RECOGNIZED BY:

HIGHER EDUCATION COMMISSION OF PAKISTAN

INDEXING

Crossref

Google Scholar

OPEN ACCESS

ResearchGate

Dimensions

LOCKSS

ICMJE
INTERNATIONAL COMMITTEE of MEDICAL JOURNAL EDITORS

IMEMR
INDEX MEDICIUS
FOR THE EASTERN MEDITERRANEAN REGION

DRJI
Directory of Research Journal Indexing

EuroPub
Directory of Academic and Scientific Journals

ASIAN Research Index

OCLC WorldCat®

Scilit

OPEN ARCHIVES

ASCI
Asian Science Citation Index

REVIEWER CREDITS

EZB Electronic Journals Library

Aims and Scope

Pakistan Biomedical Journal is an open access, peer-reviewed International journal that publishes in all fields of health, allied health and biomedical sciences for an internationally diverse authorship. Clinical studies, clinical trials, population studies, public health, discovery medicine, study of microbes, molecular and cellular biology, basic mechanisms of biology, genetics, cancer biology, molecular medicine, pharmacology, virology, chemical biology, immunobiology, chemical biology, physiological and pathological studies are within the scope of journal.

A highly-cited, multi disciplinary, international editorial board assures timely publication of manuscripts and reviews on latest advancements in biomedical sciences.

Types of Articles

- Research papers
- Short communications
- Review or mini-reviews
- Commentaries
- Perspectives, opinions
- Meta-analysis
- Case reports
- Case studies
- Case-control studies

Reviews on recent progress in biomedical sciences are commissioned by the editors. The purpose of the Pakistan Biomedical Journal is to publish scientific and technical research papers to bring attention of international researchers, scientists, academicians, health care professionals towards the recent advancements in biomedical sciences. The articles are collected in the form of reviews, original and clinical studies. It may serve as a global platform for scientists in relevant fields to connect and share ideas mutually. This journal is open to all the research professionals whose work fall within our scope. Submissions are welcome and may be submitted here.

submissions@pakistanbmj.com

@JournalPakistan
@Pakistanbmj

Title
The title of the paper should provide a concise statement of the contents of the paper. A good title is very important and will attract readers and facilitate retrieval by online searches, thereby helping to maximize citations. The title should include topical keywords and allude to the interesting conclusions of the paper. A title that emphasizes the main conclusions, or poses a question, has more impact than one that just describes the nature of the study.

Running Head
Running head should be added in the header along with the page numbers.

Type of Article
Research Article/ Case Report/ Review Article/ Opinion/ Short Communication/ Mini Review/ Letter to Editor

Running Title: A short version of the paper title.
Keywords: The major keywords used in the article have to be mentioned.

Authors
List here all author names Author[1], Author[2] and Author[3]
[1]Author department, University, Country
[2]Author department, University, Country
[3]Author department, University, Country

*Corresponding Author
Author name, Affiliation, Department Name, University Name, Address, City, State, Country, E-mail:

Abstract
Abstract should include a brief content of the article. It should be structured not more than 250 words. It should include following sub headings: Objective, Methods, Results, Conclusions.

Abbreviations
If there are any abbreviations in the article they have to be mentioned.

INTRODUCTION
Provide a context or background for the study (i.e., the nature of the problem and its significance). State the specific purpose or research objective of, or hypothesis tested by, the study or observation; the research objective is often more sharply focused when stated as a question. Both the main and secondary objectives should be made clear, and any pre-specified subgroup analyses should be described. Give only strictly pertinent references and do not include data or conclusions from the work being reported.

METHODS
The methods section should include only information that was available at the time the or plan of the protocol. All information gathered during the conduct of study should be included in the method section.
Study Design, Inclusion / Exclusion Criteria, Data Collection Procedure, Statistical Analysis.

RESULTS
Present your results in logical sequence in the text, tables, and illustrations, giving the main or most important findings first.

Do not repeat the data in text and in tables or illustrations; emphasize or summarize only important observations. When data are summarized in the results section, give numeric results not only as derivatives (for example, percentages) but also as the absolute numbers from which the derivatives were calculated, and specify the statistical methods used to analyze them. Table font should be 10 and caption should be above the table and below the figure.

Data should not be duplicated in both figures and tables. The maximum limit of tables and figures should not exceed more than 4. Mention the findings of the study in paragraph, while mentioning figure and table number in text in sequential order.

TABLE

Table should not be copy pasted or in picture form

DISCUSSION

Discuss your findings by comparing your results with other literature

REFERENCES

References should not be less than 20.
In text references should be in number style. For Example [1]
Follow the Pubmed Referencing style
Provide the DOI link

Example: Cook NR, Rosner BA, Hankinson SE, Colditz GA. Mammographic screening and risk factors for breast cancer. American Journal of Epidemiology. 2009 Dec; 170(11): 1422-32. doi: 10.1093/aje/kwp304.

If there are more than six authors, write *et al*. after the first six names.

CONCLUSION(S)

Conclusion should elucidate how the results communicate to the theory presented as the basis of the study and provide a concise explanation of the allegation of the findings.

ACKNOWLEDGEMENT

Provide the list of individuals who contributed in the work and grant details where applicable

Plagiarism policy

Similarity index should be less than 19 and less than 5 from individual sources.

Authorship Letter

Signed authorship letter by all authors including there current department, University, City, Country, Email.

Declaration Form

Signed declaration form submit by corresponding author.

The submission of article should include: manuscript according to journal guidelines, authorship letter, declaration form. It should be submitted to the following email id: submissions@pakistanbmj.com

EDITORIAL TEAM

VOLUME 07 ISSUE 07

Published by:
CrossLinks International Publishers
www.clip.com.pk
isni 0000000503896516

EDITORIAL BOARD

VOLUME 07 ISSUE 07

Advisory Board Members

Dr. Ahmad Azam Malik, Ph.D
Associate Professor
King Abdul Aziz University, Jeddah, Saudi Arabia

Dr. Haiba Kaul, Ph.D
Associate Professor
University of Veterinary and Animal Sciences, Lahore, Pakistan

Dr. Shah Jahan, Ph.D
Associate Professor
University of Health Sciences, Lahore, Pakistan

Dr. Maham Akhlaq, MBBS, Mphil, DipRCpath, Ph.D
Assistant Professor
University of Health Sciences, Lahore, Pakistan

International Members

Rafael Coveñas Rodríguez
Associate Professor
University of Salamanca, Spain

Prof. Dr. Tahir Jameel
MBBS, MCPS, Mphil, FCPS
Professor
King Abdulzaiz University Jeddah, Saudia Arabia

Jehan Zeb, Ph.D
Post Doc, Research Fellow
Hong Kong Science & Technology Park Hong Kong SAR China affiliated with The University of Hong Kong

Prof. Dr. Beatrice Paradiso
MD, Double Ph.D
Professor
Dolo Hospital, Venice, Italy

Dr. Diki, M.ED, Ph.D
Lecturer
University Terbuka, Indonesia

National Member

Dr. Muhammad Irfan Bashir, Ph.D
Assistant Professor
Gulab Devi Institute of Pharmacy, Lahore, Pakistan

Dr. Munir Bhinder, Ph. D
Associate Professor
University of Health Sciences, Lahore, Pakistan

Published by:
CrossLinks International Publishers
www.clip.com.pk
isni 0000000503896516

TABLE OF

CONTENTS

VOLUME 07 ISSUE 07

Published by:
CrossLinks International Publishers
www.clip.com.pk
isni 0000000503896516

DOI: https://doi.org/10.54393/pbmj.v7i07.1121

PAKISTAN BIOMEDICAL JOURNAL
https://www.pakistanbmj.com/journal/index.php/pbmj/index
ISSN (P): 2709-2798, (E): 2709-278X
Volume 7, Issue 7 (July 2024)

Hormonal Therapy and Endometrial Cancer: Latest Advancements

OPEN ACCESS

Riffat Mehboob[1,2]

[1]Cell and Developmental Biology Center, National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland, United States of America
[2]Lahore Medical Research Center, Lahore, Pakistan
riffat.pathol@gmail.com

ARTICLE INFO

How to Cite:

Mehboob, R. (2024). Hormonal Therapy and Endometrial Cancer: Latest Advancements. Pakistan BioMedical Journal, 7(07). https://doi.org/10.54393/pbmj.v7i07.1121

Endometrial cancer ranks as the sixth most common malignancy among women worldwide and fourth most common cancer of female reproductive system, with an incidence rate that has increased by 132% over the last 30 years [1]. It is uterine cancer which develops in inner lining of uterus (endometrium). Common symptoms include abnormal uterine bleeding, pelvic pain, and an enlarged uterus. The factors that have increased risk of getting endometrial cancer are obesity, diabetes, hypertension, menopause age, infertility, hormonal imbalance and polycystic ovary syndrome (PCOS). According to a report in 2023, it was projected that there would be over 66,000 new cases and more than 13,000 deaths attributed endometrial cancer in United States [2]. The high incidence and mortality rates are fueling growing concerns among women globally. The pathological mechanism involves invasion of stromal and myometrial tissues, often associated with Phosphatase and tensin homolog (PTEN) mutations, KRAS2 mutations, and microsatellite instability. Endometrial cancer has been categorized into type 1 and type 2 based on histological features.

