that exercise does change the endostatin concentration by

altering different mechanisms indirectly including increasing expression of enzymes involved in endostatin release [16]. Mean basal VEGF concentration of $91 + 34$ pg/ml in this study group is higher than that seen chapter 4, which was $75 + 36$ pg/ml. It is clear from the broad confidence intervals, shown in figure 6-6, that there is substantial variation in basal VEGF concentrations. A wide range of basal concentrations, between 98 to 485 pg/ml, has been reported and this is attributed to the differences in genetic regulation and makeup of these individuals [17]. Such variations make it difficult to quantify the increase in VEGF after exercise. The Mean VEGF concentration increased initially after exercise until 30 minutes. After this time point, a pattern of increase and decrease can be observed, as shown in figure 6. It can also be seen that mean VEGF concentration was never found to be lower than basal during this experiment. These results confirm our earlier results that increase in mean VEGF concentration after exercise with no specific pattern. The literature about exercise as a regulator of VEGF is conflicting and limited. On one hand, increases in VEGF concentrations after exercise have been reported [18; 19; 20; 21]. The extent of increase in mean VEGF after exercise reported, varies from as low as 30% [19] to as high as 240% [20] and as acutely as 30-minute post exercise to as long as 5 days' post exercise. These changes may reflect different exercise modalities. On the other hand, a decrease in mean VEGF concentration after acute exercise has also been reported by [22; 2]. Again the modes of exercise in the above studies were completely different. In Gustafsson study, the participants performed one knee extension for 7 sessions of 45 minutes over a period of 10 days. Timings of the blood sample collection are crucial, as the first sample was taken before 1st exercise session and the last sample was taken 24 hours after the 7th exercise session. In our study it was observed that exercise affect VEGF concentration transiently. The VEGF concentration tends to drop back towards normal at about 1 hour after exercise. So it is possible, that VEGF concentration 24 hours after exercise may be more or less the same as basal VEGF concentration. Similar results to Gustafsson have also been reported in another study, where long term endurance exercise programme for 6 months, showed no alteration in VEGF concentration. Interestingly, post intervention plasma samples were taken, on next day after the last exercise session [15]. However, the study done by Gu, has shown the decrease in mean VEGF concentration significantly up to 6 hours, a finding which could not be confirmed by published literature or this study. There is convincing evidence in the literature, that acute exercise bouts increase VEGF concentration in skeletal muscles and its subsequent release to venous circulation [19; 18; 23] but not to arterial

circulation [18]. It is plausible that after release from the stretched muscles during exercise into the venous system, the VEGF is taken by other tissues, not directly involved in the exercise. However, the possibility of increase in VEGF from cells like platelets and myocytes cannot be overruled, as electrical stimulations of cardiac myocytes has been shown to increase VEGF release [24]. Finally, correlation between endostatin and VEGF concentrations before and at all-time points after exercise were carried out. Concurrently the correlations between the changes in both mediators at each time point were also checked, as shown in table 5. No correlations of statistical importance at any time point were observed. It is established from the literature that endostatin antagonises the signalling mechanisms of VEGF [25; 26]. However, it is clear from the results, that increase in endostatin concentration after high intensity exercise has no negative effect on the plasma VEGF concentration, a finding which is in dispute with the results published by Gu and his co-workers [2]. An increase in VEGF concentration after exercise seems more logical as exercise increase the expression of mRNA in skeletal muscle [18], which enhances the production of VEGF in skeletal muscles and favours the release of VEGF from tissue to circulation [21].

CONCLUSIONS

In conclusion, the high intensity exercise increases the mean endostatin more prominently and for a longer duration than VEGF without any important interaction between the two mediators.

REFERENCES

- [1] Shah I, Arif T, Baxendale RH, Iftikhar M, Khan A. The Effect of Different Exercise Intensities on Plasma Endostatin in Healthy Volunteers. *Journal of Pharmaceutical Research International*. 2021 Mar;33(13):30-8. doi: 10.9734/jpri/2021/v33i1331263
- [2] Gu JW, Gadonski G, Wang J, Makey I, Adair TH. Exercise increases endostatin in circulation of healthy volunteers. *BioMed Central Physiology*. 2004 Jan; 4:2. doi:10.1186/1472-6793-4-2.
- [3] Engeli S, Negrel R, Sharma AM. Physiology and pathophysiology of the adipose tissue renin-angiotensin system. *Hypertension*. 2000 Jun; 35(6):1270-7. doi: 10.1161/01.hyp.35.6.1270.
- [4] Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. *Diabetes Care*. 1994 Sep; 17(9):961-9. doi: 10.2337/diacare.17.9.961
- [5] Folsom AR, Rasmussen ML, Chambless LE, Howard G, Cooper LS, Schmidt MI et al. Prospective associations of fasting insulin, body fat distribution, and diabetes with risk of ischemic stroke. The Atherosclerosis Risk in Communities (ARIC) Study Investigators. *Diabetes Care*. 1999 Jul; 22(7):1077-83. doi: 10.2337/diacare.22.7.1077
- [6] Kim JA, Montagnani M, Koh KK, Quon MJ. Reciprocal relationships between insulin resistance and endothelial dysfunction: molecular and pathophysiological mechanisms. *Circulation*. 2006 Apr; 113(15):1888-904. doi: 10.1161/Circulationaha.105.563213.
- [7] Deaton C, Froelicher ES, Wu LH, Ho C, Shishani K, Jaarsma T. The global burden of cardiovascular disease. *European Journal of Cardiovascular Nursing*. 2011 Jul; 10 Suppl 2:S5-13. doi: 10.1016/S1474-5151(11)00111-3.
- [8] Kluwer W. ACSM'S guidelines for exercise testing and prescription. Philadelphia, US: Lippincott Williams & Wilkins. 2013 Feb; 480.
- [9] Taylor HL, Buskirk E, Henschel A. Maximal oxygen intake as an objective measure of cardio-respiratory performance. *Journal of Applied Physiology*. 1955 Jul; 8(1):73-80. doi: 10.1152/jappl.1955.8.1.73.
- [10] Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry*. 1972 Jun; 18(6):499-502.
- [11] Suhr F, Brixius K, de Marées M, Bölck B, Kleinöder H, Achtzehn S, et al. Effects of short-term vibration and hypoxia during high-intensity cycling exercise on circulating levels of angiogenic regulators in humans. *Journal of Applied Physiology* (1985). 2007 Aug; 103(2):474-83. doi: 10.1152/japplphysiol.01160.2006. Epub 2007 Apr 19.
- [12] Sponder M, Sabri A, Dangl D, Stanek B, Kosi L, Kautzky-Willer A, Fritzer-Szekeres M, Marculescu R, Strametz-Juranek J. Influence of age, smoking and diabetes on exercise related antiangiogenic endostatin/collagen XVIII release in men. In *EUROPEAN HEART JOURNAL*. Great Clarendon ST, Oxford OX2 6dp, England: Oxford University Press. 2011 Aug; 32: 1029.
- [13] Sponder M, Sepiol K, Lankisch S, Priglinger M, Kampf S, Litschauer B, et al. Endostatin and physical exercise in young female and male athletes and controls. *International Journal of Sports Medicine*. 2014 Dec; 35(13):1138-42. doi: 10.1055/s-0034-1375692.
- [14] Bruslerud O, Grovan F, Lindås R, Blymke Møinichen C, Osterhus KK. Serum levels of angioregulatory mediators in healthy individuals depend on age and physical activity: studies of angiogenin, basic fibroblast growth factor, leptin and endostatin.

- Scandinavian Journal of Clinical and Laboratory Investigation. 2005; 65(6):505-11. doi: 10.1080/00365510500209306.
- [15] Brixius K, Schoenberger S, Ladage D, Knigge H, Falkowski G, Hellmich M, et al. Long-term endurance exercise decreases antiangiogenic endostatin signalling in overweight men aged 50-60 years. *British Journal of Sports Medicine*. 2008 Feb;42(2):126-9; discussion 129. doi: 10.1136/bjism.2007.035188.
- [16] Suhr F, Rosenwick C, Vassiliadis A, Bloch W, Brixius K. Regulation of extracellular matrix compounds involved in angiogenic processes in short- and long-track elite runners. *Scandinavian Journal of Medicine & Science in Sports*. 2010 Jun; 20(3):441-8. doi: 10.1111/j.1600-0838.2009.00960.x. Epub 2009 Jun 23.
- [17] Gunga HC, Kirsch K, Röcker L, Behn C, Koralewski E, Davila EH, et al. Vascular endothelial growth factor in exercising humans under different environmental conditions. *European Journal of Applied Physiology and Occupational Physiology*. 1999 May; 79(6):484-90. doi: 10.1007/s004210050541.
- [18] Hiscock N, Fischer CP, Pilegaard H, Pedersen BK. Vascular endothelial growth factor mRNA expression and arteriovenous balance in response to prolonged, submaximal exercise in humans. *American Journal of Physiology-Heart and Circulatory Physiology*. 2003 Oct; 285(4):H1759-63. doi: 10.1152/ajpheart.00150.2003.
- [19] Kraus RM, Stallings HW 3rd, Yeager RC, Gavin TP. Circulating plasma VEGF response to exercise in sedentary and endurance-trained men. *Journal of Applied Physiology* (1985). 2004 Apr; 96(4):1445-50. doi: 10.1152/jappphysiol.01031.2003. Epub 2003 Dec 5.
- [20] Schobersberger W, Hobisch-Hagen P, Fries D, Wiedermann F, Rieder-Scharinger J, Villiger B, et al. Increase in immune activation, vascular endothelial growth factor and erythropoietin after an ultramarathon run at moderate altitude. *Immunobiology*. 2000 Apr; 201(5):611-20. doi: 10.1016/S0171-2985(00)80078-9.
- [21] Rullman E, Rundqvist H, Wågsäter D, Fischer H, Eriksson P, Sundberg CJ, et al. A single bout of exercise activates matrix metalloproteinase in human skeletal muscle. *Journal of Applied Physiology* (1985). 2007 Jun; 102(6):2346-51. doi: 10.1152/jappphysiol.00822.2006.
- [22] Gustafsson T, Knutsson A, Puntchart A, Kaijser L, Nordqvist AC, Sundberg CJ, et al. Increased expression of vascular endothelial growth factor in human skeletal muscle in response to short-term one-legged exercise training. *Pflügers Archiv: European Journal of Physiology*. 2002 Sep; 444(6):752-9. doi: 10.1007/s00424-002-0845-6.
- [23] Höffner L, Nielsen JJ, Langberg H, Hellsten Y. Exercise but not prostanoids enhance levels of vascular endothelial growth factor and other proliferative agents in human skeletal muscle interstitium. *Journal of Physiology*. 2003 Jul; 550(1):217-25. doi: 10.1113/jphysiol.2002.037051.
- [24] Seko Y, Seko Y, Takahashi N, Shibuya M, Yazaki Y. Pulsatile stretch stimulates vascular endothelial growth factor (VEGF) secretion by cultured rat cardiac myocytes. *Biochemical and Biophysical Research Communications*. 1999 Jan; 254(2):462-5. doi: 10.1006/bbrc.1998.9969.
- [25] Eriksson K, Magnusson P, Dixelius J, Claesson-Welsh L, Cross MJ. Angiostatin and endostatin inhibit endothelial cell migration in response to FGF and VEGF without interfering with specific intracellular signal transduction pathways. *FEBS Letters*. 2003 Feb; 536(1-3):19-24. doi: 10.1016/s0014-5793(03)00003-6.
- [26] Yamaguchi N, Anand-Apte B, Lee M, Sasaki T, Fukai N, Shapiro R, et al. Endostatin inhibits VEGF-induced endothelial cell migration and tumor growth independently of zinc binding. *The EMBO Journal*. 1999 Aug ; 18(16):4414-23. doi: 10.1093/emboj/18.16.4414



Original Article

Effect of Chemotherapy Induced Hair-loss on Distress Levels among Cancer Patients Visiting Public and Private Hospitals of Punjab

Muhammad Ali¹, Qandeel Tahir², Mahak Khizar³, Maryam Munawar² and Ali Saif¹¹GDMO Pakistan Rangers, Pakistan²Alshifa School of Public Health Al-Shifa Trust Eye Hospital, Rawalpindi, Pakistan³Punjab Rangers Teaching Hospital, Lahore, Pakistan

ARTICLE INFO

Key Words:

Chemotherapy induced hair- loss, Distress levels, Public and Private Hospitals, Punjab.

How to Cite:

Muhammad Ali, Tahir, Q. ., Khizar, M. ., Munawar, M. ., & Saif, A. (2022). Effect of chemotherapy induced hair-loss on distress levels among cancer patients visiting public and private hospitals of Punjab: Effect of chemotherapy induced hair-loss on distress levels among cancer patients. *Pakistan BioMedical Journal*, 5(6).<https://doi.org/10.54393/pbmj.v5i6.536>

*Corresponding Author:

Muhammad Ali
 GDMO Pakistan Rangers, Pakistan
alyalianz620@gmail.com

Received Date: 28th May, 2022Acceptance Date: 13th June, 2022Published Date: 30th June, 2022

ABSTRACT

Chemotherapy is an essential part of a multimodal strategy in the treatment of many cancers. Chemotherapy-induced hair loss is believed to affect 65 percent of people. According to the study, chemotherapy-induced hair loss has been associated to anxiety, depression, a poor body image, low self-esteem, and a decreased sense of health. **Objectives:** To find out chemotherapy-induced alopecia distress levels among cancer patients' in Punjab's public and private hospitals. To find out the relationship between demographic variables and chemotherapy induced alopecia distress. **Methods:** A cross sectional study was conducted in public and private hospitals of Punjab, over the duration of 6 months, from October 2021 to March 2022. A sample of 323 respondents with the age range 19-54 was obtained. Data collection tool was adapted version of chemotherapy-induced alopecia distress scale (CASD). Frequencies and percentages of categorical variables were reported and Chi-square test was used to find out associations. **Results:** High distress level was 61% (n=196) while low distress level was 39% (n=127). Majority of the sample population consisted of participants belonging to age group 18-34 (n=146, 45.2%). Most of them were male 53% (n=173). Respondents diagnosed at stage2 had low distress level (54%) as compare to respondents who were diagnosed at stage3 and stage 4. Significant association (p-value ≤0.05) was found between Gender, family income, employment status, disease stage at diagnosis, number of chemotherapy cycles received and current active treatment. **Conclusion:** Chemotherapy-induced alopecia distress was associated with all of five domains i.e. physical, emotional, daily activities, relationships and treatment. To reduce the suffering caused by alopecia in cancer patients, appropriate therapies must be developed.

INTRODUCTION

Cancer is the second leading cause of mortality in the world [1]. Cancer incidence is anticipated to rise from 6.1 million to 10.7 million in Asia by 2030, with a corresponding rise in death from 4.1 million to 7.5 million [2]. Similarly, cancer is on the rise in Pakistan; in 2012, 1.4 million of the country's 173 million inhabitants were diagnosed with cancer, with an annual increase of 150,000 cases projected [3]. The number of cancer cases is increasing at an exponential rate. Chemotherapy is an essential part of the multimodal strategy in the treatment of many malignancies. Chemotherapeutic drugs cause hair loss, which is one of the most prevalent cutaneous side effects and one of the most painful aspects of cancer treatment [4].

Chemotherapy-induced hair loss affects about 65 percent of people. Anagen effluvium is the most prevalent kind of hair loss linked with cancer treatment. It generally appears 1-2 weeks after commencing treatment and worsens over the next 4-8 weeks [5]. Regardless of the fact that chemotherapy-induced hair loss is a common and serious side effect of cancer treatment, little is known about how it affects patients' mental health [6]. Chemotherapy-induced hair loss, on the other hand, has been associated in the literature to anxiety, sadness, a negative body image, low self-esteem, and a decreased sense of well-being [7]. Alopecia is a psychologically and socially distressing side effect of systemic cancer therapy that is typically (but not

always) reversible. Some individuals may experience such severe emotional trauma that they refuse or postpone treatment that may otherwise be useful [8]. Alopecia is a common adverse effect of chemotherapeutic antineoplastic drugs, with 62.1 percent of patients reporting it. Chemotherapy-induced alopecia can range from partial to complete hair loss, depending on the treatment strategy. Alopecia has a significant emotional impact on individuals, in addition to its physical repercussions [9]. The adverse effects of alopecia on body image is identical for male and female respondents, and patients in both groups who suffered partial or total hair loss had a more negative body image than those who did not [10]. Females' psychological well-being was shown to be more impaired than men' in the same study, because to the greater frequency of alopecia in females. This might possibly be because baldness in males is a culturally acceptable condition [11]. Furthermore, alopecia is linked to major psychological issues including sadness and anxiety. Previous research has looked at the overall relationship between alopecia and quality of life [8]. Given that patients' discomfort and body image might vary according on their emotional dimension and the effect of peers and social settings, it's important to assess particular alopecia distress and its psychological cost [12]. The alopecia that appeared 2-3 weeks after the initial therapeutic application might be a serious issue that affects the patient's physical appearance, self-confidence, familial and social environment, and cancer treatment [13]. Hair loss is one of the most commonly reported and psychologically distressing adverse effects of chemotherapy [14]. It negatively affects the compliance and coping strength of patients receiving chemotherapy [15]. This study will highlight the impact of alopecia on the distress level of patients, as the mental health of a cancer patient is one of the crucial factor for the successful outcome of the treatment.

METHODS

A cross sectional study was conducted over a period of six months in oncology Department of Public and Private Hospitals of Punjab. Data collection tool was an adapted version of chemotherapy- induced Alopecia Distress Scale (CADS) taken from previous study (I. Baati et al., 2020). It consisted of two section A and B. Section A consisted of Socio-Demographic variables (Age, Education, Profession....). Section B was consisted of Chemotherapy-induced Alopecia Distress Scale (CADS) consisting up of 25 items in five domains which are physical, emotional, daily activity, relationship, and treatment. Questionnaire was translated in Urdu, pilot study was conducted to validate the questionnaire, followed by commencement of actual study. Reliability was tested by calculating Cronbach's

alpha by using SPSS 17.0. Cronbach'S alpha was 0.8. Statistical significance was set up to $p \leq 0.05$. Convenient sampling was used. Sample size was calculated through open epi software. At Margin of error 5%, 95% confidence interval and 30% prevalence (I. Baati et al., 2020) the sample size was 323. Data analysis was done through SPSS version 17.0. Descriptive analysis for categorical variables was done through frequencies and percentages. Inferential analysis was done through Chi-square test for independence and 95% level of confidence was used for establishment of statistical significance and to find the association between independent and dependent variables

RESULTS

Total sample of 323 respondents were included in the study. Regarding gender of respondents 53% were male and 47% were female. Most of participants were with the age of 18-34 (45%), 31% were with the age of 35-45, 6% were with the age of 55 and above. Regarding education of respondents; 27% were primary educated, 5% were matric, 37% were having high school education and 31% were professionals. Concerning respondent living area; 63% were from rural areas and 37% were from urban areas. Out of 330; 54% were married, 31% were unmarried and 15% respond others. 37% of the respondents were working, 31% was retired while 32% was housewife/unemployed regarding employment status. Concerning family income 14% with less than 50000, 54% were with 50000-100000, 32% were with more than 100000. Out of 330, 69% of respondents were currently active treatment while 31% were not getting treatment.