Traditional methods for treatment of endometrial cancer (surgery, chemotherapy) are effective and essential but recent advancements in the field of endometrial oncology have raised hopes of people, particularly hormonal therapy is emerging as promising option for non-toxic treatment in type 1 (estrogen dependent) and recurrent endometrial cancer. Estrogen and progesterone work antagonistically and the endometrium, which is responsive to hormones, grows when exposed to estrogen and stops growing when exposed to progesterone during the menstrual cycle. The exposure to estrogen hormone for long time causes hormonal imbalance which increases thickness of uterus walls and provide site for cancerous cell growth. As a result, hormone therapy uses progesterone to counter the effects of estrogen and decrease tumor growth. The success of hormone therapy relies on the existence of hormone receptors such as progesterone receptors (PRs) in cancer cells. Patients with grade 1 and 2 endometrial cancer undergo standard hormonal therapy which yields high response rates such as progestin and aromatase inhibitors. Tamoxifen is considered as second line hormonal agent due to low response rate. These medications play a key role in targeting specific hormonal pathways in endometrial carcinoma treatment and management. Hormonal therapies offer a favorable safety profile to manage recurrent tumors after chemotherapy.

As the landscape of hormonal therapy for endometrial cancer evolves rapidly, the integration of traditional hormonal treatment with targeted therapies represents a significant advance. Personalized medicine—understanding the distinctive hormonal characteristics of each tumor—will shape hormonal therapy for the future. Endometrial cancer research and clinical trials hold promise for developing more effective and less invasive treatments.

REFERENCES

[1] Crosbie EJ, Kitson SJ, McAlpine JN, Mukhopadhyay A, Powell ME, Singh N. Endometrial cancer. The Lancet. 2022 Apr; 399(10333): 1412-28.

[2] Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics, 2023. CA: A Cancer Journal for Clinicians. 2023 Jan; 73(1): 17-48. doi: 10.3322/caac.21763.

DOI: https://doi.org/10.54393/pbmj.v7i07.1080

PAKISTAN BIOMEDICAL JOURNAL
https://www.pakistanbmj.com/journal/index.php/pbmj/index
ISSN (P): 2709-2798, (E): 2709-278X
Volume 7, Issue 7 (July 2024)

Review Article

OPEN ACCESS

The Scope and Challenges of Medical Technology Allied Health Professionals in Pakistan

Khadija Shah[1*], Fahad Ahmed[1], Nazish Nizar Ali[1] and Atiya Rahman Rohilla[1]

[1]Department of Allied Health Sciences, Indus College of Medical Technology and Allied Health, Indus Hospital and Health Network, Karachi, Pakistan

ARTICLE INFO

Keywords:
Allied Health Professionals, Healthcare Workforce, Professional Recognition

How to Cite:
Shah, K., Ahmed, F., Nizar Ali, N., & Rohilla, A. R. (2024). The Scope and Challenges of Medical Technology Allied Health Professionals in Pakistan: Challenges of Allied Health Professionals. Pakistan BioMedical Journal, 7(07). https://doi.org/10.54393/pbmj.v7i07.1080

***Corresponding Author:**
Khadija Shah
Department of Allied Health Sciences, Indus College of Medical Technology and Allied Health, Indus Hospital and Health Network, Karachi, Pakistan
khadijashah17feb18@gmail.com

Received Date: 25th April, 2024
Acceptance Date: 26th July, 2024
Published Date: 31st July, 2024

ABSTRACT

WHO and the US Department of Health and Human Services both define AHPs as healthcare professionals with specific connections to the art and science of healthcare, and expertise in therapeutic, diagnostic, and preventive interventions, showing leadership in clinical and technical proficiency. AHPs include dental hygienists, diagnostic medical sonographers, dieticians, medical technologists, occupational therapists, physical therapists, and speech-language pathologists. A growing number of AHPs in Pakistan are becoming stronger and more well-known in the healthcare system. The growing population and increased demand for health care professionals. In this modern era, where the country faces a brain drain of other known professions, increasing the demand for skilled AHPs who play a vital role in patient care, diagnosis, treatment, and rehabilitation. The increasing scope of AHPs is highlighted by factors such as public awareness of preventive and rehabilitative healthcare, government initiatives supporting workforce development, and the growth of academic institutions providing AH sciences programs. On March 5, 2022, the Pakistan AHPC was established to strengthen the unified professional body on a single platform. AHPs in Pakistan face challenges such as gaining formal recognition, enhancing education by implementing master's programs in all specialties, strategizing workforce planning, and boosting advocacy to empower the council in granting global acknowledgment to registered professionals. The AHPC is in its initial stages and must develop formal job descriptions for technicians and technologists, as well as establish pay scale recognition.

INTRODUCTION

The health workforce, which includes medical, nursing, and allied health professionals, is the backbone of any healthcare system. Investments and advancement in healthcare sector lead to reduced disease burden, increased productivity, and positive economic growth. Pakistan is generally facing a dire shortage of skilled healthcare workers [1-3]. Pakistan is one of several nations suffering from the growing disparity between patient care and the healthcare staff, which has become a global concern [4, 5]. According to The Pakistan Medical Commission (PMC) 249,371 registered physicians, including specialists, and 128,744 nurses, including lady health visitors (LHVs), community-based midwives (CMWs), midwives (MWs), and family welfare workers (FWWs), to cater to the nation's population of over 232 million people [4]. As per the 2021 Universal Health Coverage-Monitoring Report-Pakistan shows the healthcare worker ratio on population. The results indicate a doctor-to-population ratio of 1.09 per 1,000 and a nurse-to-population ratio of 0.59 per 1,000 in Pakistan [4]. According to the Pakistan Economic Survey 2020–2021. The current nurse-patient ratio in Pakistani hospital general wards is 1:40, but the Pakistan Nursing Council recommended a ratio of 3:10 [1, 6]. The country faces a brain drain of other known professions that work as a foundation of any hospital this need for skilled health professionals highlighted the skilled personnel who work along with medical and nursing parallelly this necessity lamplight the upbringing profession of allied health professional [1]. Although the scope of allied health has been in the limelight since 1966

DOI: https://doi.org/10.54393/pbmj.v7i07.1080

this profession is still underappreciated as compared to other professions like nursing. During the discussions leading up to the 1967 passage of the Allied Health Professions Personnel Training Act, the term "allied health sciences" gained popularity [5-7]. The terms used may differ according to the nation and the situation. Still, typically it is seen as separate from nursing, medicine, and pharmacy [8-10]. According to The Center for Health Professions, California, Allied Health Professionals makeup 60% of the entire health workforce [11]. Medical technology, commonly referred to as allied health professionals in Pakistan, is essential to the country's overall healthcare system [12]. This line of work deals with the technical aspects of medicine and surgery, encompassing their rewards and problems [13, 14]. Effective healthcare services are essential to a successful society's foundation. Allied health assistants are an emerging group in allied health practice with the potential to improve the quality of care and safety of patients [15]. The scope of Allied health professionals is significantly elaborated as they play an important role in the diagnosis, treatment, prevention, and rehabilitation of illness or injury. Without a doubt, allied health sciences form the foundation of any nation's healthcare system [16, 17].

The aim of this article was to discuss and elaborate role and challenges of allied health professionals in Pakistan. Allied health professionals or "AHP" means a Person who provides diagnostic, therapeutic, Preventive, curative, or rehabilitative services in health care, in a prescribed manner and has undergone a prescribed course of training in a recognized institution and is registered as an Allied Health Professional by the body formed for the purpose. (Allied Health Professional Council Act, 2022). Classification and affiliated bodies of AHPs in Pakistan. Allied Health professionals are typically divided into two categories as shown in table 1: Technicians/Diploma (assistants)and Therapists/ technologists(Degree holder).

Table 1: Classification and Affiliated Bodies of AHPs in Pakistan

S.No.	Disciplines	Years of education	Role Domain	Affiliated body
1	Technicians	1-year certificate	Assistant	SMF, PMF, BMF and KMF
2	Diploma	2-year certificate	Assistant	
3	Technologists /Therapists	4-year degree	Supervisors/ managers	Provisional Universities

Abbreviations: SMF (Sindh medical faculty), PMF (Punjab medical faculty), BMF (Baluchistan medical faculty), KMF (Khyber Pakhtunkhwa medical faculty).

Table 2 showed specific roles performed by Allied health professionals [18-22].

Table 2: Specific Roles Perform by AHP

S.No.	Areas	Specific Roles
1	Diagnostic	Cardiovascular technologists/technicians, Clinical laboratory technologists/technicians, Radiological technologists/technicians, Ultrasound technicians and X-ray technicians
2	Medical services	Dental technologists/technicians, Emergency medical technicians, ICU technicians, Anesthesia technologists /technicians, Operation Theater technologists/ technicians, Pead's oncology Technicians, and Health technicians
3	Non-direct care	CSSD technicians, medical appliance technicians, and Pharmacy Technicians
4	Rehabilitative	Occupational therapists, Speech-language therapists, Respiratory Therapists, and Physiotherapy technicians

As Allied health workers bridge gaps in service delivery and address patients' multiple needs across diverse settings, they play a crucial role in providing comprehensive and holistic treatment in Pakistan, where access to healthcare services is still a chronic difficulty [23]. One cannot emphasize the importance of allied health professionals in Pakistan, especially given the country's rapidly changing healthcare system and growing population [18]. Current challenges faced by health professionals were mentioned in figure1.

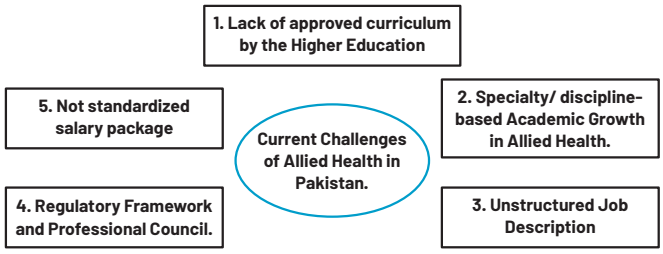

Figure 1: Current Challenges of Allied Health in Pakistan

Current Challenges of Allied Health in Pakistan: The Allied Health Medical Technology programs, particularly Bachelor of Science (BS) in Medical Technology, face several pressing challenges in Pakistan. These challenges contribute to inconsistencies in curriculum, lack of standardized job descriptions, and insufficient regulatory frameworks [24-26]. Lack of approved curriculum by the Higher Education: Unlike other healthcare programs such as Bachelor of Science in Nursing, Doctor of Physical Therapy (DPT), and Pharmacy, which have approved curricula by the Higher Education Commission (HEC), BS in Medical Technology programs lack this standardization. Each private or government universities have its own syllabus outline leading to disparities in the quality and content of education provided to students across different institutions. Academic Career Growth in Allied health: In Pakistan, there is limited academic career growth in all allied health profession specialties except in the clinical laboratory sciences. Pakistan offers master's and PhD programs in clinical laboratory science. Unstructured Job Description: The Allied health personnel face a significant challenge in the absence of a clear standardized job description for graduates/Therapists, diplomas, and technicians. Unlike professions regulated by established councils such as the Pakistan Medical Council and the Pakistan Nursing Council. workforce effectively [25]. Regulatory Framework and Professional Council: While

DOI: https://doi.org/10.54393/pbmj.v7i07.1080

efforts have been made to address some of these challenges, such as the establishment of the Allied Health Professions Council, the regulatory framework for medical technologists is still in the process of development and implementation. The Allied Health Professions Council, although recently created, is still undergoing registration and documentation processes [25]. Not standardized salary package: As compared to Registered nurses' standardized salary package in both private and government bodies. AHPs are still facing the underrated salary package.table 3 showed current allied health scenario in Pakistan. The allied health sector in Pakistan encompasses a diverse range of professions essential to the delivery of comprehensive healthcare services Despite the critical role these professionals play in enhancing patient care and supporting the healthcare system, the allied health sector in Pakistan faces a complex landscape shaped by various factors. Rapidly evolving healthcare needs, limited resources, and infrastructural challenges contribute to a dynamic environment where opportunities and constraints coexist. A small effort was made to do a SWOT analysis of the current scenario of Allied health professionals in Pakistan. This section aims to provide an in-depth examination of the sector's current state, including its key strengths and weaknesses, as well as potential opportunities for growth and external threats. By analyzing these factors through a SWOT framework, we seek to offer a strategic perspective on how the allied health sector can navigate its challenges and leverage its strengths to improve healthcare outcomes in Pakistan.

Table 3: SWOT Analysis for The Current Allied Health Scenario in Pakistan

Strengths	Weaknesses	Opportunities	Threats
1. Allied health professionals cover various domains within the healthcare system. 2. The health care system provides a Safe and healthy working environment for allied health workers. 3. Allied health professionals play an integral role in supporting the health care system. 4. Job availability	1. Lacking recognition and public awareness about the allied health profession. 2. Limited chances for advancing in career and opportunities for professional growth. 3. Lack of standardized regulatory framework for licensing and accreditation of allied health professionals. 4. Limited research and evidence-based practice initiatives within the allied health sector. 5. Overworked and stressful. 6. Annual increment too less	1. Growing demand for healthcare services due to population growth and aging demographics. 2. New opportunities for jobs due to the high demand for technical skill professionals. 3. High demand in the international healthcare market.	1. High turnover. 2. Salary structure not segregated between qualified and non-qualified staff. 3 No structured professional development progress. 4. Nonfunctional licensing system. 5. Lack of standardized education.

Global Context of AHP: Around the world, there is growing proof healthcare can only get better if we focus on training and supporting healthcare workers. Over the past ten years, technology has advanced a lot, but there hasn't been enough consistency in the skills needed for these jobs [26, 27]. The classification of health professionals varies from one country to another, leading to confusion about the roles of paramedical, paraprofessional, and allied health service providers. For instance, the title given to someone who diagnoses and treats speech disorders differs among countries. In Australia, they're referred to as speech pathologists, while in the United States, they're called speech-language pathologists [28]. In the United Kingdom, they're known as speech and language therapists [29]. The definition and understanding of paramedical professionals can vary within and between countries. According to the International Standard Classification of Occupations (ISCO), these professionals work independently or with limited supervision. Paramedics are the emergency medical technicians (EMTs) who respond to medical emergencies outside hospitals in the United States, they're categorized based on their training level as compared with France, where there is a central control function for the regulation of medical emergency services [30, 31]. Nearly more than 90,000 university-trained, autonomous AHPs play a significant role in managing the Australian health care system. Besides doctors and nurses [28]. In England, there are over 84,000 Allied Health Professionals (AHPs) working in different roles in the National Health Service (NHS). AHPs work in hospitals, clinics, and communities. They do important jobs like diagnosing and treating illnesses, from preventing problems to helping patients recover [32-36].

CONCLUSIONS

The Allied Health Council of Pakistan must take all stakeholders including educational institutions, regulatory bodies, and the higher education commission on board to develop a standardized curriculum and recruitment policy. The Allied Health Council of Pakistan must take initiative in the professional licensing to accredit the profession in the international market.

DOI: https://doi.org/10.54393/pbmj.v7i07.1080

Authors Contribution

Conceptualization: KS
Methodology: FA
Formal analysis: NNA
Writing, review and editing: ARR, NNA, FA, KS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Hassan S. Nursing Shortage in Pakistan: Nursing Shortage in Pakistan. NURSEARCHER (Journal of Nursing & Midwifery Sciences). 2023 Jun; 24-5. doi: 10.54393/nrs.v3i01.39.

[2] Smiley RA, Ruttinger C, Oliveira CM, Hudson LR, Allgeyer R, Reneau KA et al. The 2020 national nursing workforce survey. Journal of Nursing Regulation. 2021 Apr; 12(1): S1-96. doi: 10.1016/S21558256(21)00027-2.