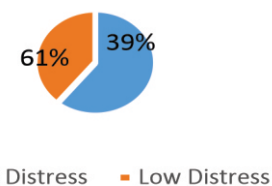


Figure 1: Effects of chemotherapy induced alopecia on distress levels

Association of various demographic factors to effects of chemotherapy induced hair loss on distress levels. A strong association was found out between gender and chemotherapy induced hair loss on distress levels, 53% of women had high distress level as compare to male $\chi^2(1, df) 2.191(4)$, $p = 0.031$. Cross tabs between family income and chemotherapy induced hair loss on distress levels were significant 56% of respondents having family income less than 50000 had high distress level as compare to high income $\chi^2(1, df) 20.232(4)$, $p 0.001$. A strong association between employment status and chemotherapy induced hair loss on distress levels 36% of respondents who were

unemployed had high level of distress as compare to others $\chi^2(df) 16.477(5)$, $p= 0.041$. Chi-square depicted significant association between disease stage of diagnosis and dependent variable 54% of respondents who diagnosed at stage2 had low distress level as compare to respondents who diagnosed at stage3 and stage 4 $\chi^2(df) 12.633(3)$, $p = 0.037$. There was strong association between number of chemo cycle received and dependent variable 51% of respondents who received 1-2 cycles had low distress level as compare to the respondents who received more chemo cycles $\chi^2(df) 3.141(6)$, $p= 0.011$.

S.NO	Variables	High	Low	X	Df	p-value
1	Gender					
	Male	70(42.2%)	85(54.8%)	2.191	4	0.031*
Female	100(53.2)	88(46.8%)				
2	Family income					
	≤ 50000	84(56.0%)	74(48.7%)	20.232	4	0.001
	50000-100000	78(51.3%)	66(44.0%)			
≥ 100000	3(13.6%)	19(86.4%)				
3	Employment status					
	Working	69(62.7%)	41(37.3%)	16.477	5	0.041*
	Retired	59(45.7%)	70(54.3%)			
	Housewife/ unemployed	23(36.5%)	40(63.5%)			
4	Disease stage at diagnosis					
	Stage-2	78(54.2%)	66(45.8%)	12.633	3	0.037*
	Stage-3	30(49.2%)	31(50.8%)			
	Stage-4	15(41.7%)	21(58.3%)			
Don't know	11(22.9%)	37(77.1%)				
5	Number of chemo cycles received					
	1-2 cycles	31(48.4%)	33(51.6%)	3.141	6	0.011*
	3-4 cycles	83(61.0%)	53(39.0%)			
	5-6 cycles	20(29.0%)	49(71.0%)			
	more than 6 cycles	20(48.8%)	21(51.2%)			
6	Current active treatment					
	Yes	70(42.2%)	85(54.8%)	2.191	1	0.033*
No	100(53.2)	88(46.8%)				

Table 1: Association of demographic factors to effects of chemotherapy induced hair loss on distress levels

DISCUSSION

Alopecia is a significant body image concern. Hair is a sign of life and identity, and it is used to communicate social status, sex, occupation, and religious beliefs. Chemotherapy-induced alopecia is a condition that can negatively impact a cancer patient's psychological well-being and quality of life, causing anxiety, depression, a poor body image, and low self-esteem [16]. The goal of this study was to determine the level of distress in cancer patients with chemotherapy-induced alopecia. The level of distress and chemotherapy-induced alopecia were assessed using the chemotherapy-induced alopecia distress scale. This

study found that the majority of the respondents (61%) had high distress level, which is in line with the study conducted in Turkey reported that 61.4% [17]. On the other hand, this finding was higher than the study conducted in Europe 50.6% of respondents had high distress level [18]. Gender, financial source for therapy, diagnosis, kind of chemotherapeutic agent, and number of cycles administered were all important variables related with distress, according to the literature review [19]. This study revealed that 56% of respondents having family income less than 50000 had high distress level as compare to high income with p-value of 0.001, similarly 54% of respondents who diagnosed at stage2 had low distress level as compare to respondents who diagnosed at stage3 and stage 4 with p-value of 0.037. Patients who were more worried about their looks and hair were more likely to feel alopecia-related distress than those who were not, and patients with high CIA distress had a two-fold worse body image than those with low CIA distress [20]. Participants in our study had a body image that was around two times poorer than that reported in studies of breast cancer patients in the United States or Europe [21]. As Tiggeman hypothesized, this might be related to distinct cultural, peer, and social variables in Korea. Negative attitudes, stereotypes, and discriminatory behavior regarding cancer and persons afflicted by the disease were too prevalent in Korea, and Korean breast cancer patients may suffer with high CIA distress and a negative body image as a result [22]. In a qualitative research in Korea, cancer patients with CIA felt uneasy in public places and found it difficult to go grocery shopping or running because they were afraid that people would recognize them as cancer patients. In this research, 57% of respondents said they felt uneasy in public places [23].

CONCLUSION

Chemotherapy-induced alopecia distress was linked with all of five domains i.e. physical, emotional, daily activities, relationships and treatment. High distress level was 61% (n=196) while low distress level was 39% (n=127). To reduce the distress caused by alopecia in cancer patients, specific interventions must be developed. Psychosocial support and socially suitable education or initiatives for self-care approaches related to alopecia and lowered body image should also be provided by health professionals.

REFERENCES

- [1] American Cancer Society. Cancer facts and figures. Explore Research, Cancer Facts and Statistics.2015 May15.
- [2] Sankaranarayanan R, Ramadas K, Qiao YI. Managing the changing burden of cancer in Asia. BMC Medicine. 2014;12(3): 10-186.doi.org/10.1186/1741-7015-12-3

- [3] Noronha V, Tsomo U, Jamshed A, Hai MA, Wattedgama S, Baral RP, et al. A fresh look at oncology facts on south central Asia and SAARC countries. *South Asian journal of cancer*. 2012 Jul;1(01):01-4. doi.org/10.4103/2278-330X.96489
- [4] Del Mastro L, Costantini M, Morasso G, Bonci F, Bergaglio M, Banducci S, et al. Impact of two different dose-intensity chemotherapy regimens on psychological distress in early breast cancer patients. *European Journal of Cancer*. 2002 Feb;38(3):359-66. doi: 10.1016/s0959-8049(01)00380-x.
- [5] Miteva M, Misciali C, Fanti PA, Vincenzi C, Romanelli P, Tosti A. Permanent alopecia after systemic chemotherapy: a clinicopathological study of 10 cases. *American Journal of Dermatopathology* 2011 Jun;33(4):345-50. doi: 10.1097/DAD.0b 013e3181f9cfc25.
- [6] Kanat O, Ertas H, Caner B. Platinum-induced neurotoxicity: A review of possible mechanisms. *World journal of clinical oncology* 2017 Aug 10;8(4):329-335. doi: 10.5306/wjco.v8.i4.329.
- [7] Rice BA, Ver Hoeve ES, DeLuca AN, Esserman LJ, Rugo HS, Melisko ME. Registry study to assess hair loss prevention with the Penguin Cold Cap in breast cancer patients receiving chemotherapy. *Breast Cancer Research and Treatment*. 2018 Jan 1;167(1):117-122. doi: 10.1007/s10549-017-4506-z.
- [8] Breed WPM, Van Den Hurk CJG, Peerbooms M. Presentation, impact and prevention of chemotherapy-induced hair loss: Scalp cooling potentials and limitations. *Expert Review of Dermatology*. 2011 Feb;6(1):109-25. doi.org/10.1586/edm.10.76
- [9] Haslam IS, Smart E. Chemotherapy-induced hair loss: the use of biomarkers for predicting alopecic severity and treatment efficacy. *Biomarker Insights*. 2019 Apr;14:1177271919842180.
- [10] Rubio-Gonzalez B, Juhász M, Fortman J, Mesinkovska NA. Pathogenesis and treatment options for chemotherapy-induced alopecia: a systematic review. *International Journal of Dermatology*. 2018 Dec;57(12):1417-1424. doi: 10.1111/ijd.13906.
- [11] Paus R, Haslam IS, Sharov AA, Botchkarev VA. Pathobiology of chemotherapy-induced hair loss. *The Lancet Oncology*. 2013 Feb;14(2): e50-9. doi: 10.1016/S1470-2045(12)70553-3.
- [12] Marks DH, Okhovat JP, Hagigeorges D, Manatis-Lornell AJ, Isakoff SJ, Lacouture ME, et al. The effect of scalp cooling on CIA-related quality of life in breast cancer patients: a systematic review. *Breast Cancer Research Treatment*. 2019 Jun 15;175(2):267-76.
- [13] Ozusağlam E, Can G. Alterations in sperm long RNA contribute to the epigenetic inheritance of the effects of postnatal trauma. *Molecular Psychiatry*. 2021;29(3):361-70.
- [14] Trüeb RM. Chemotherapy-Induced Alopecia. *Seminars in Cutaneous Medicine and Surgery* 2009 Mar;28(1):11-4. doi: 10.1016/j.sder.2008.12.001
- [15] Grevelman EG, Breed WPM. Prevention of chemotherapy-induced hair loss by scalp cooling. *Annals of Oncology*. 2005 Mar;16(3):352-8. doi.org/10.1093/annonc/mdi088
- [16] Rossi A, Anzalone A, Fortuna MC, Caro G, Garelli V, Pranteda G, et al. Multi-therapies in androgenetic alopecia: review and clinical experiences. *Dermatologic therapy* 2016 Nov 1;29(6):424-32. doi.org/10.1111/dth.12390
- [17] Rugo HS, Klein P, Melin SA, Hurvitz SA, Melisko ME, Moore A, et al. Association between use of a scalp cooling device and alopecia after chemotherapy for breast cancer. *Journal of the American Medical Association* 2017 Feb 14;317(6):606-14. doi.org/10.1001/jama.2016.21038
- [18] Macduff C, Mackenzie T, Hutcheon A, Melville L, Archibald H. The effectiveness of scalp cooling in preventing alopecia for patients receiving epirubicin and docetaxel. *European Journal of Cancer Care*. 2003 Jun 1;12(2):154-61. doi.org/10.1046/j.1365-2354.2003.00382.x
- [19] Lemieux J, Maunsell E, Provencher L. Chemotherapy-induced alopecia and effects on quality of life among women with breast cancer: A literature review. *Psychooncology*. 2008 Apr;17(4):317-28. doi.org/10.1002/pon.1245
- [20] Chon SY, Champion RW, Geddes ER, Rashid RM. Chemotherapy-induced alopecia. *Journal of the American Academy of Dermatology* 2012 Jul 1;67(1):e37-47. doi.org/10.1016/j.jaad.2011.02.026
- [21] Prochilo T, Huscher A, Andreis F, Mirandola M, Zaina E, Pomentale B, et al. Hair Loss Prevention by a Scalp Cooling Device in Early Breast Cancer Patients: The Poliambulanza Preliminary Experience. *Reviews on Recent Clinical Trials* 2018 Nov 20;14(1):66-71. doi.org/10.2174/157488711366618112011104
- [22] Shin H, Jo SJ, Kim DH, Kwon O, Myung SK. Efficacy of interventions for prevention of chemotherapy-induced alopecia: A systematic review and meta-analysis. *International Journal of Cancer*. 2015 Mar 1;136(5):E442-54. doi.org/10.1002/ijc.29115
- [23] Choi EK, Kim I-R, Chang O, Kang D, Nam S-J, Lee JE, et al. Impact of chemotherapy-induced alopecia distress on body image, psychosocial well-being, and depression in breast cancer patients 2014. doi.org/10.1002/pon.3531



Original Article

Impact of Educational Intervention in the Frequency of Nosocomial Infection among Patients Admitted in ICU of Tertiary Care Hospital: Interventional Study

Muhammad Azizullah¹, Ejaz Mahmood Ahmad Qureshi^{1*}, Muhammad Saleem Rana¹, Asif Hanif¹, Faisal Izhar² and Ahmad Humayun Asghar³

¹Department of Public Health, University of Lahore, Pakistan

²Department of Community Dentistry, FMH College of Dentistry, Lahore, Pakistan

³Department of Medicine, Govt. M. Nawaz Sharif Hospital, Lahore, Pakistan

ARTICLE INFO

Key Words:

Educational intervention, Nosocomial Infection and Intensive Care Unit.

How to Cite:

Azizullah, M. ., Ahmad Qureshi, E. M. ., Saleem Rana, M. ., Hanif, A. ., Izhar, F. ., & Humayun Asghar, A. . (2022). Impact of Educational Intervention in the Frequency of Nosocomial Infection among Patients Admitted in ICU of Tertiary Care Hospital: Interventional Study: Improvement in Hospital Acquired Infections among ICU patients after Education. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.481>

***Corresponding Author:**

Dr. Ejaz Mahmood Ahmad Qureshi
Department of Public Health, University of Lahore,
Pakistan.
ejaz_qureshi@hotmail.com

Received Date: 29th May, 2022

Acceptance Date: 17th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Objectives: Infection is one of the leading causes of death in the world especially in low and lower-middle income countries. **Methods:** Patients (n=270) were included in a study that was conducted in ICU of a tertiary care public sector, Jinnah Hospital, Lahore for a period of 18 months. Patients were divided into two groups (pre and post educational intervention). During this period, information about patient's nosocomial infection rate, its distribution and patient's excess length of stay in hospital collected. **Results:** Total of 115 (42.6%) were males and 155 (57.4%) were females. Results showed 42 (15.9%) out of 270 participants suffered in Nosocomial Infection/Hospital Acquired Infection during treatment and stay in ICU. **Conclusion:** It was concluded that educational intervention played a significant role in controlling the nosocomial infection among patients admitted in the ICU.

INTRODUCTION

"Nosocomial infection or hospital acquired infection is defined as an infection that begins 48 hours after hospitalization or within 48 hours after being discharged that was not incubating at the time of admission at hospital"(1). Infection is one of the leading causes of death in the world (2). specially in low and lower-middle income countries (3). Although the global mortality rate due to infections has dropped over the past three decades;⁴ it still remains the leading cause of death and Pakistan is no exception, showing similar tendency (5,6). Intensive care units (ICUs) are often called the hubs" of infections.

Extremely vulnerable population group with reduced host defenses and deregulated immune responses, multiple procedures, and use of invasive devices such as endotracheal intubation (7). central venous cannulations (8) mechanical ventilation (9). and urinary catheterizations (10). which distorts the anatomical integrity-protective barriers of patients are more prone to infection. The rate of both primary infection (at the time of admission) and secondary infection (ICU-derived infection occurs during stay) is higher in the ICU (11). Many high-income countries have well-established surveillance system to report

hospital acquired infections (HAI). These systems include reporting the nature and site of the infection as well as programs of intermittent point prevalence survey studies. Hospital acquired infection is one of the world's greatest health burden. According to WHO, 4 million patients suffer from HAI in Europe each year. The prevalence is estimated at 7.1% in the United States (USA) and the annual nosocomial infection rate is estimated at 1.7 million patients with an average of 4 to 12 million cases with prevalence of 4% - 5% (12). Among the developing countries, only 23 of the 147 countries reported their national data. The prevalence rate in these countries ranged from 5.7% to 19% (12). The World Health Organization (WHO) estimates that hundreds of millions of patients in developed and developing countries suffer from the hospital acquired infections each year. The rate of health care associated infection in developing countries is higher as compared to developed countries (12). Data compiled by the European Center for Disease Prevention and Control (ECDC) between 1996 and 2007 showed that the frequency of nosocomial infections ranged from 3.5% to 10.5%, with mean 1 to 7% (4). European Centre for Disease Prevention and Control (ECDC) conducted a point prevalence study in acute care hospital to estimated HAIs from 2011 to 2012, the results showing a prevalence rate of 6% of all patients (13). ECDC also reported that the prevalence rate of HAI in tertiary care hospitals was 4-7% higher than specialized hospitals and secondary level hospital, where rate was 4.5-6.5% (13,14). The rate of hospital acquired pneumonia (HAP) was 8.1% in intensive care units (ICU) (12). The incidence of HAI in USA was estimated 4.5%.in 2002 (12). USA conducted a multistate point-prevalence survey of health care-associated infections in 183 acute care hospitals in 2011. The estimated value of health care-associated infections was 4.0% (15). Little information about HAI is available for low and middle-income countries. According to the World Health Organization (WHO) report on the "Burden of Endemic Health Care-Associated Infection Worldwide" a systematic review of literature in 2011, only 23 developing countries out of 147(16%) reported this problem and in 97 out of 147(66 %), there is no monitoring system as well as any published data.¹ A study from the intensive care unit of Al-Shifa International Hospital, Islamabad found that 88 out of 346 patients (25.4%) aged 16 to 82 with an average age of 46 had hospital-acquired pneumonia (HAP) (16). Due to its increasing prevalence and lack of local data on its management, we designed current study in-order to evaluate its prevalence in our setups. Data compiled by the European Center for Disease Prevention and Control (ECDC) between 1996 and 2007 showed that the frequency of nosocomial infections ranged from 3.5% to 10.5%, with

mean 1 to 7%.⁴ European Centre for Disease Prevention and Control (ECDC) conducted a point prevalence study in acute care hospital to estimated HAIs from 2011 to 2012, the results showing a prevalence rate of 6% of all patients.¹³ ECDC also reported that the prevalence rate of HAI in tertiary care hospitals was 4-7% higher than specialized hospitals and secondary level hospital, where rate was 4.5-6.5% (13,14). The rate of hospital acquired pneumonia (HAP) was 8.1% in intensive care units (ICU).¹² The incidence of HAI in USA was estimated 4.5%.in 2002.¹² USA conducted a multistate point-prevalence survey of health care-associated infections in 183 acute care hospitals in 2011. The estimated value of health care-associated infections was 4.0% (15). Little information about HAI is available for low and middle-income countries. According to the World Health Organization (WHO) report on the "Burden of Endemic Health Care-Associated Infection Worldwide" a systematic review of literature in 2011, only 23 developing countries out of 147(16%) reported this problem and in 97 out of 147 (66 %), there is no monitoring system as well as any published data.¹ A study from the intensive care unit of Al-Shifa International Hospital, Islamabad found that 88 out of 346 patients (25.4%) aged 16 to 82 with an average age of 46 had hospital-acquired pneumonia (HAP) (16). Due to its increasing prevalence and lack of local data on its management, we designed current study in-order to evaluate its prevalence in our setups.

METHODS

Patients (n=270) were included in a study that was conducted in ICU of a tertiary care public sector, Jinnah Hospital, Lahore for a period of 18 months. Patients were divided into two groups (pre and post educational intervention). Patients acquiring nosocomial infection after 48 hours of admission in the ICU identified during a 6-month period following Infection Prevention and Control training sessions and then compared with retrospective data of same duration. All the patients 16 years and above admitted in ICU for more than 48 hours included in the study according to the defined criteria. Immuno-compromised patients and those suffering from chronic infection before admission in ICU were excluded. Date and site of infection, patient demographic information and device use, collected for each infection. During this period, information about patient's nosocomial infection rate, its distribution and patient's excess length of stay in hospital collected by using following method: Patient's nosocomial infection rate calculated by dividing the total number of patients with nosocomial infections by the total number of patients in the ICU($\times 100$). Written consent was taken.