[3] a Sreedharan JK, Subbarayalu AV, AlRabeeah SM, Karthika M, Shevade M, Al Nasser MA *et al.* Quality assurance in allied healthcare education narrative review. Canadian Journal of Respiratory Therapy: CJRT= Revue Canadienne de La Thérapie Respiratoire: RCTR. 2022 Jul; 58: 103-110. doi: 10.29390/cjrt-2022-009.

[4] Khan R. Causes and Consequences of the Shortage of Physicians in Sindh, Pakistan: A Local Perspective. The Journal of the Pakistan Medical Association. 2023 Aug; 73(8): 1693-9. doi: 10.47391/JPMA.7593.

[5] Karamat J, Shurong T, Ahmad N, Afridi S, Khan S, Mahmood K. Promoting healthcare sustainability in developing countries: Analysis of knowledge management drivers in public and private hospitals of Pakistan. International Journal of Environmental Research and Public Health. 2019 Feb; 16(3): 508. doi: 10.3390/ijerph16030508.

[6] Firdos UZ, Asghar RS, Ashraf S. Managing Nursing brain drain from Pakistan. European Academic Research. 2020 Jan; 7(10): 5231-41.

[7] Lapchmanan LM, Hussin DA, Mahat NA, Ng AH, Bani NH, Hisham S *et al.* Developing criteria for a profession to be considered as profession of allied health in Malaysia: a qualitative study from the Malaysian perspective. BioMed Central Health Services Research. 2024 Feb; 24(1): 165. doi: 10.1186/s12913-024-10569-0.

[8] Snowdon DA, Sargent M, Williams CM, Maloney S, Caspers K, Taylor NF. Effective clinical supervision of allied health professionals: a mixed methods study. BioMed Central Health Services Research. 2020 Dec; 20: 1-1. doi: 10.1186/s12913-019-4873-8.

[9] Mason J. Review of Australian Government Health Workforce Programs. Canberra: Australian Government Department of Health; 2013.

[10] Turnbull C, Grimmer-Somers K, Kumar S, May E, Law D, Ashworth E. Allied, scientific and complementary health professionals: a new model for Australian allied health. Australian Health Review. 2009 Feb; 33(1): 27-37. doi: 10.1071/AH090027.

[11] McConville S, Bohn S, Beck L. Training Allied Workers. Public Policy Institute of California; 2017.

[12] Saqib A, Atif M, Ikram R, Riaz F, Abubakar M, Scahill S. Factors affecting patients' knowledge about dispensed medicines: A Qualitative study of healthcare professionals and patients in Pakistan. PLOS One. 2018 Jun; 13(6): e0197482. doi: 10.1371/journal.pone.0197482.

[13] Issenberg SB, McGaghie WC, Hart IR, Mayer JW, Felner JM, Petrusa ER et al. Simulation technology for health care professional skills training and assessment. Journal of the American Medical Association. 1999 Sep; 282(9): 861-6. doi: 10.1001/jama.282.9.861.

[14] Kneebone R. Simulation in surgical training: educational issues and practical implications. Medical Education. 2003 Mar; 37(3): 267-77. doi: 10.1046/j.1365-2923.2003.01440.x.

[15] Lizarondo L, Kumar S, Hyde L, Skidmore D. Allied health assistants and what they do: a systematic review of the literature. Journal of Multidisciplinary Healthcare. 2010 Aug; 143-53. doi: 10.2147/JMDH.S12106.

[16] Hay J, LaBree L, Luo R, Clark F, Carlson M, Mandel D *et al.* Cost-effectiveness of preventive occupational therapy for independent-living older adults. Journal of the American Geriatrics Society. 2002 Aug; 50(8): 1381-8. doi: 10.1046/j.1532-5415.2002.50359.x.

[17] Keane S, Lincoln M, Smith T. Retention of allied health professionals in rural New South Wales: a thematic analysis of focus group discussions. BioMed Central Health Services Research. 2012 Dec; 12: 1-1. doi: 10.1186/1472-6963-12-175.

[18] Penman M, Raymond J, Kumar A, Liang RY, Sundar K, Thomas Y. Allied health professions accreditation standards for work integrated learning: A document analysis. International Journal of Environmental Research and Public Health. 2023 Jul; 20(15): 6478. doi: 10.3390/ijerph20156478.

DOI: https://doi.org/10.54393/pbmj.v7i07.1080

[19] Meo SA, Eldawlatly AA, Sultan T. Impact of unstable environment on the brain drain of highly skilled professionals, healthcare workers, researchers, and research productivity in Pakistan. Saudi Journal of Anaesthesia. 2024 Jan; 18(1): 48-54. doi: 10.4103/sja.sja_549_23.

[20] Grimmer K and Kumar S. Allied health task-related evidence. Journal of Social Work Research and Evaluation. 2005 Oct; 6(2): 143.

[21] Alhurishi SA, Aljuraiban GS, Alshaikh FA, Almutairi MM, Almutairi KM. Predictors of students' academic achievements in allied health professions at King Saud University: a retrospective cohort study. BioMed Central Medical Education. 2021 Dec; 21: 1-7. doi: 10.1186/s12909-021-02525-x.

[22] Rawekar A, Gotarkar S, Patond S, Dakhode S. Challenges of Allied Healthcare Professionals in India—Establishing the Council is Need of the Hour. Indian Journal of Forensic Medicine & Toxicology. 2020 Oct; 14(4). doi: 10.37506/ijfmt.v14i4.11485.

[23] McPherson K, Kersten P, George S, Lattimer V, Breton A, Ellis B *et al.* A systematic review of evidence about extended roles for allied health professionals. Journal of Health Services Research & Policy. 2006 Oct; 11(4): 240-7. doi: 10.1258/135581906778476544.

[24] Sequeira U, Faculty R, Nayar S. Development in Medical Education: International Perspectives. New York: Nova Science Publishers; 2019.

[25] Rajani A and Khan MH. Career and Service Structure of Allied Health Science in Pakistan, a Perspective in Question. PJR (Polish Journal of Radiology). 2016 Jul; 18(3).

[26] Gaur V. An overview of redefining paradigm: India's allied health professional. International Journal of Biochemistry Research. 2018 Jul; 1(1): 20-34.

[27] Seaton J, Jones A, Johnston C, Francis K. Allied health professionals' perceptions of inter-professional collaboration in primary health care: an integrative review. Journal of Interprofessional Care. 2021 Mar; 35(2): 217-28. doi: 10.1080/13561820.2020.1732311.

[28] National Academies of Sciences, Division of Behavioral, Social Sciences, Medicine Division, Board on Behavioral, Sensory Sciences, Board on Health Sciences Policy, Committee on the Health, Medical Dimensions of Social Isolation, Loneliness in Older Adults. Social isolation and loneliness in older adults: Opportunities for the health care system. National Academies Press; 2020 Jun 14.

[29] McGee P and Cole D. Advanced practice in allied health professions. Advanced practice in nursing and the allied health professionals. 3rd ed. Oxford: Wiley-Blackwell. 2009 Jun: 29-42.

[30] Giroud M. SAMU-System of Emergency Medical Assistance in France. Samu De France, France. 2016.

[31] Allana A. The Role of Paramedics in Integrated Care (Master's thesis). University of Toronto (Canada); 2019.

[32] McLean S, Charlesworth L, May S, Pollard N. Healthcare students' perceptions about their role, confidence and competence to deliver brief public health interventions and advice. BioMed Central Medical Education. 2018 Dec; 18: 1-9. doi: 10.1186/s12909-018-1224-0.

[33] Comer C, Collings R, McCracken A, Payne C, Moore A. Allied Health Professionals' Perceptions of Research in the United Kingdom National Health Service: a survey of research capacity and culture. BioMed Central Health Services Research. 2022 Aug; 22(1): 1094. doi: 10.1186/s12913-022-08465-6.

[34] Singh V, Pollard K, Okasheh R, Percival J, Cramp F. Understanding the role of allied health professional support workers with exercise qualifications in the delivery of the NHS Long Term Plan within allied health professional services in England. British Medical Journal Open Sport & Exercise Medicine. 2023 Aug; 9(3): e001625. doi: 10.1136/bmjsem-2023-001625.

[35] Coombs C, Arnold J, Loan-Clarke J, Bosley S, Martin C. Allied health professionals' intention to work for the National health service: a study of stayers, leavers and returners. Health Services Management Research. 2010 May; 23(2): 47-53. doi: 10.1258/hsmr.2009.009019.

[36] DeLuca MA, Kurth AE, Hagopian A. Investing strategically in the global health workforce. New York University College of Nursing; 2013.