RESULTS

Total of 115 (42.6%) were males and 155 (57.4%) were females. According to table-1, 54 (40.0%) and 61 (45.2%) were in group I and group II respectively, while 81 (60.0%) and 74 (54.8%) were in these two groups respectively. Results showed insignificant difference between groups with p-value of 0.742.

		Group		Total	P-value
		Group I	Group II		
Gender	Male	54 (40.0%)	61 (45.2%)	115 (42.6%)	.742
	Female	81 (60.0%)	74 (54.8%)	155 (57.4%)	

Table 1: Comparison of Gender in Both Groups

Regarding length of stay of participants in ICU, study showed that 52 (19.3%) participants stayed in ICU for 3 days, followed by 35 (13%) and 34 (12.6%) stayed in ICU for 4 and 5 days respectively as shown in figure-1.

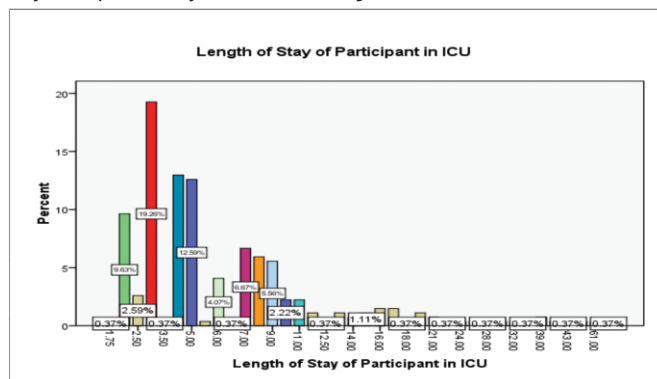


Figure 1: Length of stay of patients in ICU

Table-2 showed that 135 Group II patients belonged to pre and 135 post intervention groups. Regarding ventilator days mean was 7.7259 and 5.3870 respectively in pre and post intervention groups, with standard deviation (Std.) 11.15038 and 5.57854 in these two groups. Similarly mean and standard deviation of central line days pre and post intervention groups were 8.7481 and 6.3593 and standard error mean 0.98105 and 0.51821 respectively. Regarding urinary catheter days mean was 8.7815 and 8.7815 respectively in group I and Group II, while standard deviation (Std.) was 11.34970 and 6.30541 respectively

	Group	N	Mean	Std. Deviation	Std. Error Mean
Age	Group I	135	35.99263	17.51566	1.50751
	Group II	135	8.7407	17.98339	1.54776
ICU Adm. Days	Group I	135	8.8926	11.48042	.98808
	Group II	135	6.7241	6.33769	.54546
Vent. Days	Group I	135	7.7259	11.15038	.95967
	Group II	135	5.3870	5.57854	.48012
Cent. Line Days	Group I	135	8.7481	11.39879	.98105
	Group II	135	6.3593	6.02100	.51821
U Cath. Days	Group I	135	8.7815	11.34970	.97683
	Group II	135	6.5926	6.30541	.54268

Table 2: Information about Length of Patient's Stay in Different

Processes at Icu

Figure-2 showed death and survival rate of patients during stay in ICU. It showed that 54.07% patients died and 45.93% survived during study period.

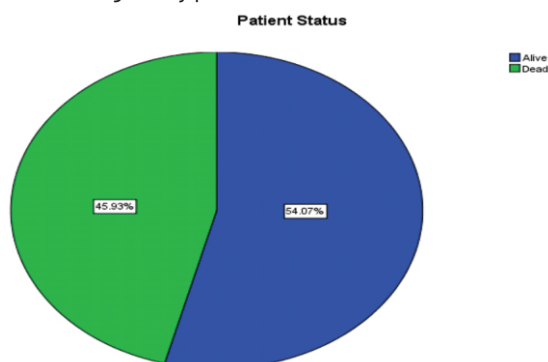


Figure 2: Frequency Distribution Of Participant's Survival And Death

Figure-3 showed that 42 (15.9%) out of 270 participants suffered in Nosocomial Infection/Hospital Acquired Infection during treatment and stay in ICU. Where 228 of 270 (84.44%) had no Hospital Acquired Infection.

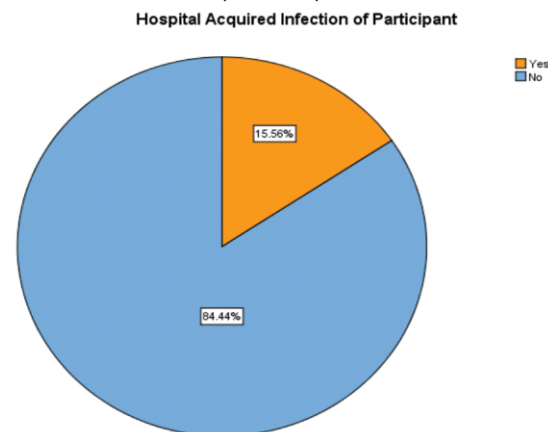


Figure 3: Frequency Distribution Of HAI at ICU

Table-3 showed that 27 (20.0%) patients in group I and 15 (11.1%) in group II had sign and symptoms of HAI, while 108 (11.1%) of group I and 120 (11.1%) patients in group II did not showed any sign and symptoms of HAI. Results showed that the association of hospital acquired infection among groups was insignificant with p-value (0.064).

		Group		Total	P-value
		Group I	Group II		
HAI	Yes	27 (20.0%)	15 (11.1%)	42 (15.6%)	.064
	No	108 (80.0%)	120 (11.1%)	228 (84.4%)	
		135 (100.0%)	135 (100.0%)	270 (100.0%)	

Table 3: Comparison of HAI in Both Groups

DISCUSSION

As far as gender of the patients is concerned, study demonstrated that in both groups, most of the patients were females in Group-I Pre Educational intervention

(60.0%) and in Group-II Post Educational intervention (54.8%). However, no significant association was found ($P=0.742$). But the findings of a similar study carried out by Abramczyk and associates (2011) in a teaching health care facility of Brazil highlighted that in both groups majority of the patients were males. Study reported that in pre-interventional group, 51.4% patients were male and 48.6% were females while in post-interventional group, 60.3% patients were males and 39.7% were females. However, this study was also unable to provide significant results ($P=0.383$) (17). A study carried out at International Shifa Hospital Islamabad also reported that 25.4% patients aged 16-82 years with an average age of 36 years had hospital acquired pneumonia (16). It has been reported that gender related difference of nosocomial infection, reflecting potential confounders (18). A study carried out in a tertiary care health facility revealed that among patients who admitted in the intensive care unit from 1995 to 2004, 34% women developed nosocomial infection. While pneumonia was more frequent in men, whereas urinary tract infections (UTI) were predominant in women, during mechanical ventilation while stay in ICU did not differ between genders. This study concluded that female patients developed more nosocomial infections and were at increased risk of ICU mortality (18). Health care associated infections not only threaten the patient's health and life but also bring additional burden to patients and healthcare system, direct economic loss and prolong hospitalization. Information regarding the length of patient stay in different processes in ICU varies from 6.7 to 8.8 days. Similar results were reported by Huixiu Jia et.al who mentioned that length of stay due to hospital acquired infection increased from 9.7 to 10.7 days in different hospitals also and also revealed the intensity of hospital acquired infections increased with the increase in the length of stay (18). Similar results were also reported a study done in France (19), Iran (20) and Saudi Arabia (21). Several studies have shown the increased length of stay due to hospital acquired infections but had poor comparability, because most studies were limited to infections of single site or caused by a single organism, and the characteristics of patient were different (22-24). The effect of different infection on length of stay were analyzed, among them blood stream infection prolonged hospital stay for 6.3 to 8.7 days in comparison of multicenter study involved 69 tertiary care ICU of 37 cities in 11 counties revealed that the extra length of stay due to blood stream infection was 9.8 days (25). Through these studies, it can be said that the blood stream infection can cause longer stay of hospitalization. In ICU the mortality is associated with several risk factors of which nosocomial infection is the most significant. Critical ill patients are treated in intensive care units; death rate and treatment

success depend upon proper utilization of technological and human resources as well as ICU staff training. Among ICU patients, mortality is associated with duration of hospital stay, patients condition, sedation, immobility, coma, mechanic ventilation, intubation, neurological disease, vasopressors drugs usage, glycemic index and agitation. Prolonged stay in the ICU enhance the risk of mortality (26). Mortality rate in both groups was evaluated in the present study in which found that patients of both groups who stayed in the intensive care unit, death occurred more than half (54.1%) of the patients died while 45.93% survived during the study period. In Group-I, 58.5% and in Group-II, 49.6% patients survived while mortality was observed in 41.5% and 50.4% in Group-I and Group-II, respectively. It showed the impact of intervention as mortality rate among ICU patients reduced after the post educational intervention. However, no significant association was found between both groups ($P=2.148$). The findings of this study are comparable with a study performed by Mitsogianni and collaborators (2016), who confirmed the post intervention impact on the mortality rates, as mortality rate among ICU patients was 32.2% which reduced to 30.6% after educational intervention, however the result was found statistically insignificant ($P=0.789$) (27). Nosocomial infection is transmitted to the patients during hospital stay. WHO data showed that the most significant factors associated with incidence of HAI among high income countries are: age above 65 years, admission in ICU and stay >7 days etc. Hospital stay in ICU can reduce the probability of transmission of nosocomial infection (12).

CONCLUSION

It was concluded that nosocomial infection among patients admitted in the ICU is reliant on duration of hospital stay but educational intervention played a significant role in controlling the nosocomial infection among patients admitted in the ICU.

REFERENCES

- [1] Shaikh JM, Devrajani BR, Shah SZA, Akhund T, Bibi I. Frequency, pattern and etiology of nosocomial infection in intensive care unit: an experience at a tertiary care hospital. *Journal of Ayub Medical College Abbottabad*. 2008 Dec; 20(4):37-40.
- [2] Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012 Dec; 380(9859):2095-128. doi: 10.1016/S0140-6736(12)61728-0.
- [3] Martin-Loeches I, Wunderink RG, Nanchal R, Lefrant

- JY, Kapadia F, Sakr Y, et al. Determinants of time to death in hospital in critically ill patients around the world. *Intensive Care Medicine*. 2016 Sep; 42(9):1454-60. doi: 10.1007/s00134-016-4479-0.
- [4] Corrêa RA, José BPS, Malta DC, Passos VMA, França EB, Teixeira RA, et al. Burden of disease by lower respiratory tract infections in Brazil, 1990 to 2015: estimates of the Global Burden of Disease 2015 study. *Revista Brasileira de Epidemiologia*. 2017 May; 20(Suppl 01(Suppl 01)):171-181. Portuguese, English. doi: 10.1590/1980-5497201700050014.
- [5] Haque A, Ahmed SA, Rafique Z, Abbas Q, Jurair H, Ali SA. Device-associated infections in a paediatric intensive care unit in Pakistan. *Journal of Hospital Infection*. 2017 Jan; 95(1):98-100. doi: 10.1016/j.jhin.2016.10.021.
- [6] Saleem Z, Hassali MA, Godman B, Hashmi FK, Saleem F. A multicenter point prevalence survey of healthcare-associated infections in Pakistan: findings and implications. *American Journal of Infection Control*. 2019 Apr; 47(4):421-424. doi: 10.1016/j.ajic.2018.09.025.
- [7] Bell T, O'Grady NP. Prevention of central line-associated bloodstream infections. *Infectious Disease Clinics of North America*. 2017 Sep; 31(3):551-559. doi: 10.1016/j.idc.2017.05.007.
- [8] Keane S, Martin-Loeches I. Host-pathogen interaction during mechanical ventilation: systemic or compartmentalized response? *Critical Care*. 2019 Jun; 23(Suppl 1):134. doi: 10.1186/s13054-019-2410-0.
- [9] Parker V, Giles M, Graham L, Suthers B, Watts W, O'Brien T, et al. Avoiding inappropriate urinary catheter use and catheter-associated urinary tract infection (CAUTI): a pre-post control intervention study. *BMC Health Services Research*. 2017 May; 17(1):314. doi: 10.1186/s12913-017-2268-2.
- [10] Chaudhry D, Prajapat B. Intensive care unit bugs in India: how do they differ from the western world. *Journal of Association of Chest Physicians*. 2017 Jan; 5(1):10.
- [11] Qadeer A, Akhtar A, Ain QU, Saadat S, Mansoor S, Assad S, et al. Antibigram of medical intensive care unit at tertiary care hospital setting of Pakistan. *Cureus*. 2016 Sep; 8(9): e809. doi: 10.7759/cureus.809.
- [12] World Health Organization (WHO). Report on the burden of endemic health care-associated infection worldwide. Geneva: WHO; 2011.
- [13] Walter J, Haller S, Quinten C, Kärki T, Zacher B, Eckmanns T, et al. Healthcare-associated pneumonia in acute care hospitals in European Union/European Economic Area countries: an analysis of data from a point prevalence survey, 2011 to 2012. *Euro Surveill*. 2018 Aug; 23(32):1700843. doi: 10.2807/1560-7917.ES.2018.23.32.1700843.
- [14] Cassini A, Plachouras D, Eckmanns T, Abu Sin M, Blank HP, Ducomble T, et al. Burden of six healthcare-associated infections on European population health: estimating incidence-based disability-adjusted life years through a population prevalence-based modelling study. *PLoS Medicine*. 2016 Oct; 13(10): e1002150. doi: 10.1371/journal.pmed.1002150.
- [15] Magill SS, Edwards JR, Bamberg W, Beldavs ZG, Dumyati G, Kainer MA, et al. Multistate point-prevalence survey of health care-associated infections. *New England Journal of Medicine* 2014 Mar 7; 370(13):1198-208. doi: 10.1056/NEJMoa1306801.
- [16] Imran M, Amjad A, Haidri FR. Frequency of hospital acquired pneumonia and its microbiological etiology in medical intensive care unit. *Pakistan Journal of Medical Sciences*. *Pakistan Journal of Medical Sciences*. 2016 Aug; 32(4):823-6. doi: 10.12669/pjms.324.8942.
- [17] Abramczyk ML, Carvalho WB, Medeiros EAS. Preventing catheter-associated infections in the pediatric intensive care unit: impact of an educational program surveying policies for insertion and care of central venous catheters in a Brazilian teaching hospital. *Brazilian Journal of Infectious Diseases*. 2011 Dec; 15(6):573-7. doi: 10.1590/s1413-86702011000600012.
- [18] Jia H, Li L, Li W, Hou T, Ma H, Yang Y, et al. Impact of Healthcare-Associated Infections on Length of Stay: A Study in 68 Hospitals in China. *Biomed Research International*. 2019 Apr; 2019:2590563. doi: 10.1155/2019/2590563.
- [19] Ohannessian R, Gustin MP, Bénet T, Gerbier-Colomban S, Girard R, Argaud L, et al. Estimation of Extra Length of Stay Attributable to Hospital-Acquired Infections in Adult ICUs Using a Time-Dependent Multistate Model. *Critical Care Medicine*. 2018 Jul; 46(7):1093-1098. doi: 10.1097/CCM.0000000000003131.
- [20] Karkhane M, Pourhosiengholi MA, Torkabad MR, Kimiia Z, Mortazavi SM, Aghdam SK, et al. Annual antibiotic related economic burden of healthcare associated infections; a cross-sectional population based study. *Iranian Journal of Pharmaceutical Research: IJPR*. 2016; 15(2): 605.
- [21] Al-Mousa HH, Omar AA, Rosenthal VD, Salama MF, Aly NY, El-Dossoky Noweir M, et al. Device-associated infection rates, bacterial resistance, length of stay, and mortality in Kuwait: International Nosocomial Infection Consortium findings. *American Journal of*

- Infection Control. 2016 Apr; 44(4):444-9. doi: 10.1016/j.ajic.2015.10.031.
- [22] Vardakas KZ, Rafailidis PI, Konstantelias AA, Falagas ME. Predictors of mortality in patients with infections due to multi-drug resistant Gram negative bacteria: the study, the patient, the bug or the drug? *Journal of Infection*. 2013 May; 66(5):401-14. doi: 10.1016/j.jinf.2012.10.028.
- [23] Gandra S, Barter DM, Laxminarayan R. Economic burden of antibiotic resistance: how much do we really know? *Clinical Microbiology and Infection*. 2014 Oct; 20(10):973-80. doi: 10.1111/1469-0691.12798.
- [24] Rosenthal VD, Olarte N, Torres-Hernandez H, Villamil-Gomez W. Catheter-associated blood stream infection rates, extra length of stay and mortality in 69 adult ICUs of 37 cities of 11 developing countries. Findings of the INICC. *American Journal of Infection Control*. 2007 Jun; 35(5): E68-9.
- [25] Soares Pinheiro FGM, Santana Santos E, Barreto ÍDC, Weiss C, Vaez AC, Oliveira JC, et al. Mortality Predictors and Associated Factors in Patients in the Intensive Care Unit: A Cross-Sectional Study. *Critical Care Research and Practice*. 2020 Aug; 2020:1483827. doi: 10.1155/2020/1483827.
- [26] Mitsogianni M, Vasileiadis I, Parisi M, Tzanis G, Kampisiouli E, Psaroudaki et al. A Multifaceted Intervention Program to Prevent Bloodstream Infection in an Intensive Care Unit Running Head: An Intervention for the Reduction of Bacteraemia in ICU. *Health Science Journal*. 2016; 10(2):1.



Original Article

Knowledge, Attitudes, and Practices towards Novel COVID-19 among Pakistani Population during Pandemic Period

Asif Mahmood Mattoo¹, Saadia Hameed², Hina Javed³, Fakher un Nisa⁴, Asif Maqsood Butt^{5*} and Mehboob Ahmad⁶

¹AERO Hospital, Hasanabdal, Pakistan

²Holy Family Hospital, Rawalpindi, Pakistan

³Ambitious college of Advance Studies, Rawalpindi, Pakistan

⁴Private Setup, Rawalpindi

⁵Department of Community Medicine, Rawalpindi Medical University, Rawalpindi, Pakistan

⁶District Health Officer, Bhimber, Health Department, Azad Kashmir, Pakistan

ARTICLE INFO

Key Words:

COVID-19; Knowledge, attitudes, practice; health education, mask, gloves, sanitizer.