DOI: https://doi.org/10.54393/pbmj.v7i07.1104

PAKISTAN BIOMEDICAL JOURNAL
https://www.pakistanbmj.com/journal/index.php/pbmj/index
ISSN (P): 2709-2798, (E): 2709-278X
Volume 7, Issue 7 (July 2024)

Review Article

OPEN ACCESS

Prevalence and Transmission Factors of Shiga Toxin 0157:H7 in Pakistan; A Review

Fiza Rafi[1], Hassan Raza[2], Bushra Nisar Khan[3*], Sarfraz Kiani[2], Shaheer Azhar[4], Tatheer Zahra[5] and Muhammad Mehmood Imran[6]

[1]Department of Biological Sciences, Superior University, Lahore, Pakistan
[2] Upscaling Green Program, Ministry of Climate Change, Islamabad, Pakistan
[3]Institute of Zoology, University of the Punjab, Lahore, Pakistan
[4]Sheikh Zayed Hospital, Lahore, Pakistan
[5]Walsall Manor Hospital, United Kingdom
[6]Service Hospital, Lahore, Pakistan

ARTICLE INFO

Keywords:
Escherichia. coli, Shiga Toxin 0157:H7, Gut Microbiome, Hemolytic Uremic Syndrome (HUS), Antibiotics

How to Cite:
Rafi, F., Raza, H., Khan, B. N., Kiani, S., Azhar, S., Zahra, T., & Imran, M. M. (2024). Prevalence and Transmission Factors of Shiga Toxin 0157:H7 in Pakistan; A Review: Prevalence and Transmission Factors of Shiga Toxin 0157:H7. Pakistan BioMedical Journal, 7(07). https://doi.org/10.54393/pbmj.v7i07.1104

***Corresponding Author:**
Bushra Nisar Khan
Institute of Zoology, University of the Punjab, Lahore, Pakistan
bushra.zool@gmail.com

Received Date: 11th June, 2024
Acceptance Date: 26th July, 2024
Published Date: 31st July, 2024

ABSTRACT

Shiga toxin-producing *E. coli* is a definitive strain of the very commensal microbe *Escherichia coli*. It is a resident of the vertebrate gut with hundreds of microbial colonies that comprise the versatile gut microbiome. Stx is a toxin, which is a protein in nature that has evolved in such a way that it can specifically target a host cell and deliver a payload inside the target cell's cytosol. These pathogens can trigger complications such as thrombotic microangiopathy and acute kidney injury. It is transmitted by food consumed in raw form (salads, milk, and curd), floods, contaminated ponds, and petting farms. Ruminants, floods, zoo fauna, and untreated sewage water were found to be the primary sources of STEC reservoirs nationally. Alarmingly, there is a high prevalence of neonatal diarrhea in Pakistan. Antibiotics are devoured in STEC-caused infections, especially. Diarrhea, as they aggravate the toxin production. Plant extracts and chemical purification methods have shown potential for shiga toxins reduction. Application of biosafety measurements can significantly reduce the chances of infection in developing countries, including Pakistan.

INTRODUCTION

Shiga-toxin-producing E. coli is the definitive strain of a very commensal microbe, Escherichia coli. As a resident of a vertebrate gut, it makes hundreds of microbial colonies that comprise the versatile gut microbiome. Kiyoshi Shiga became the name bearer of this bacterial strain in 1898 when he described S. dysenteriae, which produced Shiga toxins [1]. Later, isolation from the kidney cells of African monkeys also designated it as Vero-toxin E. coli. Over the years, the impact of gut microbes on dietary digestion, mediation of infection, and even modifying behaviour and cognition has been well proven and undeniable [2-4]. The fitness, health, and ecology of an organism are impacted by the vertebrate gut microbiome because these microbes provide a large physiological and pathophysiological contribution [4, 5]. Escherichia. coli is the widespread aerobe of the mammalian intestine that is present in soil, food, animal, and human manure [5, 6]. Despite being a part of any mammalian gastrointestinal tract's healthy microbiota [7] few strains develop virulence after attaining new genetic information. These strains are broadly classified as extra-intestinal (ExPEC) and intestinal pathogenic E. coli (InPEC). InPEC is further classified into

DOI: https://doi.org/10.54393/pbmj.v7i07.1104

individual strains as adherent-invasive E. coli (AIEC), diffuse adherent E. coli (DAEC), enteroaggregative E. coli (EAEC), enteroinvasive E. coli (EIEC), enteropathogenic E. coli (EPEC), and Shiga toxin-producing E. coli (STEC) [7, 8]. The unique capacity of some strains of bacteria to release toxins can lead to infections and serious illnesses, including mortality in humans. Globally, these pathogenic strains are the primary culprits of infectious mortality in hospitalised patients. In humans, a large number of microbial pathogens are transmitted via food products, known as foodborne pathogens (FBP) [9]. Stx [10,11] toxin is a key virulent factor, which is a protein in nature. It has evolved in such a way that it can specifically target a host cell and deliver a payload inside the target cell's cytosol [12]. Stx family came under the medical spotlight in 1983 because of two documented reports presented at almost the same time [3]. The most commonly studied STEC serotype is E. coli 0157:H7. This predominance is partly related to its inability to ferment sorbitol on agar plates [3]. Both shiga toxin 1 and 2 consist of two subunits: the single A plus the disease-causing B subunit, which, after passing from the Golgi apparatus and endoplasmic reticulum, inhibits protein synthesis. The degree of expression of both shiga toxin 1 and 2 determines the pathogenicity [1]. Typically, a lambdoid bacterium possesses such genes. Critically listed infectious foodborne pathogens include STEC [2]. It can be the cause of severe human illnesses that include simple diarrhoea, hemorrhagic diarrhoea, bloody diarrhoea (BD) (5–15% of which leads to the life-threatening HUS), and haemolytic uremic syndrome [13].

Hosts Species

Complex pathways of transmission are built because of the very diverse species of reservoirs and spillover hosts. Host organisms can be categorized as reservoir hosts, who are essential for maintaining pathogens in the natural environment; spillover hosts, which transmit infection to other species of interest from reservoirs; and dead-end hosts. Cattle and livestock are primary reservoirs hosts. Birds, Swine and dogs constitute spillover host while Fish and shellfish act as dead-end hosts for the shiga toxin producing Escherichia coli (STEC) in animals [14]. STEC has been characterised by wild and captive species of ruminants, including yaks, moose, antelope, and llamas. Direct transmission to humans is also reported at petting zoos, along with indirect transmission via faecal droplets in agriculture fields, water sources, and on meat [12]. E. coli reservoirs in white-tailed deer have been reported using 16S r DNA pyrosequencing [15] in the intestinal tract of domestic cows [6] and in apparently healthy captive Nilgiri Langur and colonies of laboratory Rhesus macaques [16].

Food Borne Factors

Pakistan has a voluminous consumption rate of suspected foods, including dairy products (curds, milk, and cheese), minced meat, fresh juices, vegetables, and nowadays poultry meat. Raw meat nurtures important pathogenic microbes [17], chicken in particular. Water contaminated with faeces, raw manure, or fertilizers used for washing vegetables and fruits has been a trigger for pandemics. Studies summarizing contamination methods and prevalence rates are presented here (Table 1).

Table 1: Prevalence Rate of STEC in Different Foods in Pakistan

Food Source	City	Pathotype/ Serotype	Prevalence Rate (%)	Year	Reference
Milk	Peshawar	0157:H7	8.75	2009	[18]
	Lahore	STEC	01	2016	[19]
	Khyber Pakhtunkhwa (Kpk)	STEC	05	2024	[20]
	Lahore	0157:H7	50	2013	[21]
Meat (Cattle & Goat)	Quetta	0157:H7	12	2018	[22]
	Quetta	0157:H7	10	2018	[23]
	Islamabad & Rawalpindi	0157:H7	1.33	2021	[24]
	Islamabad & Rawalpindi	STEC	43.5	2020	[25]
Chicken Meat	Northern Punjab	0157:H7	18	2023	[26]
	Southern Punjab	STEC	2.7	2021	[27]
	Lahore	0157:H7	30	2017	[28]
Sugarcane Plum, Peach & Lemonade Juice	Lahore	0157:H7	13	2014	[29]
			41		
			53		
			50		
Salads	South KPK	STEC	05	2015	[30]
Apple & Tomatoes	Lahore	STEC	17	2022	[5]
			26		

* Where rate was not present, it was calculated from sample size by using this formula. No of infected samples/No of total samples *100. Where particular serotype was not found, pathotype is mentioned.