How to Cite:

Mahmood Mattoo, A. ., Hameed, S. ., Javed, H. ., Nisa, F. U. ., Maqsood Butt, A. ., & Ahmad, M. . (2022). Knowledge, Attitudes, And Practices Towards Novel COVID-19 Among Pakistani Population During Pandemic Period: Knowledge, Attitudes, and Practices towards Novel COVID-19 among Pakistani Population during Pandemic Period. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.403>

***Corresponding Author:**

Asif Maqsood Butt

Department of Community Medicine, Rawalpindi Medical University, Rawalpindi, Pakistan

rcap2017dme@gmail.com

Received Date: 26th April, 2022

Acceptance Date: 3rd June, 2022

Published Date: 30th June, 2022

ABSTRACT

Special control measures have been taken by government of Pakistan during COVID-19 pandemic. Implementation of these measures were dependent on knowledge, attitudes, and practices (KAP) of population towards disease. **Objectives:** To assess KAP of residents of Pakistan towards COVID-19 during outbreak. **Methods:** It was a web-based, cross-sectional study. The study was designed using Google Forms and was distributed through "WhatsApp" groups. The objectives and purpose were explained to respondents. The survey was completed by clicking on responses to closed-ended multiple choice questions measured on Likert Scale. **Results:** Overall awareness for all respondents was adequate with majority reporting correct answers. Less than half of respondents knew about correct use of sanitizer and gloves. Frequently missed questions with correct responses were about use of alcohol base sanitizer to disinfect hands 104 (32%), disinfect gloves 56 (17%), ideally required concentration of alcohol 131 (40%) and primary use of gloves 71 (228%). **Conclusion:** Knowledge about disease was found acceptable with encouraging attitude and satisfactory practices. However, most respondents lacked knowledge about use of sanitizer and gloves. It is important to devise a Health Education campaign and public guidelines at national level to target all socio-economic groups, to stop spread of COVID-19.

INTRODUCTION

Coronavirus disease 2019 (abbreviated "COVID-19") a viral disease of respiratory system was first detected in Wuhan, China, November 2019. An extremely infectious and communicable disease with symptoms of fatigue, dry cough, myalgia, fever, followed by shortness of breath, dyspnea and later respiratory failure or acute respiratory distress syndrome and coagulation dysfunction [1]. Medical professionals being first line workers have a

serious occupational threat, caused by this pandemic because of frequent exposure to infected people [2]. They should know about intra-hospital transmission, symptoms and preventive measures of disease [3]. A study highlighted that misunderstandings and lack of knowledge among medical professionals resulted in improper diagnosis and poor management of disease [4]. Primary prevention is based on measures adopted to break

communication of epidemiologic triangle (agent, host and environment) at any level. Patients primarily rely on conservative treatment and management for agent, has no specific anti-viral medicine. Preventive measures for host include social distancing, masks, personal hygiene (hand washing, sanitizers use) avoiding gatherings, wearing protective clothes, and screening of population for disease. Being air borne/droplet infection, environment plays vital role in communication of disease, therefore disinfection of floors is very important to keep environment clean. Preventive measures such as avoidance of public gatherings, wearing face masks, hand washing practices with soap or disinfection with 60 - 80% alcohol-based sanitizers (if soap and water not available), avoid touching mouth, nose, eyes with unsterilized hands, screening of cases, tracing contacts, and quarantine being recommended for reduction of transmission of disease [5]. Similar study conducted in Latin America pointed out that people developed different reactions, massive fear with anguish and were reluctant to adopt preventive measures [6]. Another study highlighted that attitude of people to adopt preventive measures was associated with level of knowledge. Positive attitude develops with more information and education towards preventive measures of COVID-19 [1]. Similarly, disinformation, type of information or no information would be another barrier towards attitude and practices against COVID-19 [7]. On the other hand, in developed nations like Singapore, a study revealed that people trusted their government and took measures implemented by government even with little information [8]. CDC recommended to cover face with surgical masks when in community to minimize public transmission of disease [9]. However, WHO recommended to wear mask only if person is suffering from disease symptoms to protect others from getting infection [10]. Neighbors of Pakistan, China, India, and Iran with religious and ethnic groups traveling to and from these countries. First case of COVID-19 reported on 26th February 2020 in Pakistan had also travelled back from Iran and currently our neighbour India having highest number of delta variant [11]. New strategies were developed and implemented for prevention and control of pandemic and as days passed, government response became more forceful. Social distancing, use of face masks, hand sanitizers, wearing of gloves and later followed by lockdown [12]. This article emphasizes on exploration of Knowledge, Attitude and Practices (KAP) of prevention and control measures adopted for COVID-19 by population of Pakistan.

METHODS

It was a web-based, cross-sectional study, designed using Google Forms and were distributed through "WhatsApp" groups and emails. Survey was distributed to WhatsApp

groups of medical professionals including doctors, nurses, paramedics, pharmacists and non-medicals like engineers, army officers, teachers, bankers, and college students. Respondents were free to take part as a volunteer in study. Those who agreed were asked to complete response to questions on survey that was measured on Likert Scale. Survey questionnaire consisted of four parts: demographics, knowledge, attitude, and practices. Questionnaire included questions related to COVID-19 i.e. use of masks, hand hygiene techniques, use of sanitizers and gloves (Table 1). A score of 1 was awarded for each correct answer. Descriptive data analysis was performed using SPSS-20 and MS-Excel.

RESULTS

From 11/05/2020 to 17/05/2020, a total of 324 respondents completed survey. Respondents were predominantly male 202 (62%), with a mean age of 37.5 years. Two hundred and twelve (65%) were married. Education level of respondents included 145 (45%) postgraduates, 141 (43%) graduate, 32 (10%) FSc and 6 (2%) with matric qualification. Majority of respondents were doctors 124 (38%), engineers 46 (14%), nurses 29 (9%), students 29 (9%), teachers 15 (5%) and 81 (25%) from miscellaneous occupational backgrounds (Table 2). Knowledge test about symptoms of disease, dry cough, fatigue, myalgia and fever were correctly replied by 180 (56%) respondents and difference between COVID-19 and common cold was rightly known to 176 (54%). Answers about rate of infectivity by asymptomatic person was correctly responded by 136 (42%) and mode of spread of disease by 156 (48%). Prevention of disease by wearing mask was correctly responded by 134 (41%) and 162 (50%) respondents knew that it was important to avoid public places and transport as preventive measure. Accurate approach towards treatment methods was known to 160 (49%). However, knowledge about use of 70% alcohol-based sanitizer for hand sanitization in 30 seconds was only known to 104 (32%) respondents and 90 seconds for latex gloves sanitization to 56 (17%) respondents only. About attitude towards COVID-19 pandemic only 109 (34%) were satisfied, by timely measures adopted by government. Majority of respondents 179 (55%) attentively listened preventive measures and 192 (59%) took self-measures against disease. Also, majority 188 (58%) agreed that it was responsibility of all citizens to take measures to control it. More than half 170 (52%) were quite certain that pandemic would be controlled after some time. Practicing safety measures significantly different among age-groups, genders, marital status, and education levels. Most 174 (54%) said that they wear mask and 175 (51%) used gloves when going out of home. Additionally, 142 (44%) did not visit any crowded place during recent days. Also, most 127 (39%) preferred to wash hands with soap, while only 91 (28%) used

hand sanitizer. Mostly respondents were not aware of preferred hygiene method of hand sanitization and wearing gloves. Only 131 (40%) know that 70% is correct alcohol base concentration for hand sanitization and 71(22%) were aware that advantage of wearing gloves is a reminder to avoid touching face. It was 12 points scored questionnaire and with 8.12 average points, 8 median and 1-12 was range of respondents scores.



Figure 1: Total points scored distribution

Frequently asked questions were about use of alcohol base sanitizer to disinfect hands, disinfect gloves, ideally required concentration of alcohol and primary use of gloves. Inference clearly indicates that mostly respondents were lacking knowledge about use of sanitizer and gloves.

Groups	Sub-Groups	N	%	SD	t stat	p value
Gender	Male	201	62%	56.5	3.3	0.04
	Female	121	37%			
	Not preferred to	2	1%			
Age	15 to 29 years	120	37%	12.97	7.69	0.01
	30 to 49 years	124	38%			
	50 years and above	80	25%			
Marital status	Married	212	65%	70.71	3.24	0.09
	Single	112	35%			
Occupation	Doctor	124	38%	34.03	0.63	0.27
	Engineer	46	14%			
	Nurse	29	9%			
	Student	29	9%			
	Teacher	15	5%			
	Miscellaneous	81	25%			
Education	Postgraduate	145	45%	72.39	2.24	0.05
	Graduate	141	44%			
	Fsc	32	10%			
	Matric	6	2%			

Table 1: Demographic data of respondents(n=324)

No	Knowledge	True (%)	False (%)	I don't know (%)	SD	t stat	p value
1	Dry cough, fatigue, myalgia, and fever are main clinical symptoms of disease.	180 (56%)	94 (29%)	50 (15%)	66.1	2.82	0.052
2	Common cold with stuffy or runny nose or sneezing are some common symptoms.	176 (54%)	101 (31%)	47 (15%)	64.7	2.88	0.051
3	COVID-2019 infected person without fever do not infect others.	136 (42%)	159 (49%)	29 (9%)	69.3	2.69	0.057
4	Mode of disease spread is airborne/droplets.	156 (48%)	141 (44%)	27 (8%)	70.5	2.65	0.059
5	People should wear masks to prevent spread of disease	134 (41%)	158 (49%)	32 (10%)	66.9	2.79	0.054
6	Disease can be prevented by avoiding crowded places and public transport.	162 (50%)	132 (41%)	30 (9%)	69.1	2.70	0.057
7	Quarantine and medical treatment of patients is effective ways to reduce spread of disease.	160 (49%)	130 (40%)	34 (10%)	65.8	2.84	0.052

Table 2: Knowledge towards COVID-19(n=324)

No	Knowledge	Immediately	15 Sec	30 Sec	60 Sec	90 Sec & more	I don't know	SD	t stat	p value
8	Time required to disinfect hands by a 70% alcohol-based hand sanitizer.	55 (17%)	62 (19%)	104 (32%)	17 (5%)	21 (6%)	65 (20%)	32.0	4.1	0.005
9	Time required to disinfect latex gloves by a 70% alcohol-based hand sanitizer.	35 (11%)	36 (11%)	45 (14%)	24 (7%)	56 (17%)	28 (40%)	37.8	3.4	0.009

Table 3: Knowledge towards the use of hand sanitizer and gloves

No	Knowledge	True (%)	False (%)	I don't know (%)	SD	t stat	p value
1	Satisfied with measures adopted by government.	109 (34%)	154 (48%)	61 (19%)	46.50	4.02	0.028
2	Listened preventive measures against disease.	179 (55%)	145 (45%)	-	24.02	9.52	0.033
3	Any self-measures taken against disease.	192 (59%)	132 (41%)	-	42.4	5.40	0.058
4	It's responsibility of every citizen to control pandemic.	188 (58%)	136 (42%)	-	36.7	6.23	0.051
5	COVID-19 will be controlled after some time.	170 (52%)	73 (23%)	81 (25%)	53.8	3.47	0.037

Table 4: Attitude towards COVID-19(n=324)

Sr No	Practices	Yes	No	SD	t stat	p value	
1	Wearing mask when going out of home.	174 (54%)	150 (46%)	16.9	13.5	0.024	
2	Wearing gloves when going out of home	175 (54%)	149 (46%)	18.3	12.4	0.025	
3	Visited crowded place during recent days.	142 (44%)	182 (56%)	28.2	8.1	0.039	
4	Preference for protection of hand.	Hand wash with soap: 127 (39%) Hand sanitizer: 91 (28%)	Gloves: 20 (5%) Others: 6 (2%)	44.4	2.75	0.017	
5	Alcohol base concentration for hand sanitization.	35% 125 (46%)	50% 14 (4%) 70% 131 (40%)	85% & more 31 (10%)	58.04	2.4	0.034
6	Advantage of wearing gloves.	Protecting hands to get environmental contamination: 172 (53%)	Protect other surfaces to get contamination: 65 (20%) A reminder to avoid touching face: 71 (22%)	60.7	1.88	0.051	

Table 5: Practices towards COVID-19(n=324)

	Value	df	Asymptotic Significance (2-sided)
The main clinical symptoms of COVID-19 are fever, fatigue, dry cough, and myalgia.	155.320 ^a	20	0.000
Unlike the common cold, stuffy nose, runny nose, and sneezing are less common in persons infected with the COVID-19 virus.	107.145 ^a	20	0.000
Persons with COVID-19 cannot infect with the virus to others when a fever is not present.	112.053 ^a	20	0.000
The COVID-19 virus spreads via airborne / respiratory droplets of infected individuals.	208.560 ^a	20	0.000
Ordinary residents can wear general medical masks to prevent the infection by the COVID-19 virus.	149.017 ^a	20	0.000
To prevent the infection by COVID-19, individuals should avoid going to crowded places such as shopping malls and avoid taking public transportation.	247.512 ^a	20	0.000
Isolation and treatment of people who are infected with the COVID-19 virus are effective ways to reduce the spread of the virus.	183.628 ^a	20	0.000
How much time a hand sanitizer with 35% alcohol takes to disinfect hands?	177.807 ^a	50	0.000
How much time a hand sanitizer with 35% alcohol takes to disinfect latex gloves?	215.519 ^a	50	0.000
Are you satisfied with the measures adopted by government against COVID-19 virus?	13.864 ^a	20	0.837
Have you paid attention to the preventive measures against COVID-19 virus?	167.635 ^a	10	0.000
Are you willing to take measures through your own efforts against COVID-19 virus?	121.012 ^a	10	0.000
Do you agree every citizen is responsible for the control of COVID-19 virus pandemic?	30.575 ^a	10	0.001
Do you agree that COVID-19 will finally be successfully controlled?	42.305 ^a	20	0.003
Do you wear gloves when leaving home?	8.925 ^a	10	0.539
Have you gone to any crowded place in recent days?	24.163 ^a	10	0.007
What concentration of alcohol is ideal for hand sanitization?	141.313 ^a	40	0.000
Gloves primarily serves.....	327.726 ^a	80	0.000

Table 6: Pearson Chi-Square Test

DISCUSSION

56% respondents, contributing to study were having good knowledge about disease with a positive and encouraging attitude with optimistic practices to take preventive procedures which was instrumental in limiting prevalence of disease. Pandemic disease spread globally in almost all countries of world with a mortality rate of about 5.7% [1]. Government of Pakistan took measures to minimize prevalence of disease but additional efforts were required to further educate population with more correct and reliable information using social media, internet or Television channels. Results of this study were in conformity with Chinese study where educated population were more knowledgeable and followed preventive measures with zeal and zest [13]. It was also noted just like another similar study carried out in China that it made them to realize and take more effective measures against disease if respondents have a clear knowledge about symptoms and mode of transmission and understanding about disease [14]. Our study just like Egyptian study showed an encouraging attitude of respondents towards policies adopted by government. They were found confident that by adopting these measures and self-practice of hand washing, using sanitizers, and limiting personal contact, they would be able to restrict and ultimately stop spread of disease [15]. It was observed from study that mostly respondents were following CDC and WHO recommendations to wearing face masks. Although wearing mask is most important measure to restrict human to human spread of disease beside other measures like hand washing, sanitization, and social distancing. Another

study evaluated that wearing medical mask was found more effective as compared to cotton cloth masks to restrict spread. However, use of N95 respirator face mask should only be restricted to medical staff attending patients [16]. CDC recommended use of alcohol-based hand sanitizers to restrict transmission of communicable disease [17]. Questions of this study focused on KAP of hand washing hygiene techniques of soap. Most respondents were lacking knowledge about use of sanitizers, gloves and were not following as recommended by CDC or WHO [18]. Our study had limitations since survey sample size was small and geographically limited and therefore results of study may not generalizable. Additionally, survey also had inherent limitations of cross-sectional study. Impact of following guidelines and practices in prevention and control of COVID-19 transmission could not be ascertained and would require future research [19-20].

CONCLUSION

It is concluded that about 56% of educated population and higher level of socio-economic status were found with acceptable knowledge, encouraging attitude and satisfactory practices. Mostly knowledge was gained through social media and TV channels, which have advantages and disadvantages. Therefore, areas of gap in knowledge, attitude and practice were observed among studied population. It is very important to devise a Health Education campaign of public health policies and guidelines at national level to target all socio-economic groups to further increase KAP among population to restrict spread of COVID-19.

REFERENCES

- [1] Zhong BL, Luo W, Li HM, Zhang QQ, Liu XG, Li WT, et al. Knowledge, attitudes, and practices towards COVID-19 among Chinese residents during the rapid rise period of the COVID-19 outbreak: a quick online cross-sectional survey. *International Journal of Biological Sciences*. 2020 Mar 15;16(10):1745-1752. doi: 10.7150/ijbs.45221
- [2] Gan WH, Lim JW, Koh D. Preventing Intra-hospital Infection and Transmission of Coronavirus Disease 2019 in Health-care Workers. *Safety and Health at Work*. 2020 Jun;11(2):241-243. doi: 10.1016/j.shaw.2020.03.001
- [3] Nemati M, Ebrahimi B, Nemati F. Assessment of Iranian nurses' knowledge and anxiety toward COVID-19 during the current outbreak in Iran. *Archives of Clinical Infectious Diseases*. 2020 Apr 1;15(COVID-19). doi: 10.5812/archcid.102848
- [4] Omrani AS and Shalhoub S. Middle East respiratory syndrome coronavirus (MERS-CoV): what lessons

- can we learn? *Journal of Hospital Infection*. 2015 Nov;91(3):188-96. doi: 10.1016/j.jhin.2015.08.002.
- [5] Adhikari SP, Meng S, Wu Y, Mao Y, Ye R, Wang Q, et al. A literature review of 2019 Novel Coronavirus during the early outbreak period: Epidemiology, causes, clinical manifestation and diagnosis, prevention and control. doi: 10.1186/s40249-020-00646-x
- [6] Zegarra-Valdivia J, Vilca BN, Guerrero RJ. Knowledge, perception and attitudes in Regard to COVID-19 Pandemic in Peruvian Population. doi:10.31234/osf.io/kr9ya
- [7] Janjua NZ, Razaq M, Chandir S, Rozi S, Mahmood B. Poor knowledge—predictor of nonadherence to universal precautions for blood borne pathogens at first level care facilities in Pakistan. *BMC Infectious Diseases*. 2007 Jul 24;7:81. doi: 10.1186/1471-2334-7-81
- [8] Deurenberg-Yap M, Foo LL, Low YY, Chan SP, Vijaya K, Lee M. The Singaporean response to the SARS outbreak: knowledge sufficiency versus public trust. *Health Promotion International*. 2005 Dec;20(4):320-6. doi: 10.1093/heapro/dai010
- [9] Sharma SK, Mishra M, Mudgal SK. Efficacy of cloth face mask in prevention of novel coronavirus infection transmission: A systematic review and meta-analysis. *Journal of Education and Health Promotion*. 2020 Jul 28;9:192. doi: 10.4103/jehp.jehp_533_20
- [10] Coronavirus disease (COVID-19) advice for the public: When and how to use masks (2020). Retrieved April 4, 2020, from <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public/when-and-how-to-use-masks>.
- [11] Saqlain M, Munir MM, Rehman SU, Gulzar A, Naz S, Ahmed Z, et al. Knowledge, attitude, practice and perceived barriers among healthcare workers regarding COVID-19: a cross-sectional survey from Pakistan. *Journal of Hospital Infection*. 2020 Jul;105(3):419-423. doi: 10.1016/j.jhin.2020.05.007
- [12] Baud D, Qi X, Nielsen-Saines K, Musso D, Pomar L, Favre G. Real estimates of mortality following COVID-19 infection. *Lancet Infectious Diseases*. 2020 Jul;20(7):773. doi: 10.1016/S1473-3099(20)30195-X
- [13] Fitzgerald DA. Human swine influenza A [H1N1]: practical advice for clinicians early in the pandemic. *Paediatric Respiratory Reviews*. 2009 Sep;10(3):154-8. doi: 10.1016/j.prrv.2009.06.005
- [14] World Health Organization. Advice on the use of masks in the context of COVID-19: interim guidance, 6 April 2020. World Health Organization; 2020.
- [15] MacIntyre CR, Seale H, Dung TC, Hien NT, Nga PT, Chughtai AA, et al. A cluster randomised trial of cloth masks compared with medical masks in healthcare workers. *BMJ Open*. 2015 Apr 22;5(4):e006577. doi: 10.1136/bmjopen-2014-006577
- [16] Gupta MK and Lipner SR. Hand hygiene in preventing COVID-19 transmission. *Cutis*. 2020 May;105(5):233-234. PMID: 32603385.
- [17] CDC C. Frequently asked questions about hand hygiene for healthcare personnel responding to COVID-2019.
- [18] Jindal R and Pandhi D. Hand hygiene practices and risk and prevention of hand eczema during the COVID-19 pandemic. *Indian dermatology online journal*. 2020 Jul;11(4):540. doi: 10.4103/idoj.IDOJ_448_20
- [19] Ratten V. COVID-19 and entrepreneurship: Future research directions. *Strategic Change*. 2021 Mar;30(2):91-8. doi: 10.1002/jsc.2392
- [20] Caligiuri P, De Cieri H, Minbaeva D, Verbeke A, Zimmermann A. International HRM insights for navigating the COVID-19 pandemic: Implications for future research and practice. *Journal of International Business Studies*. 2020;51(5):697-713. doi: 10.1057/s41267-020-00335-9



Systematic Review

Anti-Hypertensive Effect of Gooseberry

Arooj Attique¹, Shahnai Basharat¹, Areeja Nasir¹, Huria Arooj¹, Samman Ishtiaq², Zunaira Zulqarnain³, Ammara Akeel⁴ and Misbah Arshad^{1*}

¹The University of Lahore, Lahore, Pakistan

²Rashid Latif Medical College, Lahore, Pakistan

³Punjab University, Lahore, Pakistan

⁴University of Agriculture (FSD), Faisalabad, Pakistan

ARTICLE INFO

Key Words:

Phyllanthus emblica, hypertension, Vitamin C, Polyphenol, Systolic and Diastolic blood pressure

How to Cite:

Attique, A. ., Basharat, S. ., Nasir, A. . ., Arooj, H. ., Ishtiaq, S. ., Zulqarnain, Z. ., Akeel, A. . & Arshad, M. . (2022). Anti-Hypertensive Effect of Gooseberry: Anti-Hypertensive Effect of Gooseberry . Pakistan BioMedical Journal, 5(6). <https://doi.org/10.54393/pbmj.v5i6.538>

*Corresponding Author:

Misbah Arshad

The University of Lahore, Lahore, Pakistan

fatimamishbah10@gmail.com

Received Date: 8th June, 2022

Acceptance Date: 25th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Phyllanthus emblica, also known as emblic, Indian gooseberry, or amla, is a deciduous tree of the family Phyllanthaceae. The berries are tiny and round, with a bright or yellow-green in color. The Indian gooseberry (Phyllanthus emblica) is an Indian and Middle Eastern tree. For thousands of years, it has been prescribed in Ayurvedic treatment. **Objective:** The aim of this review was to identify scientific evidence regarding the effects of gooseberry on hypertension. **Methods:** Electronic search of Google scholar, Medline and PubMed databases were conducted. When the force of blood pushing against the walls of blood vessels, is consistently too high. It is known as hypertension. Scientific evidence indicates that polyphenols are central components in fruits and other sections of the amla tree, as well as vitamin **Results:** Previous studies suggested that Gooseberry is highly effective to manage hypertension. Indian gooseberries are able to keep both diastolic and systolic blood pressure levels in their normal ranges as well significantly decrease the high levels of both of them. It has other health benefits as well which includes normalizing blood sugar levels, protects against kidney disorders, several types of cancers, also prevents cancer from spreading to other parts of the body and many more health benefits. Most of the studies that were done on Phyllanthus emblica to determine their effects on high blood pressure of patients done by giving them in the form of capsules either in their aqueous state or in their dried powder form two or three times a day after meal for weeks. And the results were visible from second or fourth weeks onwards. **Conclusion:** These studies indicated that Indian gooseberries are highly efficient and a great remedy to treat hypertension

INTRODUCTION

Hypertension is one of the most common and major risk factors for the occurrence of cardiovascular diseases [1]. Hypertension is one of the most common and most rapidly growing diseases around the world which is also increasing the risks of more serious cardiovascular diseases as well [2]. It not only results in cardiovascular diseases but also accompany diseases like diabetes mellitus and dyslipidemia [3]. High blood pressure also increases the risk of coronary heart diseases, peripheral vascular diseases, retinal hemorrhage, vision loss and renal impairment [4]. Hypertension occurs when arterial blood pressure is abnormally high. Normal ranges of blood pressure are systolic <120 mmHg and that of diastolic is <80

mmHg. There's also a term known as prehypertension which is not a medical condition but if it's range is not controlled, it can lead to hypertension (Erem et al., 2009). Prehypertension ranges from systolic 120 - 139 mmHg and diastolic 80 - 89 mmHg. Hypertension occurs when blood pressure is equal or greater than 140 mmHg systolic and 90 mmHg diastolic [5,6]. Hypertension is sometimes unable to be diagnosed because it is initially asymptomatic. But if left untreated, it can result in stroke, heart attack and kidney failure [5,7]. Most common symptoms to detect high blood pressure are headaches, lightheadedness, blurry vision or in some cases even faintness [7]. According to a national family health survey held in 2015 and 2016, hypertension is

more prevalent in people of urban areas than those living in rural areas. The main reason for this is rapid urbanization and lifestyle changes which is unhealthy. Sedentary lifestyle and unhealthy eating habits are the most common reasons for the development of high blood pressure in the body along with high blood glucose levels, obesity and other several chronic diseases as well. *Phyllanthus emblica*, which is an Indian Gooseberry belonging to the family of Euphorbiaceae, is native to India and Southeast Asia. It is also known as amla or amla fruit. It is an important medicinal herb in Ayurvedic medicine [6]. Indian gooseberry is a deciduous tree in small to medium size. It is found abundantly in India, Pakistan, Sri Lanka, Malaysia, China, and South East Asia. The gooseberry plant is about 8 to 18 meters in height. It has a thin light gray bark with light green colored leaves and greenish yellow flowers. Its fruit is pale yellow in color, spherical in shape and fleshy [8]. Indian gooseberry is a highly nutritious fruit. It is a rich source of several amino acids and minerals. It also has high amounts of vitamin C in it [9]. The quantity of vitamin C found in Indian gooseberries is more than that present in citrus fruits such as lemons and oranges. Indian gooseberries also contain proteins, carbohydrates, and vitamin B complex. It has iron and phosphorus in abundance. The nutrients that are present in very low amounts in amla are saturated fats and sodium which means it is greatly beneficial to reduce heart diseases, hypertension and obesity [10]. Amla is also an important dietary source of various polyphenols of which tannins are found in abundance which has lower molecular weight and can be easily hydrolyzed in the body [11]. It also contains chemical constituents such as alkaloids and phenols which are also easily hydrolysable and more biologically active in the body [12]. It contains two types of hydrolysable tannins which are Emblicanin A and B [13]. Both of these have antioxidant properties. Emblicanin A gives glucose, gallic acid and ellagic acid upon hydrolysis whereas Emblicanin B gives only glucose and gallic acid [14]. Amla also contains flavonoids, of which most commonly found is quercetin. The alkaloids that are found in abundance in Indian gooseberries are phyllantine and phyllantidine [12]. Almost every part of the gooseberry plant has medicinal properties, but its fruit holds the most importance in the treatment of various ailments. It has a lot of Ayurvedic properties and is used for the treatment of a number of various diseases [12]. It is highly used for the cure of diseases like heart diseases, high blood glucose as well as jaundice, diarrhea and hair problems. It is also used as laxatives and diuretics as well as a liver tonic [15]. There has been much research done on amla that shows its medicinal properties and makes it stand out in plant based medicine around the globe. This berry is also an important dietary

source of polyphenolic compounds. According to various studies, it is reported that amla is most important in lowering high blood glucose, high cholesterol, and also has antioxidant and anti-inflammatory properties [16]. The free radical scavenging properties of amla prevent various types of cancers. It prevents cancer from spreading in the body as it has strong anti-mutagenic properties as well. It also prevents the need for chemotherapy and radiotherapy for cancer patients [16,17,18]. There have been many researches made that indicate the importance of Indian gooseberries in the treatment of heart diseases of which one of the most common is hypertension and hyperlipidemia. Hypertension can be a leading risk factor in the development of cardiovascular diseases which can be fatal for some patients as well. It is important to control this disease by raising awareness and by making healthy lifestyle changes in one's life. There are several low cost treatments available that can reduce the risk of developing hypertension. A study was conducted worldwide to measure the prevalence of hypertension and the methods of its diagnosis, treatment and controlling of its risk factors from the year 1990 to 2019. This study was conducted for over 200 countries. The data were collected from 1990 to 2019 of the patients aging from 30 to 79 years. The data contained all the hypertensive patients and the treatment they have received. Around 49% of men and 59% of women reported a previous diagnosis of hypertension globally. And 47% women and 38% men were treated. Around 23% of women and 18% of men have successfully controlled their hypertension as per reports globally. According to study, since 1990, treatment and control rate have been improved especially in high income countries as compared to low-income countries which have fewer improvements in controlling hypertension among patients [19]. A study was conducted to get to know the awareness about hypertension among patients of the age of above 18 years. The study was conducted on the patients belonging from rural and middle-class social group. The study was conducted on 202 patients out of which 49 (24%) were males and 153 (76%) were females. Around 80% of the patients know that hypertension can lead to severe cardiovascular diseases. Upon further inquiries, over 77% of these patients were not doing any physical activity and not avoiding oily foods to reduce their weight. A large number of patients use ghee for cooking purposes. The study concluded that more awareness is needed among patients on how to change their lifestyle so that hypertension can be prevented or controlled which can further help in the reduction of risk of developing cardiovascular diseases [20]. The *Phyllanthus emblica* fruit is considered to be highly efficient in lowering the risks of cardiovascular diseases out of which the most common

are high blood pressure and high cholesterol levels in the body. One of the studies indicate the efficiency of amla fruit in the prevention of hypertension, hyperlipidemia, arrhythmia, cardiotoxicity and heart failure. This study was performed on nineteen in vitro and animal samples. Its clinical trials were accessed by Jadad scale and animal studies were accessed by ARRIVE checklist. The study showed that *Phyllanthus emblica* influences various risk factors of cardiovascular diseases and can be efficient in protecting against serious heart problems [21]. Another study indicated that hypertension can be a reason for cardiovascular morbidity and motility as well. This study was conducted in 150 hypertensive patients which were given a capsule of 500mg of *Phyllanthus emblica* (in the form of aqueous extract) two times a day. It was added in their regular medication of the day for a period of 12 weeks in total. The effects of the capsule started showing the results of controlling blood pressure of the patients in 2, 4 and 8th weeks of the study. Other health parameters such as lipid profile, uric acid, oxidant and antioxidants enzyme levels and HbA1c were also measured at the end of the study. *Phyllanthus emblica* showed good results in controlling high blood pressure but did not additionally lower the diastolic and systolic blood pressure levels [22]. Another study was done on *Phyllanthus emblica* which was conducted on 12 patients of hypertension. In this study, the patients were given 250mg of *Phyllanthus emblica* extract in aqueous form two times a day for 14 days in total. The aqueous extract of *Phyllanthus emblica* was highly standardized on high performance liquid chromatography so that low molecular weight hydrolysable tannins can be obtained as well. These tannins include Emblicanin A, Emblicanin B, pedunculagin and punigluconin. Heart rate, augmentation pressure, radical and aortic blood pressure were assessed at the baseline of this study. The study showed significant decrease in the arterial stiffness by lowering radical and aortic blood pressure. The treatment was performed very well and did not show any adverse side effects [23]. A study was conducted on patients with primary hypertension. These patients were divided into two groups in which one used amla fruit and the other group used placebo with their routine medications. Amla was given in a 500mg capsule form three times a day after every meal. The placebo was also given in a 500mg of capsule three times a day after every meal. The capsule contained powder of dried amla fruit. The study continued for about a month. The study indicated that there was a significant difference in the condition of patients of hypertension. Their systolic and diastolic blood pressures were both controlled as compared to before taking the amla capsule [21]. Another study was performed on 20 patients of hypertension who were all men and also potential smokers.

These people have compromised immune systems, decreased appetite, as well as cardiovascular abnormalities and also some other disorders. The group of 20 people were divided in half. Group with first 10 patients were given 250mg of *Phyllanthus emblica* fruit extract which contained almost 60% of hydrolysable tannins including Emblicanin A, Emblicanin B and punigluconin. It was given two times a day or after meals. The other group of 10 people received a placebo of 250mg capsule of the same ingredients including lactose, magnesium stearate and microcrystalline cellulose. The study continued for almost 60 days. The results were assessed by giving the participants a symptoms frequency questionnaire at the end of their trial. The subjective parameters that were assessed were mouth hygiene, cough, shortness of breath, palpitations, heartburn and fatigue. The objective parameters that were assessed included blood pressure, lipid profile, lipoprotein A, high sensitivity C-reactive protein, fasting glucose, ECG. The results of the study indicated significant differences in the group given *Phyllanthus emblica* capsule as compared to those who were given placebo capsule. The blood pressure and lipid profile were much controlled [24]. Patients with uncontrolled hypertension were randomized divided into two equal groups. First group was assigned to take 500mg of *Phyllanthus emblica* in capsule form and the other group was assigned to take a placebo consisting of standard antihypertensive drugs. Both the capsules were assigned to take two times a day after meal for a time period of about eight weeks. Systolic blood pressure, diastolic blood pressure and heart rate were measured after 2, 4, 6 and 8 weeks of the study. The study indicated that systolic blood pressure was decreased by 8-15% in patients who were given *Phyllanthus emblica* capsules and 6-7% in those who were given placebo capsules. The study also indicated that diastolic blood pressure was decreased by 7-12% in the emblica group and 3-7% in the placebo group. This indicated that patients given *Phyllanthus emblica* reduced their blood pressure more efficiently than those patients who took standard hypertensive drugs [25]. Another study performed the effect of Indian gooseberries on blood pressure and lipid profile of the patients. In the study, a total of 60 patients were taken out of which 40 were given 500mg of *Phyllanthus emblica* powder and the rest of 20 patients were given 20mg of simvastatin as a placebo both in capsule form for 42 days. After 42 days, the samples of the patients were analyzed to determine the lipid profile as well as monitoring of blood pressure. The result of both the samples showed significant effect in the reduction of high blood pressure and controlled lipid profile of the patients but most effective results were given by Indian gooseberry. It provides significant protection against diseases like

coronary artery disease and atherosclerosis without having any negative effects on blood pressure and lipid profile of patients [26]. Another study was conducted on over 150 patients with essential hypertension. These patients were given an aqueous extract of 500mg of *Phyllanthus emblica* and placebo in capsule form for a time period of 12 weeks. Both the *Phyllanthus emblica* and placebo results were compared at the baseline and after the completion of 12 weeks. It showed that *Phyllanthus emblica* was significantly effective in reducing the blood pressure of patients with hypertension [3].

Research	Year	Sample Size	Results	Reference
Faculty opinions recommendation of worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019.	1990-2019	Over 200 countries	23% women 18% men successfully controlled their hypertension	19
Awareness of Hypertension among patients attending Primary Health Care Centre and Outpatient Department of tertiary care hospital of Karachi	2007	202 patients 49 males 153 females	80% of patients know hypertension and related risks. 77% of patients were not avoiding oily food, no physical activity.	20
The cardiovascular pharmacology of <i>Emblca officinalis</i> .	2018	19 vitro and animal samples.	<i>Phyllanthus emblica</i> shows effective in protecting against serious heart diseases.	21
Antihypertensive and pleiotropic effects of <i>Phyllanthus emblica</i> extract as an add-on therapy in patients with essential hypertension-A randomized double-blind placebo-controlled trial.	2021	150 hypertensive patients.	<i>Phyllanthus emblica</i> showed good results in controlling high blood pressure.	22
Evaluation of <i>Phyllanthus emblica</i> extract on cold pressor induced cardiovascular changes in healthy human subjects.	2014	12 patients with hypertension.	Significant decrease in the arterial stiffness by lowering radical and aortic blood pressure.	23
Evaluating the use of <i>Emblca officinalis</i> standardized fruit extract in cardio-respiratory improvement and antioxidant status of volunteers with smoking history.	2014	20 male smokers with hypertension.	Good results were shown in blood pressure, lipid profile, lipoprotein A, and on other tests.	24
A randomized, triple-blind, placebo-controlled, add-on clinical trial to evaluate the efficacy of <i>emblca officinalis</i> in uncontrolled hypertension.	2020	92 patients with uncontrolled hypertension.	Systolic blood pressure was decreased by 8-15% in patients. Diastolic blood pressure was decreased by 7-12%.	25
A comparative clinical study of hypolipidemic efficacy of Amla (<i>Emblca officinalis</i>) with 3-hydroxy-3-methylglutaryl-coenzyme-A reductase inhibitor simvastatin.	2012	60 patients.	Good amount of reduction shown in high blood pressure of patients and it controlled lipid profile of the patients.	26

CONCLUSIONS

It is concluded that *Phyllanthus emblica* which is also known as Indian gooseberry or amla/amlu fruit is highly efficient in controlling high blood pressure. It also helps in maintaining lipid profile in its normal ranges and then further helps in protecting from various cardiovascular diseases. Indian gooseberries are able to keep both diastolic and systolic blood pressure levels in their normal ranges as well significantly decrease the high levels of both of them. It has other health benefits as well which includes normalizing blood sugar levels, protects against kidney disorders, several types of cancers, also prevents cancer from spreading to other parts of the body and many more health benefits. Most of the studies that were done on *Phyllanthus emblica* to determine their effects on high blood pressure of patients done by giving them in the form of capsules either in their aqueous state or in their dried powder form two or three times a day after meal for weeks. And the results were visible from second or fourth weeks onwards. These studies indicated that Indian gooseberries are highly efficient and a great remedy to treat

hypertension.