The other major pathways associated with non-food transfer include swimming in contaminated ponds, lakes, or pools, municipal water supply, stools [31, 32] and petting farms. As of now, direct transmission via human to human is low [6]. Heavy floods all over the country caused by seasonal rains are also major sources of contamination. In the 2011–2012 floods, 200 samples were obtained to examine the presence of pathogenic E. coli. This research concluded that one-third of the total 200 samples were infected with Escherichia coli pathotypes. Fifty percent of them were enterotoxigenic strains (ETEC). There were seventy-two percent enteropathogenic strains (EPEC) and eleven percent Shiga toxin isolates carrying STX1 and STX2 genes [33]. Summer and fall are peak times for STEC infection [1], and rural areas are more at risk than urban areas [3]. In Rawalpindi and Islamabad zoos, an experimental study on 110 faecal samples of 24 species to estimate the prevalence of STEC in zoo animals reported the presence of stx1, stx2, eae, and ehxA virulence genes (with 6 different combinations) in 15 samples (2-black buck, 1-chinkara deer, 4-hog deer, 1-mouflon sheep, 4-spotted

DOI: https://doi.org/10.54393/pbmj.v7i07.1104

deer, 1-baboon monkey, 1-ostrich, and 1-tiger). The techniques used in this experiment included multiplex PCR. It indicated the zoo animals as carriers and possible causes of infection for other animals as well as humans [4]. Sewage water was investigated in 2019 for E. coli from sixteen different locations in Lahore. It provided comprehensive results with the presence of 49 serotypes of E. coli, including E35, E63, and E101, through 16S rRNA gene sequencing. Antibiotic sensitivity, biofilm formation, and shiga toxin genes (stx1, stx2, stx2c, and stx2d) were also evaluated. However, shiga toxin genes weren't detected using PCR and gel electrophoresis [34].

Clinical Infections

Multiple allelic genotype variants of stx1 and stx2 have been associated with different human diseases. Each variant is grouped on the basis of the sequence of amino acids in the Stx. Subtypes of Stx1 are Stx1a, Stx1d, and Stx1e, and subtypes of Stx2 are Stx2a to Stx21. Haemolytic uremic syndrome is caused by both Stx1 and Stx2. During bacterial lysis, Stx is released from the bacterium in the intestine [5]. STEC has two main characteristics: a pathogenicity locus with chromosomal origins that is responsible for encoding "attaching effect" producing proteins and Shiga toxins encoded by bacteriophage. These "attaching effect" proteins contain Intimin which adheres bacterium to epithelial layer of microvilli and type 3 secretion system. STEC passes through gastric fluid uninterrupted and initiate intimin & T3 System expression. Their attachment in intestinal tract results in diarrhea [9].

Haemolytic Uremic Syndrome

Symptoms of STEC-induced HUS in children include fever, abdominal pain, early illness, vomiting, and diarrhoea, followed by HUS development after a few days. Other symptoms involve bloody diarrhoea, CNS involvement, severe inflammatory colitis, cardiac dysfunction, glucose intolerance, hepatomegaly, loss of the microvilli, and leucocytosis. These disease-causing organisms can trigger a thrombotic microangiopathy called TMA, non-immune hemolytic anaemia, and azotemia. TMA is further classified as primary and secondary TMA. Primary TMA in atypical HUS presents an underlying regulatory defect in the complement system [1]. It has a high incidence in young children worldwide, with an annual prevalence of about 2–3 per 100,000 people [6]. HUS is a complex disorder that results in further organ damage. It has a major impact on renal functions. Many studies have related acute renal failure or acute kidney injury to hemolytic uremic syndrome in Pakistan. A study of 116 patients with pregnancy complications involving HUS in Sindh revealed 7% positivity. 14% developed in the first trimester, while 86% developed in the later trimester of pregnancy [35]. Children have also been shown to be a vulnerable group for HUS. In a 33-patient pediatric ward study, 3% were positive for HUS. Further analysis of their stools revealed pathogenic *E. coli* positivity [36]. Another study confirmed 10.8% HUS positivity in 74 pediatric cases that caused acute kidney injury [37]. Kidney failures have been reported in pregnancy complications and pediatric units in Pakistan, which are also linked to HUS (Table 2). A strain of E. coli, O157:H7, exhibits three genetic lineages (I, II, and I/II), further separated into nine different clades. Most of the pathogenic strains belong to clades 2, 3, 7, and 8. These clades differ from each other on account of the infections they cause and the distribution and abundance of shiga toxin genes. HUS-infected patients have higher chances of clade 8 strains, as their frequency has increased in the last half decade. Young patients under 18 years old were found to be associated with the stx2a and c genotypes of clade 8 strains [38].

Diarrhea

Around four decades ago, *E. coli* 0157 was acknowledged as a source of bloody diarrhea. Bloody diarrhea is caused by STEC in America and Europe, whereas S. dysentery type 1-induced shiga toxins are the main pathogenic agent in Southern Africa and Asia [1]. All around the world, Pakistan is considered to be in 26th place in the under-five death chart, with a whooping rate of 86 out of 1000 child births, making it one of the countries with 50% of mortality caused by diarrhoea or pneumonia. *Escherichia coli* has also been responsible for meningitis and urinary tract infections (UTIs) [18]. A study in Faisalabad, Pakistan, showed how important STEC prevalence is. They took 200 stool samples from children and used them to isolate and characterise STEC. They focused on genes eae, hly, and stx1 and 2, which stand for intimin, enterohemolysin, and Shiga toxin 1 and 2. The PCR results revealed 11% stx, 6.5% hly, and 8% eae positive samples, with only three samples positive for the 0157 serotype [25]. According to a research paper, the prevalence of neonatal diarrhoea in Pakistan is at its maximum in Gilgit Baltistan, with Punjab, AJK, Sindh, Baluchistan, FATA, and KP in descending order [39]. In experimental research on 37 *E. coli* isolates obtained from various laboratories in Karachi, 16 strains were found to be positive for different toxin genes. The results showed the maximum prevalence of the stx1 gene in 10 isolates, two of which were also positive for the stx2S gene [40]. In order to find the *E. coli* 0157 serotype, the latex agglutination test was used on 52 strains from the IMAM Clinic in Karachi's culture collection. Twenty samples tested positive for the 0157 strain of *E. coli* [22] (Table 2).

Table 2: Prevalence and Suspected Pathway of STEC Disease in Pakistan

Disease	No. of cases	Suspected Pathway	Isolated Agent/Genes	Prevalence (%)	Ref
HUS	33	Stools contamination	STEC and non-STEC	3	[34]
	74	Acute renal failure	STEC and non-STEC	10.8	[36]

DOI: https://doi.org/10.54393/pbmj.v7i07.1104

Diarrhea	200	Stools contamination	Stx	11	[41]
	52	Stools contamination	0157	38.15	[38]

* Where rate was not present, it was calculated from sample size by using this formula. No of infected samples/No of total samples *100

Anti-Microbial Resistance

Cattle, poultry, and humans contain widespread E. coli, making them the best source of resistance genes. After isolating 121 different types of bacteria based on their phenotypes and genotypes, commonly used antibiotics like Cefotaxime, Ceftazidime, Sulphamethoxazole-Trimethoprim combination, Nitrofurantoin, Ciprofloxacin, and Ampicillin were tested to see if they could kill the bacteria. The results indicated the resistance of E. coli isolates to sulphamethoxazole-trimethoprim [42]. During a diarrheal episode in Faisalabad, the effects of readily available cefotaxime, ampicillin, and gentamicin on shiga toxins were elucidated. STEC was confirmed in five samples. A considerable reduction in the release of toxins and cytotoxicity level was reported after exposure to minimum inhibitory concentrations of ampicillin, gentamicin, and cefotaxime, with a maximum reduction by sub-MIC of gentamicin [43]. A related study revealed the possible impact of SubMIC on 15 bacterial isolates collected from Railway General Hospital, Rawalpindi. The results showed that shiga toxin levels went up by 6.5 and 8 times when ciprofloxacin and tigecycline Sub MIC were used. On the other hand, expression levels were very low when Fosfomycin was used (2 times) and Meropenem was used (the weakest)[44].