REFERENCES

- [1] Pickering GW. The natural history of hypertension. British medical bulletin. 1952 Jan; 8(4):305-9. doi: 10.1093/oxfordjournals.bmb.a074193.
- [2] Shafi ST, Shafi T. A survey of hypertension prevalence, awareness, treatment, and control in health screening camps of rural central Punjab, Pakistan. Journal of epidemiology and global health. 2017 Jun; 7(2):135-140. doi: 10.1016/j.jegh.2017.01.001.
- [3] Shanmugarajan D, Girish C, Harivenkatesh N, Chanaveerappa B, Prasanna Lakshmi NC. Antihypertensive and pleiotropic effects of *Phyllanthus emblica* extract as an add-on therapy in patients with essential hypertension-A randomized double-blind placebo-controlled trial. Phytotherapy Research. 2021 Jun; 35(6):3275-3285. doi: 10.1002/ptr.7043.
- [4] Mendis S. World Health Organisation; 2010. Global status report on noncommunicable diseases 2010.

- [5] Kumar M R, Shankar R, Singh S. Hypertension among the adults in rural Varanasi: a cross-sectional study on prevalence and health seeking behavior. *Indian Journal of Preventive and Social Medicine*. 2016;47(1-2):78-83.
- [6] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. National Heart, Lung, and Blood Institute; National High Blood Pressure Education Program Coordinating Committee. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003 Dec; 42(6):1206-52. doi: 10.1161/01.HYP.0000107251.49515.c2.
- [7] Prabakaran J, Vijayalakshmi N, VenkataRao E. Prevalence of hypertension among urban adult population (25-64 years) of Nellore. *International Journal of Research & Development of Health*. 2013;1(2):42-49.
- [8] Maurya U, Srivastava S, Traditional Indian herbal medicine used as antipyretic, antiulcer, anti-diabetic and anticancer: A review, *International Journal of Research in Pharmaceutical Chemistry*, 2011; 1(4):1152-9.
- [9] Srivasuki KP, Nutritional and health care benefits of Amla, *Journal of Pharmacognosy*, 2012; 3(2):141-151.
- [10] Dang GK, Parekar RR, Kamat SK, Scindia AM, Rege NN. Antiinflammatory activity of *Phyllanthus emblica*, *Plumbago zeylanica* and *Cyperus rotundus* in acute models of inflammation. *Phytotherapy Research*. 2011Jun;25(6):9048. doi:10.1002/ptr.3345.
- [11] Bhandari PR, Kamdod MA. *Emblca officinalis* (Amla): a review of potential therapeutic applications. *International Journal of Green Pharmacy (IJGP)*. 2012; 6:257-269.
- [12] Udupa KN. Ayurveda for promotion of health. *Journal of Ayurveda*. 1985Jan;3(3).
- [13] Bhattacharya SK, Bhattacharya A, Sairam K, Ghosal S. Effect of bioactive tannoid principles of *Emblca officinalis* on ischemia-reperfusion-induced oxidative stress in rat heart. *Phytomedicine*. 2002 Mar; 9(2):171-4. doi: 10.1078/0944-7113-00090.
- [14] Wang YF, Wang XY, Ren Z, Qian CW, Li YC, Kaio K, et al. Phyllaemblicin B inhibits Coxsackie virus B3 induced apoptosis and myocarditis. *Antiviral Research*. 2009 Nov; 84(2):150-8. doi: 10.1016/j.antiviral.2009.08.004.
- [15] Perianayagam JB, Sharma SK, Joseph A, Christina AJ. Evaluation of anti-pyretic and analgesic activity of *Emblca officinalis* Gaertn. *Journal of Ethnopharmacology*. 2004 Nov;95(1):83-5. doi: 10.1016/j.jep.2004.06.020.
- [16] Krishnaveni M, Mirunalini S. Chemopreventive efficacy of *Phyllanthus emblica* L. (amla) fruit extract on 7,12-dimethylbenz(a)anthracene induced oral carcinogenesis—a dose-response study. *Environ Environmental toxicology and pharmacology*. 2012 Nov;34(3):801-10. doi: 10.1016/j.etap.2012.09.006.
- [17] Adil MD, Kaiser P, Satti NK, Zargar AM, Vishwakarma RA, Tasduq SA. Effect of *Emblca officinalis* (fruit) against UVB-induced photo-aging in human skin fibroblasts. *Journal of Ethnopharmacology*. 2010 Oct; 132(1):109-14. doi: 10.1016/j.jep.2010.07.047.
- [18] Deep G, Dhiman M, Rao AR, Kale RK. Chemopreventive potential of *Triphala* (a composite Indian drug) on benzo(a)pyrene induced forestomach tumorigenesis in murine tumor model system. *Journal of experimental & clinical cancer research: CR*. 2005 Dec; 24(4):555-63.
- [19] Semplicini, A. Faculty opinions recommendation of worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: A pooled analysis of 1201 population-representative studies with 104 million participants. *Faculty Opinions - Post-Publication Peer Review of the Biomedical Literature*. 2021. doi.org/10.3410/f.740693 066.793589850
- [20] Ashfaq T, Anjum Q, Siddiqui H, Shaikh S, Vohra EA. Awareness of hypertension among patients attending primary health care centre and outpatient department of tertiary care hospital of Karachi. *Journal of Pakistan Medical Association*. 2007 Aug; 57:396-8.
- [21] Hashem-Dabaghian F, Ziaee M, Ghaffari S, Nabati F, Kianbakht S. A systematic review on the cardiovascular pharmacology of *Emblca officinalis* Gaertn. *Journal of cardiovascular and thoracic research*. 2018;10(3):118128. doi:10.15171/jcvtr.2018.20
- [22] Shanmugarajan D, Girish C, Harivenkatesh N, Chanaveerappa B, Prasanna Lakshmi NC. Antihypertensive and pleiotropic effects of *Phyllanthus emblica* extract as an add-on therapy in patients with essential hypertension—A randomized double-blind placebo-controlled trial. *Phytotherapy Research*. 2021 Jun; 35(6):3275-3285. doi: 10.1002/ptr.7043.
- [23] Fatima N, Pingali U, Pilli R. Evaluation of *Phyllanthus emblica* extract on cold pressor induced cardiovascular changes in healthy human subjects. *Pharmacognosy Research*. 2014 Jan; 6(1):29-35. doi: 10.4103/0974-8490.122914
- [24] Biswas TK, Chakrabarti S, Pandit S, Jana U, Dey SK. Pilot study evaluating the use of *Emblca officinalis*

- standardized fruit extract in cardio-respiratory improvement and antioxidant status of volunteers with smoking history. *Journal of Herbal Medicine*. 2014 Dec; 4(4):188-194. doi.org/10.1016/j.hermed.2014.09.002
- [25] Ghaffari S, Navabzadeh M, Ziaee M, Ghobadi A, Ghods R, Hashem-Dabaghian F. A Randomized, Triple-Blind, Placebo-Controlled, Add-On Clinical Trial to Evaluate the Efficacy of *Emblica officinalis* in Uncontrolled Hypertension. *Evidence-Based Complementary and Alternative Medicine*. 2020 Oct; 2020:8592869. doi: 10.1155/2020/8592869.
- [26] Gopa B, Bhatt J, Hemavathi K G. A comparative clinical study of hypolipidemic efficacy of Amla (*Emblica officinalis*) with 3-hydroxy-3-methylglutaryl-coenzyme-A reductase inhibitor simvastatin. *Indian journal of pharmacology*. 2012 Mar; 44(2): 238-242. doi.org/10.4103/0253-7613.93857
- [27] Khambatta, C. How does Amla Powder affect blood pressure? Amla Green. [Last accessed on January 9, 2022]. Retrieved from <https://amlagreen.com/blogs/news/aml-powder-for-blood-pressure>
- [28] Erem C, Hacıhasanoglu A, Kocak M, Deger O, Topbas M. Prevalence of prehypertension and hypertension and associated risk factors among Turkish adults: Trabzon Hypertension Study. *Journal of public health*. 2009 Mar; 31(1):4758. doi:10.1093/pubmed/fdn078.
- [29] Fisher ND, Williams GH. Hypertensive vascular disease. In: Kasper DL, Braunwald E, Fauci AS, et al. editors. *Harrison's Principles of Internal Medicine*. 16th. New York, NY, USA: McGraw-Hill; 2005;1463-1481.
- [30] International Institute for Population Sciences. Ministry of Health and Family Welfare, Government of India. National family Health Survey (NFHS-4) 2015-16 Factsheet, India, <http://rchiips.org/NFHS/pdf/NFHS4/India.pdf>.
- [31] Dev S. Ancient-modern concordance in Ayurvedic plants: some examples. *Environmental health perspectives*. 1999 Oct; 107(10):783-789. doi.org/10.1289/ehp.99107783

**Systematic Review****Ethical Issues and Use of Animal Models in Dentistry - A Systematic Review****Saad Liaqat^{1*}, Sahar Jamal¹, Saira Ahmad¹, Fatima Sajjad¹, Talha Falak Khalil¹, Humaira Jabeen¹, Muhammad Adnan Khan¹, Nawshad Muhammad¹**¹Department of Dental Materials, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan**ARTICLE INFO****Key Words:**

Animal studies, Ethical issues, Dentistry, Artificial Intelligence

How to Cite:Liaqat, S., Jamal, S., Ahmad, S., Sajjad, F., Khalil, T. F., Jabeen, H., Khan, M. A., & Muhammad, N. (2022). Ethical Issues and Use of Animal Models in Dentistry - A Systematic Review: Animal studies, Ethical issues, Dentistry, Artificial Intelligence. *Pakistan BioMedical Journal*, 5(6).
<https://doi.org/10.54393/pbmj.v5i6.494>***Corresponding Author:**Saad Liaqat
Department of Dental Materials, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan
saadliaqat.ibms@kmu.edu.pk

Received Date: 27th May, 2022

Acceptance Date: 20th June, 2022

Published Date: 30th June, 2022

ABSTRACT

Prior to conducting therapeutic trials on people, it is critical to do experimental studies on animal models to determine the origin and pathophysiology of the illness process. **Objective:** The objective of this systematic review was to outline the ethical issues involved in the need of animal studies in dentistry. **Methods:** This research was conducted using latest Prisma guidelines 2020. Data retrieved for this study was searched on PubMed, google scholar, and Cochrane libraries. **Results:** Safe and valid experimentation is the key for successful research. In health sector, the precision, accuracy, and validation of the experiment is very critical. It has been a common practice in health sector, that medicine and other surgical research is tested and validated on non-human primates. Once these tests on non-human subjects are replicated and validated multiple times, then the trials on human volunteers are initiated. However, over the years, researchers and different groups have raised serious questions about the abuse of animal studies. Moreover, the technology has progressed quite rapidly. **Conclusions:** The contemporary world is currently dealing with artificial intelligence, virtual reality, and augmented reality. The dentistry is also strong pillar of health services and is not alien to these issues. The outcome of this review is to explore the possibilities of using technology as an alternative to animal in dentistry.

INTRODUCTION

Prior to conducting therapeutic trials on people, it is critical to do experimental studies on animal models to determine the origin and pathophysiology of the illness process [1]. Animal models are thus utilised to analyse the etiopathogenesis, clinical features, immunological and histopathological characteristics of the diseases affecting the periodontium and by testing the success of emerging operational procedures of dental diseases, and to validate the findings before implementation on people [2]. The disorders that affect the gingiva and periodontium are a group of chronic inflammatory diseases that affect the periodontium's supporting tissues. Most importantly, the

bacterial plaque, which is a thin adherent microbial biofilm around the teeth is the primary cause of many periodontal disorders. To prevent these disorders, it's crucial to understand the disease's aetiology, pathophysiology, biomaterial use, and tissue reactions to novel procedures in animal models before applying them to humans.

METHODS

This research was conducted using latest Prisma guidelines 2020.

Search Strategy: Data retrieved for this study was searched on PubMed, google scholar, and Cochrane libraries (Figure 1).

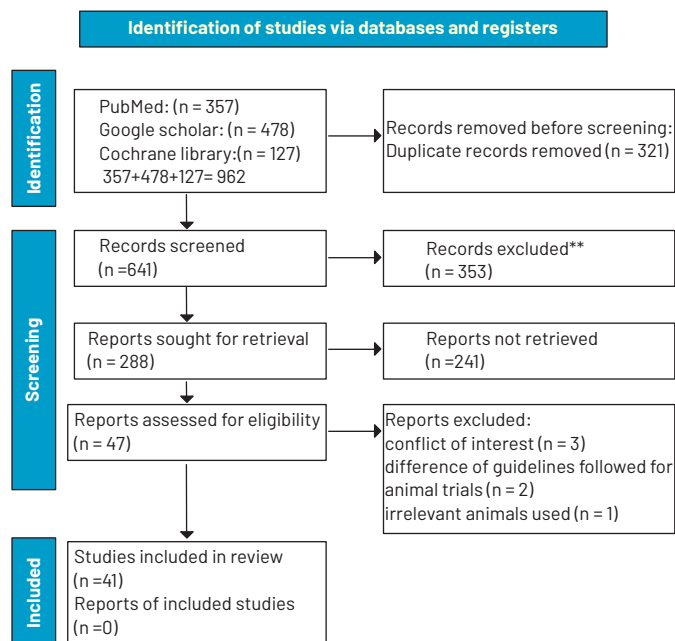


Figure 1: PRISMA flow diagram for inclusion and exclusion of articles

RESULTS

Different Models in Practice: Primates other than humans, rodents, and other animals such as dogs and hamsters are also employed in dental research, each with their own set of benefits and drawbacks. Various areas of dentistry have used the bulk of animals for the purpose of experiment for last two decades [3]. Most of the animals utilized in dental research were yet alone for the purpose of instructions and training. Smaller animals were mostly used in dental research faculties and larger animals were used as a last resort for testing new surgical methods before they were used on humans. To understand the causes and pathophysiology of periodontal diseases, experiments are done on animals for the purpose of dental research [4]. The use of animal models helped tremendously in the field of tissue engineering. A recent study conducted on rats and rabbits in the year of 2019, has shown the repair of damaged cartilage with the help of mesenchymal stem cells growth through differentiation and replacement of cells [5]. These animals were treated with exosomes which are basically the type of extracellular vesicles that contains proteins, DNA and RNA of the cells that secretes them. Thus, showing increase proliferation of cells and deposition of matrix for the regeneration of cartilage [6]. Various types of animal models were utilised in periodontal research according to the clinical studies and systematic reviews [7]. Benefits of Animal in Research: The following are some of the advantages of using animal models in research.

- The use of animals in study has aided our

understanding of biological processes significantly [8].

- Many significant biomedical breakthroughs have been made as a result of it [9].

- Antibiotics, insulin, vaccinations, and organ transplantation are just a few of the therapeutic and preventative treatments that have been developed using it [10].

General Practicing Guidelines: The amended guidelines for the use of animals in scientific study were prepared by the Indian national science academy. It is simple to obey the ethical criteria when it comes to the use of animals in research if you understand the guidelines [11].

- Allowing and providing facilities for the use of animal models for research purposes should be allowed and provided depending on the need [12].

- It is recommended to researchers that they avoid using animals unless it is necessary. They should also make certain that no unneeded strain or injury occurs [13].

- It should offer proper care and housing for the animal models utilized in research, as well as to ensure their physical comfort and their healthy life [14].

- Experiments on animals should be obtained from a well-known animal institution that can provide information on the health, genetics, and status of nutrition of each animal model [15].

- To train and give opportunities to the medical researchers as well as to support the employees who care for them [16].

Ethical Guidelines: Before beginning their research with experimental animal models, scientists should follow the rules of ethics towards animals at the level of institution and at the level of national. The animal ethics committee should be rigorously followed by everyone [17]. The committee should include a mix of stakeholders from main research institute, collaborative institute, veterinary specialist, society representative, a member of regulatory agency, and a competent professional in case expected radioactive exposure [18]. Before beginning the experiment, this committee should examine the animals, scientists, and workers managing the animals. The following are some of the ethical rules for using models of animals in dental research that must be followed.

1. Animal research should only be undertaken if they are at utmost importance to improve human or animal health and increasing knowledge in health promotion [19].
2. Ensure that minimum number of animal subjects are chosen.
3. Treat animals with respect and ensure that they have suitable living conditions [20].
4. Anaesthesia should be used for experiments that produce discomfort or pain.

5. Animals that are unable to be alleviated or healed at the conclusion of the study should be put to sleep.
6. Every person conducting animal research should be qualified or have prior experience.
7. Wherever possible, in vitro procedures and ex vivo animal models can be employed to limit the number of animals needed [21].
8. The three r's are the most important rules to follow while conducting research on experimental animal models. Russel and Burch's three r's are replacement, reduction, and refinement. When it comes to experimental animals used in research, the three rules should be followed: the animals should only be used when absolutely required. The sample size for the required number of the animals should be optimized to the minimum level [22].
9. Furthermore, the committee for the purpose of control and supervision of experiments on animals (CPCSEA) instilled the 4 r's credo - replacement, reduction, refinement, and rehabilitation of animals used in experiments [23]. The CPCSEA has made it a national policy to include post-experimentation animal rehabilitation as part of the research. The inclusion of the fourth r's to the research field encourages the researcher to take on more responsibilities [24].

Regulations of Animal Testing with Animal Welfare Act:

The best science comes from the best animal welfare. The status of an animal is referred to as animal welfare; the treatment that an animal receives is referred to as animal care, livestock farming, and fair treatment [25]. Animal welfare has recently been a major consideration when doing animal experiments. Many regulatory organizations are concerned about animal welfare, and as a result, guidelines for adequate animal care and utilisation during research are being developed [26]. Only after pressure from animal rights organizations and the general public did regulating agencies emerge [27]. These regulatory bodies passed legislation governing the treatment and use of laboratory animals. Regulatory agencies both at national and international level has set up different guidelines to oversee the experiments [28]. The ethical requirements should be met and a prior approval from these regulatory agencies is mandatory before initiating any research on animals [29].

Importance of Animal Profiles Prior to Use in Research:

Each animal and each experiment have its own pre-requisites. The potential animal subjects should be profiled. The profiling might include psychological standards, research requirements, age, breathing pattern, and temperature, but is not limited to these only. In more precise experiments, even the DNA and the living premises of the animals are tested [30].

Procedures to Reduce Unethical Ways of Animals Use in Dental Experimentation:

To reduce the unethical ways of using animals in experimentation, alternative models have been introduced. This method is useful as it is time efficient, requires less manpower and cost-effective. Stem cell, DNA chips, microfluidics chips, new image technologies are some examples to animal testing alternatives. No doubt that these alternatives will reduce animal use in and experiments.

Alternatives to Animal Models: Possibilities other than animal testing comprise of knowledgeable tests utilizing human cells and tissues which is also called as in vitro techniques, up to date computer-modelling techniques also known as in silico models, and studies involving human volunteers. Technological and scientific advancements in the discipline of toxicology and drug development have declined the demand of animal models [31]. Two new techniques have been used for dental pulp-dentin regeneration [32]. One of which is revascularization procedure while the second approach is to graft mesenchymal stem cells into canals after root canal therapy [33]. Similarly, for dentine regeneration the stem cells play a very crucial role [34]. Exploration of nano medicine cover many localities which include transfer of drugs, formation of vaccines, microbicidal, devices for recognition and imaging, implants, highly productive screening programs by operating biotic, nonbiological, bionics or combination materials [35]. Another technique is the use of macromolecular crystallography for exploratory step which focuses on the use of automated robotics and least human interference [36]. The application of Machine Learning to prognosticate the grade of printing specifying the printing process in extrusion-based 3D printing of biological substances. These procedures manifest acceptable printing situation, thus lessen the number of experimentation necessary for testing [37]. Latest progress in optogenetics have mainly concentrated on neuroscience and has recently shown progress in other fields involving stem cell research and regenerative medicine increasing awareness in well-being and illness conditions [38]. Nano electromechanical systems are developing, along with current scientific learning and technological implementations approaching latest experimental practices and offering new diagnostic and molecular interactive applications [39]. Need for nano informatics arises from some utmost challenges faced by nanotechnology, nanomaterial is helpful in sharing of data and give a way to develop methods and devices specific to the nano level [40]. New strategies have been developing after a lot of efforts for HIV-1 treatment and diagnosis, by using micro- and nano-scale technologies, objective is to

cope up with these problems using emerging technologies [41].

Future Perspectives: Science and technology have been widely accepted and integrated into the health sector. With rapid advancement, new streams of research have emerged. In the contemporary research domains, the biomedical research is more relevant to the animal studies. Moreover, the genetic and cellular engineering has been at the forefront of root causes and the solutions various human diseases and viruses.

Some objectives and suggestions to follow during the animal model usage are as follow:

- Replacement of the living subjects to computer experiments and simulations.
- By reducing animal use to by adopting in vitro methods or ex vivo methods
- Advancement to current level in biomedical research can improve the animal models.
- Animals' safety during research and experimentation must be a permanent consideration.

CONCLUSION

Initially research is an abstract idea, which should be properly tested and verified. The non-human subjects have been used for the overs for this validation. However, these experiments are sometime a source of abuse for animals and in some cases very unethical. Different regulators have set up different guidelines but still the idea of experimenting on live animals is broadly criticized. New technologies such as virtual reality, image processing, and augmented reality has emerged, which could be a good alternative and can be more convincing than other experimentation methods.

REFERENCES

- [1] Merceron G, Blondel C, Brunetiere N, Francisco A, Gautier D, Ramdarshan A. Dental microwear and controlled food testing on sheep: the TRIDENT project. *Biosurface and Biotribology*. 2017 Dec;3(4): 174-83. doi.org/10.1016/j.bsbt.2017.12.005
- [2] Guvva S, Patil MB, Mehta D. Rat as laboratory animal model in periodontology. *International Journal of Oral Health Sciences*. 2017 Jul;7(2): 68. doi.org/10.4103/ijohs.ijohs_47_17
- [3] Cao J, Zhang L, Liu YJ, Wang WL, Wang YG, Li CF, et al. Properties of a Novel Animal Model of LPR. *J Voice*. 2021 Sep;35(5): 805.e17-e26. doi.org/10.1016/j.jvoice.2020.01.021
- [4] Tan SSH, Tjio CKE, Wong JRY, Wong KL, Chew JRJ, Hui JHP, et al. Mesenchymal stem cell exosomes for cartilage regeneration: a systematic review of preclinical in vivo studies. *Tissue Engineering Part B: Reviews*. 2021 Feb;27(1): 1-13. doi.org/10.1089/ten.teb.2019.0326
- [5] Smith EL, Locke M, Waddington RJ, Sloan AJ. An ex vivo rodent mandible culture model for bone repair. *Tissue Engineering Part C: Methods*. 2010 Dec;16(6): 1287-96. doi.org/10.1089/ten.tec.2009.0698
- [6] Diaz-Gomez L, Kontoyiannis PD, Melchiorri AJ, Mikos AG. Three-dimensional printing of tissue engineering scaffolds with horizontal pore and composition gradients. *Tissue Engineering Part C: Methods*. 2019 Jul;25(7): 411-20. doi.org/10.1089/ten.tec.2019.0112
- [7] Doke SK, Dhawale SC. Alternatives to animal testing: A review. *Saudi Pharmaceutical Journal*. 2015;23(3): 223-9. doi.org/10.1016/j.jsps.2013.11.002
- [8] Guittin P, Decelle T. Future improvements and implementation of animal care practices within the animal testing regulatory environment. *ILAR journal*. 2002 Jan;43(Suppl_1): S80-S4. doi.org/10.1093/ilar.43.Suppl_1.S80
- [9] Singhrao SK, Sloan AJ, Smith EL, Archer CW. Technical advances in the sectioning of dental tissue and of on-section cross-linked collagen detection in mineralized teeth. *Microscopy research and technique*. 2010 Aug;73(8): 741-5. doi.org/10.1002/jemt.20815
- [10] Arora T, Mehta A, Joshi V, Mehta K, Rathor N, Mediratta P, et al. Substitute of animals in drug research: an approach towards fulfillment of 4R's. *Indian journal of pharmaceutical sciences*. 2011 Jan;73(1): 1. doi.org/10.4103/0250-474X.89750
- [11] Richmond J. Refinement, reduction, and replacement of animal use for regulatory testing: future improvements and implementation within the regulatory framework. *ILAR journal*. 2002 Jan;43(Suppl_1):S63-S8. doi.org/10.1093/ilar.43.Suppl_1.S63
- [12] Pereira S, Veeraraghavan P, Ghosh S, Gandhi M. Animal experimentation and ethics in India: the CPCSEA makes a difference. *Alternatives to laboratory animals*. 2004 Jan;32(1_suppl):411-5. doi.org/10.1177/026119290403201s67
- [13] Olfert ED, Cross BM, McWilliam AA. *Guide to the care and use of experimental animals: Canadian Council on Animal Care Ottawa*; 1993.
- [14] Cantley M, Bartold P, Marino V, Reid R, Fairlie D, Wyszynski R, et al. The use of live-animal micro-computed tomography to determine the effect of a novel phospholipase A2 inhibitor on alveolar bone loss in an in vivo mouse model of periodontitis. *Journal of periodontal research*. 2009 Jun;44(3): 317-

22. doi.org/10.1111/j.1600-0765.2008.01132.x
- [15] Ekuni D, Yamanaka R, Yamamoto T, Miyauchi M, Takata T, Watanabe T. Effects of mechanical stimulation by a powered toothbrush on the healing of periodontal tissue in a rat model of periodontal disease. *Journal of periodontal research*. 2010 Feb;45(1): 45-51. doi.org/10.1111/j.1600-0765.2009.01195.x
- [16] Hokamura K, Inaba H, Nakano K, Nomura R, Yoshioka H, Taniguchi K, et al. Molecular analysis of aortic intimal hyperplasia caused by *Porphyromonas gingivalis* infection in mice with endothelial damage. *Journal of periodontal research*. 2010 Jun;45(3): 337-44. doi.org/10.1111/j.1600-0765.2009.01242.x
- [17] Liang S, Hosur KB, Domon H, Hajishengallis G. Periodontal inflammation and bone loss in aged mice. *Journal of periodontal research*. 2010 Aug;45(4): 574-8. doi.org/10.1111/j.1600-0765.2009.01245.x
- [18] Park JC, Su C, Jung IH, Choi SH, Cho KS, Kim CK, et al. Mechanism of alveolar bone loss in a collagen-induced arthritis model in mice. *Journal of clinical periodontology*. 2011 Feb;38(2): 122-30. doi.org/10.1111/j.1600-051X.2010.01645.x
- [19] Barros S, Arce R, Galloway P, Lawter R, Offenbacher S. Therapeutic effect of a topical CCR2 antagonist on induced alveolar bone loss in mice. *Journal of periodontal research*. 2011 Apr;46(2): 246-51. doi.org/10.1111/j.1600-0765.2010.01340.x
- [20] Moro CA, Hanna-Rose W. Animal Model Contributions to Congenital Metabolic Disease. *Adv Exp Med Biol*. 2020 Apr; 1236: 225-44. doi.org/10.1007/978-981-15-2389-2-9
- [21] Wilson-Sanders SE. Invertebrate models for biomedical research, testing, and education. *ILAR journal*. 2011 Jan;52(2): 126-52. doi.org/10.1093/ilar.52.2.126
- [22] Robinson NB, Krieger K, Khan FM, Huffman W, Chang M, Naik A, et al. The current state of animal models in research: A review. *Int J Surg*. 2019 Dec; 72: 9-13. doi.org/10.1016/j.ijssu.2019.10.015
- [23] Öner A, Moerke C, Wolff A, Kischkel S, Schmidt W, Grabow N, et al. A preclinical animal model for evaluating the sealing capacity of covered stent grafts in acute vessel perforation. *Eur J Med Res*. 2020 Dec;25(1): 28. doi.org/10.1186/s40001-020-00429-y
- [24] Vedani A. [Computer-aided drug design-an alternative to animal testing in the pharmacological screening] [Article in German]. *ALTEX-Alternatives to animal experimentation*. 1991 Apr;8(1):39-60.
- [25] Schmidt K. Concepts of animal welfare in relation to positions in animal ethics. *Acta biotheoretica*. 2011 Jun;59(2): 153-71. doi.org/10.1007/s10441-011-9128-y
- [26] Fernandes MR, Pedroso AR. Animal experimentation: A look into ethics, welfare and alternative methods. *Rev Assoc Med Bras* (1992). 2017 Nov;63(11): 923-8. doi.org/10.1590/1806-9282.63.11.923
- [27] Lewejohann L, Schwabe K, Häger C, Jirkof P. Impulse for animal welfare outside the experiment. *Lab Anim*. 2020 Apr;54(2): 150-8. doi.org/10.1177/0023677219891754
- [28] Reaves M, Northcut B. Animal welfare is the primary concern. *Lab Anim (NY)*. 2019 Oct;48(10): 275. doi.org/10.1038/s41684-019-0396-5
- [29] Cornejo YR, Holguin L, Tu J. Considering animal welfare with scientific justification in mind. *Lab Anim (NY)*. 2018 Jun;47(6): 140. doi.org/10.1038/s41684-018-0070-3
- [30] Joers V, Tansey MG, Mulas G, Carta AR. Microglial phenotypes in Parkinson's disease and animal models of the disease. *Prog Neurobiol*. 2017 Aug; 155: 57-75. doi.org/10.1016/j.pneurobio.2016.04.006
- [31] Freires IA, Sardi JdCO, de Castro RD, Rosalen PL. Alternative animal and non-animal models for drug discovery and development: bonus or burden? *Pharmaceutical research*. 2017 Apr;34(4): 681-6. doi.org/10.1007/s11095-016-2069-z
- [32] Meigs L, Smirnova L, Rovida C, Leist M, Hartung T. Animal testing and its alternatives - the most important omics is economics. *Altex*. 2018 Jul;35(3): 275-305. doi.org/10.14573/altex.1807041
- [33] Kim S, Shin S-J, Song Y, Kim E. In vivo experiments with dental pulp stem cells for pulp-dentin complex regeneration. *Mediators of Inflammation*. 2015; Nov 24:1-6. doi.org/10.1155/2015/409347
- [34] Iohara K, Nakashima M, Ito M, Ishikawa M, Nakasima A, Akamine A. Dentin regeneration by dental pulp stem cell therapy with recombinant human bone morphogenetic protein 2. *Journal of dental research*. 2004 Aug;83(8): 590-5. doi.org/10.1177/154405910408300802
- [35] Pelaz B, Alexiou C, Alvarez-Puebla RA, Alves F, Andrews AM, Ashraf S, et al. Diverse applications of nanomedicine. *ACS nano*. 2017 Mar;11(3): 2313-81. doi.org/10.1021/acsnano.6b06040
- [36] Lawrence JM, Orlans J, Evans G, Orville AM, Foadi J, Aller P. High-throughput in situ experimental phasing. *Acta Crystallographica Section D: Structural Biology*. 2020 Aug;76(8): 790-801. doi.org/10.1107/S2059798320009109
- [37] Conev A, Litsa EE, Perez MR, Diba M, Mikos AG, Kavvaki LE. Machine Learning-Guided Three-

- Dimensional Printing of Tissue Engineering Scaffolds. *Tissue Engineering Part A*. 2020 Jun;26(23-24): 1359-68. doi.org/10.1089/ten.tea.2020.0191
- [38] Rein ML, Deussing JM. The optogenetic(r) evolution. *Molecular Genetics and Genomics*. 2012 Feb;287(2): 95-109. doi.org/10.1007/s00438-011-0663-7
- [39] Craighead HG. Nanoelectromechanical systems. *Science*. 2000 Nov;290(5496):1532-5. doi.org/10.1126/science.290.5496.1532
- [40] Panneerselvam S, Choi S. Nanoinformatics: emerging databases and available tools. *International journal of molecular sciences*. 2014 May;15(5): 7158-82. doi.org/10.3390/ijms15057158
- [41] Lifson MA, Ozen MO, Inci F, Wang S, Inan H, Baday M, et al. Advances in biosensing strategies for HIV-1 detection, diagnosis, and therapeutic monitoring. *Advanced drug delivery reviews*. 2016 Aug; 103: 90-104. doi.org/10.1016/j.addr.2016.05.01

**Systematic Review****Approval and Legislation Involved in Development of Medical Devices in Dentistry – A Systematic Review****Saad Liaqat^{1*}, Humaira Farman¹, Sabra Bibi¹, Sarmad Fayyaz¹, Sadiq Ullah¹, Humaira Jabeen¹, Muhammad Adnan Khan¹, Nawshad Muhammad¹**¹Department of Dental Materials, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan**ARTICLE INFO****Key Words:**

Legislation, Medical Devices, Dentistry, Development of Devices

How to Cite:Liaqat, S., Farman, H., Bibi, S., Fayyaz, S., Ullah, S., Jabeen, H., Khan, M. A., & Muhammad, N. (2022). Approval and Legislation Involved in Development of Medical Devices in Dentistry – A Systematic Review: Approval and Legislation of Medical Devices in Dentistry. *Pakistan BioMedical Journal*, 5(6). <https://doi.org/10.54393/pbmj.v5i6.495>***Corresponding Author:**Saad Liaqat
Department of Dental Materials, Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan
saadliaqat.ibms@kmu.edu.pk

Received Date: 27th May, 2022

Acceptance Date: 20th June, 2022

Published Date: 30th June, 2022

ABSTRACT

A medical device is defined as “any an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent” and “intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals”. **Objective:** The objective of this systematic review was to outline the steps and necessary requirements needed for approval and legislation of new medical devices. **Methods:** Two databases; PubMed and Google Scholar were electronically searched for articles published from year 2011 to 2021. The following MeSH (Medical Subjects Headings) terms; “new medical devices”, “Regulatory Bodies”, “Approval Medical Devices”, “Pre-market Post-market Approval” along with Boolean operators AND, OR and NOT were used to search for the articles. **Results:** It is evident from our study that risks associated with new medical and dental devices are being taken seriously by the governments of different countries and intensive work is done to minimize the risks and maximize the benefits of them. **Conclusions:** It is safe to say that we are entering a new era of safe medical practice along with new and better devices being available for the public. The reforms being made will help not only the hospitals and patients but will also assist the manufacturers in understanding the mechanisms involved in clearing their products for the approval. It will lead to advancement and reshaping healthcare system to combat many challenges faced by it and promote and protect the public health.

INTRODUCTION

A medical device is defined as “any an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent” and “intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals” [1]. New medical and dental devices are launched by introducing a prototype. These prototypes have to go through a number of tests and later modified and improved till they are rendered safe and fit for the desired usage [2]. These tests include in-vitro mechanical tests, in-vivo animal tests and clinical trials. A number of factors have to be considered before designing the clinical trials which

affect the final result and safety of these devices [3]. Clinical trials ensure that the new device is effective and safe when used in accordance with the advice of the manufacturers [4]. Many organizations exist to ensure the quality and efficacy of these new medical and dental devices like the Food and Drug Administration (FDA) in the United States [5] Figure 1, European Medicine Association (EMA) in Europe and The Pharmaceuticals and Medical Devices Agency (PMDA) in Japan [6]. Specifically, the Centre for Devices and Radiological Health (CDRH) within the FDA is responsible for protecting and promoting the health of the public by making sure that the patients have

prompt access to high quality, effective and safe medical and dental devices[7].

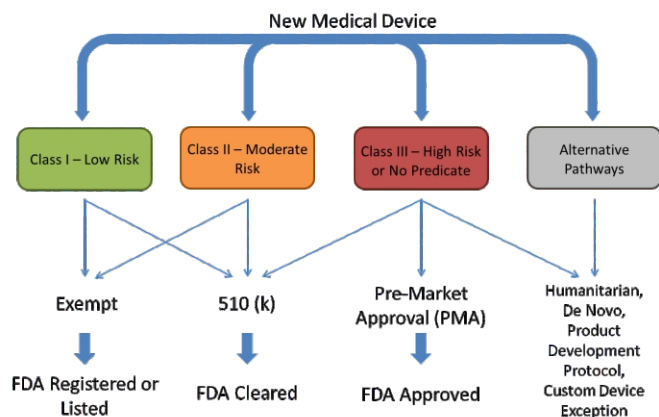


Figure 1: FDA Approval Pathway for Medical Devices

Premarket Approval: Approval of new devices is a technical process and most of the manufacturers are small scale business owners lacking the manpower and expertise to tackle these technical issues, thus delaying the approval and market entry of their product [8]. The FDA has divided medical devices into three regulatory classes according to their clinical usage; Class I, Class II and Class III [9]. The FDA depends on “valid scientific evidence” to classify and regulate medical and dental devices, “valid scientific evidence” being available to the general public. FDA was authorized to regulate the manufacturing as well the marketing processes of innovative medical and dental devices in 1976. The FDA has established two pathways for regulation of new devices, one being the 510(k) pathway and the other being the Premarket approval (PMA) [10]. 1976 onwards, devices that are rendered less complicated and risky are cleared through a rather simple process called 510(k) pathway without the need to perform clinical trials [11]. Whereas the approval of new high risk new medical and dental devices need to have Premarket approval (PMA) which requires clinical trials [12]. Premarket approval (PMA) is more rigorous than 510(k) pathway as problems in the device may lead to severe adverse and undesirable effects requiring a very strict regulatory protocol before they can be certified safe [13]. 510(k) pathway is a submission made to FDA by the manufactures to acquire a certificate that their product is legally safe and effective for the desired purpose [14]. By law, 510(k) only requires 1 feasibility study and 1 pivotal study [15] but 510(k) is the strictest marketing protocol requiring class 1 and class 2 evidence [16] Table 1. Though Class I low risk devices are generally exempted from 510(k) pathway, clinical evaluation is a must for Class III high risk devices approval [17]. For example, new implanted devices are approved through

510(k) pathway mostly but a few of them need the more rigorous premarket approval(PMA) [18]. The FDA and sponsors collaborate to plan clinical trials according to the device's design and technology, its clinical use, collection of data and patients' benefits and risks [19]. Obtaining the 510(k) may need more than 5 years for high risk devices [20,21]. Also, the trend is changing now from only PMA to continual clinical study as long as the product is in the market [22] as studies have showed that very high risk devices could not generate enough quality clinical evidence before launched. According to studies, two thirds of high risk devices that had been cleared through 510(k) pathway were recalled by the FDA due to unsatisfactory results[23].