Treatment Methods

Hydration and supportive therapy are the cornerstones of the currently advised STEC infection treatment plan. The questionable use of antibiotics has been linked to a worsening of symptoms and an increased risk of haemolytic uremic syndrome. Furthermore, by killing bacteria and causing an increase in the release of shiga toxins that may have been retained in the bacterial cell, antibiotics may exacerbate infections that are Shiga toxigenic [45]. Because there is no safe and specific therapeutic intervention, replacing intravenous fluids in infected patients and providing supportive care are the best-advised treatments. In patients with severe CNS involvement, eculizumab or plasma treatment is best recommended. When given intravenously with an isotonic solution and early parental volume expansion, the high risk of oliguria or anuria caused by renal hyper fusion is lowered [46]. Patients with suspected or confirmed STEC diarrhea should not be given antibiotics as they increase toxin production. When combined with renal replacement, supportive therapy and intensive care improvements have eventually improved the prognosis of HUS. Supportive therapy is advised to treat the following: anaemia, thrombocytopenia, fluid management, acute kidney injury and dialysis, neurological dysfunction, gastrointestinal complications, pancreatitis, and pulmonary complications [47]. Chemical additions to purification methods yielded positive treatment results. The experiment on water reservoir tanks, ground water samples, and canal water was conducted in a laboratory setting. They pasteurized the samples with the addition of ferrous salt as a coagulant and reported the highest success rate with 99% shiga toxin removal[48].

Plant Extracts

Plant extracts, particularly fruits, are a bioactive compound source for controlling *E. coli*-induced infections. It acts as either a bactericidal or bacteriostatic compound, and it could also be used as an amplifier for antibiotic activity (a synergic agent). It attenuates the pathogenic activity by acting directly on virulence characters. Fruits, either in the form of raw extracts or molecules that have been cleaned up, can help treat many different types of E. coli infections by stopping enzymes that target pathogens, preventing biofilm formation, and damaging bacterial membranes [7]. Mangosteen fruit produces α-mangostin, which in combination with β-lactams is proven useful [50]; quercetin and kemp ferol [49]; Chinese bayberry fruit; fermentation of green olives; cranberry extracts [25]; fresh and dried fruits of Chinese quince [22]; peel extract of Gabiroba; chestnut extract; grape extracts; seeds of Citrus mandarin; lemon and strawberry; cocoa beans; and grapefruit juice [12] for substantially increased efficacy; synergistic activity for amoxicillin; curing diarrhea; production of exopolysaccharides (EPS); controlling neonatal and post-weaning diarrhea; and anti-CT properties[26]. A promising study proved the efficacy of medicinal plants in combating STEC-borne pathogens. Researchers used 5 medicinal plant extracts against STEC strain 0157:H7, using extracts from Azadirachta indica, Mela azedarech, Withenia coagulans, Nigella satvia, and Calotropis procera. Calotropis procera showed the maximum inhibition zone and highest weight gain and survival rate. This enhances the potential of plant treatments without developing microbial resistance[19].

Biomedical Applications

The evolution of protein toxins, like Stx, aimed to deliver inside the cytosol of target cells while also selectively targeting host cells. These characteristics might be used to create new therapeutic proteins. The use of Stx-A and Stx-B has advanced quickly in recent years. It has been determined that Stx-A is a promising payload for creating immunotoxins that target and destroy cancer cells. Immunotoxins are fusion proteins made up of a targeting domain, which can be any protein binder that can precisely engage cell surface proteins produced in cancer cells [24,

DOI: https://doi.org/10.54393/pbmj.v7i07.1104

27]. Human volunteers are avoided because of the serious health effects associated with STEC infection, which range from neurological manifestations to death. So, the adoption of model animals, which mostly include mammals: monkeys, pigs, rabbits, and greyhounds, becomes a necessity. Some studies used chicken [20]. Greyhounds were used as test subjects for treatments. Toxin injections in these dogs caused damage to their kidneys and skin lesions. Calves and cattle had intestinal pathology. O157 infections in chickens caused intestinal pathology. Stx 1 or 2 infections in baboons caused intestinal pathology and renal damage. And streptomycin and O157 infections in ferrets caused renal damage [44].

CONCLUSIONS

This study focused on shiga toxin strains in Pakistan, specific to their transmission factors, and reported clinical infections. According to research, Shiga toxin 0157:H7 is still the most common type of STEC found around the world. Food-borne factors constitute the primary culprit of transmission especially dairy products and meat. Sewage water and floods also spread this deadly pathogen. Pakistan has seen documented outbreaks and significant clinical infections in the past decade. Pregnancy complications and neonatal vulnerability to diarrhea and HUS is primary concern in maternal and child care. This virulent pathogen is being exacerbated because of the development of anti-microbial resistance against antibiotic use. Different chemical treatments in water purification, medicinal plants, and fruit peels including Chinese bay berry fruit and cranberry extracts have shown tremendous potential in treating this emerging disease, especially in developing countries. Usage of Stx A for delivering targeted payload inside cancels cells has increased biomedical potential of protein toxins. It is recommended to increase awareness about reservoirs, transmission methods, infectious diseases, and basic preventive measures through the concerted efforts of national organizations.

Authors Contribution

Conceptualization: FR, BNK
Methodology: FR, SK
Formal analysis: SA
Writing, review and editing: HR, SK, TZ, MMI

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Joseph A, Cointe A, Mariani Kurkdjian P, Rafat C, Hertig A. Shiga toxin-associated hemolytic uremic syndrome: A narrative review. Toxins. 2020 Jan; 12(2): 67. doi: 10.3390/toxins12020067.

[2] Combrink L, Humphreys IR, Washburn Q, Arnold HK, Stagaman K, Kasschau KD *et al.* Best practice for wildlife gut microbiome research: A comprehensive review of methodology for 16S rRNA gene investigations. Frontiers in Microbiology. 2023 Feb; 14: 1092216. doi: 10.3389/fmicb.2023.1092216.

[3] Balaji P, Kumar KS, Vijayarani K, Vairamuthu S, Karunakaran K, Porteen K *et al.* Prevalence of Escherichia coli and Salmonella spp. in captive Niligiri langur (Trachypithecus johnii) in south India. International Journal of Current Microbiology and Applied Sciences. 2018 May; 7(6): 3119-26. doi: 10.20546/ijcmas.2018.706.366.

[4] Rasheed MB, Ahsan A, Irshad H, Shahzad MA, Usman M, Riaz A *et al.* Occurrence of Shiga toxin producing E. coli in zoo animals of Rawalpindi and Islamabad zoos. Asian Journal of Agriculture and Biology. 2023; 2: 2022080. doi: 10.35495/ajab.2022.080.

[5] Foster-Nyarko E, Pallen MJ. The microbial ecology of Escherichia coli in the vertebrate gut. FEMS Microbiology Reviews. 2022 May; 46(3): fuac008. doi: 10.1093/femsre/fuac008.

[6] Torti JF, Cuervo P, Nardello A, Pizarro M. Epidemiology and characterization of Shiga toxin-producing Escherichia coli of hemolytic uremic syndrome in Argentina. Cureus. 2021 Aug; 13(8). doi: 10.7759/cureus.17213.

[7] Mansfield KG, Lin KC, Newman J, Schauer D, MacKey J, Lackner AA *et al.* Identification of enteropathogenic Escherichia coli in simian immunodeficiency virus-infected infant and adult rhesus macaques. Journal of Clinical Microbiology. 2001 Mar; 39(3): 971-6. doi: 10.1128/JCM.39.3.971-976.2001.

[8] Pakbin B, Brück WM, Brück TB. Molecular mechanisms of shigella pathogenesis; recent advances. International Journal of Molecular Sciences. 2023 Jan; 24(3): 2448. doi: 10.3390/ijms24032448.

[9] Freedman SB, van de Kar NC, Tarr PI. Shiga toxin–producing Escherichia coli and the hemolytic-uremic syndrome. New England Journal of Medicine. 2023 Oct; 389(15): 1402-14. doi: 10.1056/NEJMra2108739.

DOI: https://doi.org/10.54393/pbmj.v7i07.1104

[10] Prado PC, Matias CL, Goulart JQ, Pinto AT. Most involved microorganisms in foodborne diseases outbreaks: A systematic review. Brazilian Journal of Development. Curitiba. 2021 Nov; 7(11): 106900-106916. doi: 10.34117/bjdv7n11-363.

[11] Liu Y, Tian S, Thaker H, Dong M. Shiga toxins: An update on host factors and biomedical applications. Toxins. 2021 Mar; 13(3): 222. doi: 10.3390/toxins13030222.

[12] Persad AK and Lejeune JT. Animal reservoirs of Shiga toxin-producing *Escherichia coli*. Enterohemorrhagic *Escherichia coli* and Other Shiga Toxin-Producing *E. coli*. 2015 May; 211-30. doi: 10.1128/9781555818791.ch11.