Class	Risk	Examples	Safety/Effective control	Regulatory Pathway
I	Low	Tongue depressor, hospital beds	General Control	Self-registration
II	Medium	Absorbable sutures, Blood pressure cuffs	<ul style="list-style-type: none"> General Control Special Control 	<ul style="list-style-type: none"> Mostly 510K pathway Few devices under PMA 10-15% devices require Clinical trials
III	Highest	Implantable pacemaker, Coronary stent	<ul style="list-style-type: none"> General Control Special Control Premarket Authorization 	<ul style="list-style-type: none"> PMA Almost all require Clinical Trials

Table 1: Classification of devices under FDA

Post-Market Surveillance: The post-market surveillance (PMS) is as important as the pre-market approval in ensuring the safety and effectiveness of devices [24]. After a device has been introduced, companies need a robust PMS plan including patient review to ensure the product is delivering what it was intended for [25]. Manufacturers are required by law to carry out clinical evaluation in “real life” to prove that the performance of their product is in line with the data they provided before the launch of the product [26]. Post market surveillance should provide (i) data regarding not up to the mark performance of the device, (ii) conveying benefits and risks to the manufacturers and (iii) data to the regulating authorizes for future reforms [27], Figure 2.

Much attention is given to pre-market approval(PMA) by the manufacturers to launch their product and establish themselves in the market [28] but the situation of post market surveillance remains defective with studies remaining incomplete for years[29].



Figure 2: Output of the post-market surveillance (PMS) plan [25]

Controversy: The regulatory procedures for new medical and dental devices are considerably less than that of drugs which makes the data insufficient and prone to errors [30]. Studies have shown that wearable medical devices (WMD) even though hugely marketed have less than satisfactory safety data [31]. Currently, in Europe the pre as well as post market data of a new device is not sufficient enough to declare it completely safe [24]. Though post market surveillance may be useful but reporting an unfortunate event could take several months and it may have caused many disasters till that time [32]. Tort reforms have made the matters worse by making the clinicians bolder in use of high risk devices without considering the undesirable consequences [33]. Some organizations like EMA (European Medicines Agency) have come under criticism for allegedly placing the interests of manufacturing companies above those of the patients [34]. After UK left the European Union, commonly known as "Brexit", now a device approved by MDR will have to obtain another certificate; UK MDR through a "UK responsible person". The UK responsible person will have to take over the responsibilities of the manufacturer to get their devices registered and approved in UK, adding injury to the already complicated process of the regulatory system [35]. Japan is lagging behind other countries in providing access to innovative medical devices to its public [36]. In developing countries like Pakistan where medical malpractice and negligence is already prevalent, the guidelines and training regarding using innovative medical devices do not exist. The healthcare professionals are free to guide themselves through a new device generating very serious outcomes ranging from the death of patients to violence erupting in hospitals by the kin of the patients [37].

METHODS

Two databases: PubMed and Google Scholar were

electronically searched for articles published from year 2011 to 2021. Our question was "Are the current regulatory system for new medical and dental devices around the world satisfactory?". The following MeSH (Medical Subjects Headings) terms; "new medical devices", "Regulatory Bodies", "Approval Medical Devices", "Pre-market Post market Approval" along with Boolean operators AND, OR and NOT were used to search for the articles. Exclusion and inclusion criteria were established before the searches were made:

Exclusion Criteria:

1. Articles published in languages other than English
2. Studies done more than ten years ago.
3. Regulatory studies of drugs but not containing information about medical devices.
4. Commentaries
5. Editorial
6. Studies about the performance of innovative medical and dental devices but not their regulation and approval.

Inclusion Criteria:

1. Since articles regarding regulation of dental devices specifically were not available, medical and dental devices were included in the searches.
 2. Articles from 2011 onwards containing information about the regulatory processes of new medical and dental devices.
 3. Systematic reviews.
 4. Review articles.
 5. Original studies regarding the regulatory processes.
- Studies on reforms on regulatory processes.

RESULTS

40 articles according to the inclusion and exclusion criteria were selected among the searches. Among the 40 articles, 29 (72.5%) were in the view that the current regulatory mechanism lacks authenticity and seriously need reforms owing to the following factors:

1. Insufficient clinical data provided to the regulatory bodies.
2. Poor and ambiguous clinical data.
3. Incomplete post market studies after being approved.
4. Clinical studies not done in different countries among different populations for safety evaluation while being provided to them after being approved in one country.
5. Regulatory authorities favoring manufacturers instead of the public health concerns.
6. Needing more filters for regulation of different

medical devices.

7. Time consuming and tedious regulatory processes.

8. High risk wearable devices not having clinical trials before being launched.

9. Not holding manufacturing companies responsible for their products' disasters.

10. UK leaving the European Union and MDR not being application to the UK.

The regulatory bodies seem to be aware of the challenges and limitations of the innovative medical devices and remain committed to the cause of improving the system. Several steps are being taken and reforms are made to ease the pathways for cost-effective production of innovative medical devices. In this regard, dental devices are constantly undergoing reforms by the FDA and other agencies after they have been proven to be less risky after being successfully utilized by the clinicians and patients. A number of dental devices have been reclassified by the FDA like the endosseous dental implants were reclassified into Class II from Class III [38]. Similarly, FDA has also moved "saliva stimulator system" [39] and another dental device called "temporary mandibular condyle prosthesis" into Class II from previous Class III making the regulatory process more convenient and reasonable [39]. The FDA is also trying to exclude over the counter (OTC) denture kits (powder and liquid system) from the 510(k) pathway to be readily available without having to undergo tight scrutiny before they are made available to the consumers [40].

DISCUSSION

Instead of Medical Devices Directive (MDD), The Medical Device Regulation (MDR) was implemented in Europe in 2017 for new medical devices [41]. MDR will transform the medical device industry by moving many devices to higher risk category [42]. After MDR was implemented, manufactures were required to observe higher standards of protocol and regulatory pathways for their products [43]. Also, flexibility is allowed in the new reforms in MDR for special situation and devices where an innovative device may be used for rare disease not having any other treatment options and can benefit the patient or save their lives [44]. China too is seeking reforms in their medical devices industry owing to a demand in innovative technologies and huge growth of their market. Just like the FDA, China is reclassifying a number of medical devices, so the total time consumed by the regulatory authority China Food and Drug Administration (CFDA) for simple devices is considerably shortened making more time for the monitoring of medium and high risk medical and dental devices [45]. The Japanese government has done a

commendable job of shortening the review and regulatory time period of new medical and dental devices from 21.1 months in 2015 to 10 months in 2015 which will benefit not only the patients but also the manufacturing companies [46].

CONCLUSION

It is safe to say that we are entering a new era of safe medical practice along with new and better devices being available for the public. The reforms being made will help not only the hospitals and patients but will also assist the manufacturers in understanding the mechanisms involved in clearing their products for the approval. It will lead to advancement and reshaping healthcare system to combat many challenges faced by it and promote and protect the public health.

REFERENCES

- [1] Marjenin T, Scott P, Bajaj A, Bansal T, Berne B, Bowsher K et al. FDA Perspectives on the Regulation of Neuromodulation Devices. *Neuromodulation*. 2020 Jan;23(1):3-9. doi:10.1111/ner.13085.
- [2] Niimi S. [Practice of Regulatory Science (Development of Medical Devices)]. *Yakugaku Zasshi*. 2017 Jan;137(4):431-437. Japanese. doi: 10.1248/yakushi.16-00244-3.
- [3] Mack MJ, Adams DH. Regulatory approval and practice guidelines involving cardiovascular valve devices: determining the right evidentiary bar. *Journal of the American College of Cardiology*. 2020 Aug 25;76(8):992-5.
- [4] Jiang N, Mück JE, Yetisen AK. The Regulation of Wearable Medical Devices. *Trends Biotechnol*. 2020 Feb;38(2):129-133. doi: 10.1016/j.tibtech.2019.06.004.
- [5] Van Norman GA. Drugs, Devices, and the FDA: Part 1: An Overview of Approval Processes for Drugs. *JACC Basic Transl Sci*. 2016 Apr 25;1(3):170-179. doi: 10.1016/j.jacbts.2016.03.002.
- [6] Mori K, Watanabe M, Horiuchi N, Tamura A, Kutsumi H. The role of the Pharmaceuticals and Medical Devices Agency and healthcare professionals in post-marketing safety. *Clinical Journal of Gastroenterology*. 2014 Apr;7(2):103-7. doi.org/10.1007/s12328-014-0474-6.
- [7] Mann EA, Nandkumar S, Addy N, Demko BG, Freedman NS, Gillespie MB et al. Study design considerations for sleep-disordered breathing devices. *J Clin Sleep Med*. 2020 Mar 15;16(3):441-449. doi: 10.5664/jcsm.8226.
- [8] Lee SY, Kim JR, Kim ER, Lee JH, Lee CH, Park CW. A study on development of guideline on writing

- technical document for electrical medical devices: Bone absorptiometric X-ray System. *Journal of radiological science and technology*. 2016 Jun; 39(2):263-71. doi.org/10.17946/JRST.2016.39.2.16.
- [9] Sorenson C, Drummond M. Improving medical device regulation: the United States and Europe in perspective. *Milbank Q*. 2014 Mar;92(1):114-50. doi: 10.1111/1468-0009.12043.
- [10] Jones AD III, Mi G, Webster TJ. A Status Report on FDA Approval of Medical Devices Containing Nanostructured Materials. *Trends Biotechnol*. 2019 Feb;37(2):117-120. doi: 10.1016/j.tibtech.2018.06.003.
- [11] Jarow JP, Baxley JH. Medical devices: US medical device regulation. *Urol Oncol*. 2015 Mar;33(3):128-32. doi: 10.1016/j.urolonc.2014.10.004.
- [12] Rome BN, Kramer DB, Kesselheim AS. Approval of high-risk medical devices in the US: implications for clinical cardiology. *Curr Cardiol Rep*. 2014 Jun;16(6):489. doi: 10.1007/s11886-014-0489-0.
- [13] Jazowski SA, Winn AN. The Role of the FDA and Regulatory Approval of New Devices for Diabetes Care. *Curr Diab Rep*. 2017 Jun;17(6):40. doi: 10.1007/s11892-017-0871-6.
- [14] Marcus HJ, Payne CJ, Hughes-Hallett A, Marcus AP, Yang GZ, Darzi A et al. Regulatory approval of new medical devices: cross sectional study. *BMJ*. 2016 May 20;353:i2587. doi: 10.1136/bmj.i2587.
- [15] Rath VK, Krumholz HM, Masoudi FA, Ross JS. Characteristics of Clinical Studies Conducted Over the Total Product Life Cycle of High-Risk Therapeutic Medical Devices Receiving FDA Premarket Approval in 2010 and 2011. *JAMA*. 2015 Aug 11;314(6):604-12. doi: 10.1001/jama.2015.8761.
- [16] Fargen KM, Frei D, Fiorella D, McDougall CG, Myers PM et al. The FDA approval process for medical devices: an inherently flawed system or a valuable pathway for innovation? *J Neurointerv Surg*. 2013 Jul;5(4):269-75. doi: 10.1136/neurintsurg-2012-010400.
- [17] Hihara H, Tagaino R, Washio J, Laosuwan K, Wicaksono DP, Izumita K et al. Effectiveness and safety of a new dental plaque removal device utilizing micro mist spray for removing oral biofilm in vitro. *BMC Oral Health*. 2021 Dec;21(1):1-8. doi.org/10.1186/s12903-021-01647-4.
- [18] Zuckerman D, Brown P, Das A. Lack of publicly available scientific evidence on the safety and effectiveness of implanted medical devices. *JAMA Intern Med*. 2014 Nov;174(11):1781-7. doi: 10.1001/jamainternmed.2014.4193.
- [19] Faris O, Shuren J. An FDA viewpoint on unique considerations for medical-device clinical trials. *New England Journal of Medicine*. 2017 Apr 6;376(14):1350-7. DOI: 10.1056/NEJMra1512592.
- [20] Johnston JL, Dhruva SS, Ross JS, Rath VK. Early experience with the FDA's Breakthrough Devices program. *Nat Biotechnol*. 2020 Aug;38(8):933-938. doi:10.1038/s41587-020-0636-7.
- [21] Jokura Y, Yano K, Yamato M. Comparison of the new Japanese legislation for expedited approval of regenerative medicine products with the existing systems in the USA and European Union. *J Tissue Eng Regen Med*. 2018 Feb;12(2):e1056-e1062. doi: 10.1002/term.2428.
- [22] Rath VK, Krumholz HM, Masoudi FA, Ross JS. Characteristics of Clinical Studies Conducted Over the Total Product Life Cycle of High-Risk Therapeutic Medical Devices Receiving FDA Premarket Approval in 2010 and 2011. *JAMA*. 2015 Aug 11;314(6):604-12. doi: 10.1001/jama.2015.8761.
- [23] Zuckerman DM, Brown P, Nissen SE. Medical device recalls and the FDA approval process. *Arch Intern Med*. 2011 Jun 13;171(11):1006-11. doi: 10.1001/archinternmed.2011.30.
- [24] Fink M, Akra B. Regulatory clearance: How are outcome measurements critical? *Injury*. 2020 May;51 Suppl 2:S67-S70. doi: 10.1016/j.injury.2019.10.071.
- [25] Pane J, Francisca RDC, Verhamme KMC, Orozco M, Viroux H, Rebollo I et al. EU postmarket surveillance plans for medical devices. *Pharmacoepidemiol Drug Saf*. 2019 Sep;28(9):1155-1165. doi: 10.1002/pds.4859.
- [26] Wilkinson J, Crosbie A. A UK medical devices regulator's perspective on registries. *Biomed Tech (Berl)*. 2016 Apr 1;61(2):233-7. doi: 10.1515/bmt-2015-0142.
- [27] Howard JJ. Balancing innovation and medical device regulation: the case of modern metal-on-metal hip replacements. *Med Devices (Auckl)*. 2016 Aug 9;9:267-75. doi: 10.2147/MDER.S113067.
- [28] Beckers R, Kwade Z, Zanca F. The EU medical device regulation: Implications for artificial intelligence-based medical device software in medical physics. *Phys Med*. 2021 Mar;83:1-8. doi: 10.1016/j.ejmp.2021.02.011.
- [29] Cipriani A, Ioannidis JPA, Rothwell PM, Glasziou P, Li T, Hernandez AF et al. Generating comparative evidence on new drugs and devices after approval. *Lancet*. 2020 Mar 21;395(10228):998-1010. doi: 10.1016/S0140-6736(19)33177-0.
- [30] Wong KA, Hodgson L, Garas G, Malietzis G, Markar S, Rao C et al. How can cardiothoracic and vascular medical devices stay in the market? *Interact Cardiovasc Thorac Surg*. 2016 Dec;23(6):940-948.

- doi: 10.1093/icvts/ivw257.
- [31] Tahir H, Tahir R, McDonald-Maier K. On the security of consumer wearable devices in the Internet of Things. *PLoS One*. 2018 Apr 18;13(4):e0195487. doi: 10.1371/journal.pone.0195487.
- [32] Kramer DB, Baker M, Ransford B, Molina-Markham A, Stewart Q, Fu K et al. Security and privacy qualities of medical devices: an analysis of FDA postmarket surveillance. *PLoS One*. 2012 Jul;7(7):e40200. doi: 10.1371/journal.pone.0040200.
- [33] Galasso A, Luo H. Tort reform and innovation. *The journal of law and economics*. 2017 Aug 1;60(3):385-412. doi.org/10.1086/694337.
- [34] Greer SL, Hervey TK, Mackenbach JP, McKee M. Health law and policy in the European Union. *The Lancet*. 2013 Mar 30;381(9872):1135-44. doi.org/10.1016/S0140-6736(12)62083-2.
- [35] Green JIJ. Medical Device Regulation: Requirements for Dental Professionals Who Prescribe and Manufacture Custom-Made Devices. *Prim Dent J*. 2021 Mar;10(1):64-88. doi: 10.1177/2050168420980980.
- [36] Ikeno F, Ikeda K, Uchida T. Patient access to medical devices-what about Japan, the second largest medical device market? *Cardiovasc Interv Ther*. 2014 Jan;29(1):1-3. doi:10.1007/s12928-013-0202-z.
- [37] Chughtai AA, Khan W. Use of personal protective equipment to protect against respiratory infections in Pakistan: A systematic review. *J Infect Public Health*. 2019 Jul-Aug;12(4):522-527. doi: 10.1016/j.jiph.2019.01.064.
- [38] Food and Drug Administration, HHS. Dental devices; reclassification of blade-form endosseous dental implant. Final order. *Fed Regist*. 2014 Jun 18;79(117):34623-5.
- [39] Dental Devices. Reclassification of Electrical Salivary Stimulator System. Final order. *Federal register*. 2015 Nov;80(224):72585-6.
- [40] Food and Drug Administration, HHS. Medical Devices; Exemption From Premarket Notification; Class II Devices; Over-the-Counter Denture Repair Kit. Final order. *Fed Regist*. 2018 Mar 14;83(50):11144-5.
- [41] Stanley A. A new era for the dental industry. *BDJ In Practice*. 2020 Apr;33(4):18-9. doi.org/10.1038/s41404-020-0362-3.
- [42] Martelli N, Eskenazy D, Déan C, Pineau J, Prognon P, Chatellier G et al. New European Regulation for Medical Devices: What Is Changing? *Cardiovasc Intervent Radiol*. 2019 Sep;42(9):1272-1278. doi: 10.1007/s00270-019-02247-0.
- [43] Gibbs S, Kosten I, Veldhuizen R, Spiekstra S, Corsini E, Roggen E et al. Assessment of metal sensitizer potency with the reconstructed human epidermis IL-18 assay. *Toxicology*. 2018 Jan 15;393:62-72. doi: 10.1016/j.tox.2017.10.014.
- [44] Fraser AG, Byrne RA, Kautzner J, Butchart EG, Szymański P, Leggeri I et al. Implementing the new European Regulations on medical devices-clinical responsibilities for evidence-based practice: a report from the Regulatory Affairs Committee of the European Society of Cardiology. *Eur Heart J*. 2020 Jul 14;41(27):2589-2596. doi: 10.1093/eurheartj/ehaa382.
- [45] Liu W, Shi X, Lu Z, Wang L, Zhang K, Zhang X. Review and approval of medical devices in China: Changes and reform. *J Biomed Mater Res B Appl Biomater*. 2018 Aug;106(6):2093-2100. doi: 10.1002/jbm.b.34031.
- [46] Konishi A, Isobe S, Sato D. New Regulatory Framework for Medical Devices in Japan: Current Regulatory Considerations Regarding Clinical Studies. *J Vasc Interv Radiol*. 2018 May;29(5):657-660. doi: 10.1016/j.jvir.2017.12.022