[13] Delgado ML, Singh P, Funk JA, Moore JA, Cannell EM, Kanesfsky J *et al.* Intestinal microbial community dynamics of white-tailed deer (Odocoileus virginianus) in an agroecosystem. Microbial ecology. 2017 Aug; 74: 496-506. doi: 10.1007/s00248-017-0961-7.

[14] Abdullah UY, Al-Sultan II, Jassim HM, Ali YA, Khorsheed RM, Baig AA. Hemolytic uremic syndrome caused by Shiga toxin-producing Escherichia coli infections: an overview. Cloning & Transgenesis. 2014 Mar; 3(2): 1-9. doi: 10.4172/2168-9849.1000125.

[15] Ismail S, Ullah K, Sunnya H, Bingjie X. Overview of O157 in Pakistan: An Important Food-Borne Disease of Public Health. The Journal of Microbiology and Molecular Genetics. 2021 Dec; 2(3): 1-21. doi: 10.52700/jmmg.v2i3.34.

[16] Feng Y, Mannion A, Madden CM, Swennes AG, Townes C *et al.* Cytotoxic Escherichia coli strains encoding colibactin and cytotoxic necrotizing factor (CNF) colonize laboratory macaques. Gut pathogens. 2017 Dec; 9: 1-5. doi: 10.1186/s13099-017-0220-y.

[17] Rehman A, Andleeb S, Ullah SR, Mustafa Z, Gul D, Mehmood K. Antibiotic-mediated expression analysis of Shiga toxin 1 and 2 in multi-drug-resistant Shiga toxigenic *Escherichia coli*. Folia Microbiologica. 2021 Oct; 66(5): 809-17. doi: 10.1007/s 12223-021-00882-0.

[18] Abid H, Ali J, Waqas M, Anwar Y, Ullah J. Microbial quality assessment study of branded and unbranded milk sold in Peshawar City, Pakistan. Pakistan Journal of Nutrition. 2009; 8(5): 704-9. doi: 10.3923/pjn.2009.704.709.

[19] Razzaq A, Shamsi S, Nawaz A, Nawaz A, Ali A, Malik KA. 12. Occurrence of Shiga toxin producing *E. coli* from raw milk. Pure and Applied Biology. 2021 Oct; 5(2): 270-6. doi: 10.19045/bspab.2016.50035.

[20] Ullah S, Khan SU, Khan MJ, Khattak B, Fozia F, Ahmad I *et al.* Multiple-drug resistant Shiga toxin-producing *E. coli* in raw milk of dairy bovine. Tropical Medicine and Infectious Disease. 2024 Mar; 9(3): 64. doi: 10.3390/tropicalmed9030064.

[21] Shahzad KA, Muhammad K, Sheikh AA, Yaqub T, Rabbani M, Hussain T *et al.* Isolation and molecular characterization of Shiga toxin producing E. coli O157. The Journal of Animal & Plant Sciences. 2013; 23(6): 1618-1621.

[22] Samad A, Abbas F, Ahmad Z, Tanveer Z, Ahmad I, Patching SG *et al.* Multiplex polymerase chain reaction detection of Shiga toxin genes and antibiotic sensitivity of Escherichia coli O157: H7 isolated from beef meat in Quetta, Pakistan. Journal of Food Safety. 2018 Dec; 38(6): e12540. doi: 10.1111/jfs.12540.

[23] Samad A, Abbas F, Ahmad Z, Pokryrshko O, Asmat TM. Prevalence of foodborne pathogens in food items in Quetta, Pakistan. Pakistan Journal of Zoology. 2018 Aug; 50:1-4. doi: 10.17582/journal.pjz/2018.50.4.sc17.

[24] Shahzad A, Ullah F, Irshad H, Ahmed S, Shakeela Q, Mian AH. Molecular detection of Shiga toxin-producing Escherichia coli (STEC) O157 in sheep, goats, cows and buffaloes. Molecular Biology Reports. 2021 Aug; 48(8): 6113-21. doi: 10.1007/s11033-021-06631-3.

[25] Irshad H, Binyamin I, Ahsan A, Riaz A, Shahzad MA, Qayyum M *et al.* Occurrence and Molecular Characterization of Shiga Toxin-Producing Escherichia coli Isolates Recovered from Cattle and Goat Meat Obtained from Retail Meat Shops in Rawalpindi and Islamabad, Pakistan. Pakistan Veterinary Journal. 2020 Jul; 40(3): 295-300. doi: 10.29261/pakvetj/2020.045.

[26] Kanwal B, Shah S, Hassan S, Shaheen F. Prevalence of Shiga Toxin Producing Enterohemorrhagic Escherichia coli O157: H7 Isolated from Chicken Meat in Northern Punjab, Pakistan. Veterinary Sciences Research and Reviews. 2023; 9(1): 50-6. doi: 10.17582/journal.vsrr/2023/9.1.50.56.

[27] Amir M, Riaz M, Chang YF, Ismail A, Hameed A, Ahsin M. Antibiotic resistance in diarrheagenic Escherichia coli isolated from broiler chickens in Pakistan. Journal of food quality and hazards control. 2021 Jun; 8(2): 78-86. doi: 10.18502/jfqhc.8.2.6472.

[28] Tanveer A, Muneer B, Mehboob K, Rafique R, Sharif F. Isolation, Identification and Characterization of Escherichia Coli O157: H7 from Poultry Meat-A Worldwide Public Health Threat!. Infectious Diseases Journal of Pakistan. 2017 Apr; 26(4): 65-71.

[29] Iqtedar ME and Yasin AY. Incidence of *E. coli* O157: H7 in fresh fruit juices of street vendors from different areas of Lahore City, Pakistan. BIOLOGIA (PAKISTAN). 2014; 60(2): 185-91.

DOI: https://doi.org/10.54393/pbmj.v7i07.1104

[30] Shah MS, Eppinger M, Ahmed S, Shah AA, Hameed A, Hasan F. Multidrug-resistant diarrheagenic *E. coli* pathotypes are associated with ready-to-eat salad and vegetables in Pakistan. Journal of the Korean Society for Applied Biological Chemistry. 2015 Apr; 58: 267-73. doi: 10.1007/s13765-015-0019-9.

[31] Shah MS, Eppinger M, Ahmed S, Shah AA, Hameed A, Hasan F. Flooding adds pathogenic Escherichia coli strains to the water sources in southern Khyber Pakhtunkhwa, Pakistan. Indian journal of medical microbiology. 2016 Oct; 34(4): 483-8. doi: 10.4103/0255-0857.195350.

[32] Bano A and Ali B. Isolation and culture dependent characterization of Escherichia coli from the sewage waste water of Lahore, Pakistan. South Asian Journal of Research in Microbiology. 2019 Nov 15;5(1):1-3. doi: 10.9734/sajrm/2019/v5i130122.

[33] Bokhari H, Shah MA, Asad S, Akhtar S, Akram M, Wren BW. *Escherichia coli* pathotypes in Pakistan from consecutive floods in 2010 and 2011. The American journal of tropical medicine and hygiene. 2013 Mar; 88(3): 519. doi: 10.4269/ajtmh.12-0365.

[34] Ansari MR, Laghari MS, Solangi KB. Acute renal failure in pregnancy: one year observational study at Liaquat University Hospital, Hyderabad. JPMA. The Journal of the Pakistan Medical Association. 2008 Feb; 58(2): 61.

[35] Ibrahim SH, Bhutta ZA, Khan IA. Haemolytic uraemic syndrome in childhood: an experience of 7 years at the Aga Khan University. Journal of Pakistan Medical Association. 1998 Apr; 48(4): 100-103.

[36] Tresa V, Yaseen A, Lanewala AA, Hashmi S, Khatri S, Ali I *et al.* Etiology, clinical profile and short-term outcome of acute kidney injury in children at a tertiary care pediatric nephrology center in Pakistan. Renal failure. 2017 Jan; 39(1): 26-31. doi: 10.1080/0886022X.2016.1244074.

[37] Baloch DG. An overview of diarrheagenic *Escherichia coli* among infants in Pakistan. Pak-Euro Journal of Medical and Life Sciences. 2021 May; 4: 11-24. doi: 10.31580/pjmls.v4iSpecial%20Is.1865.

[38] Sohail A and Mazhar E. Screening of *Escherichia coli* O157 Strain from Stool Samples in Karachi, Pakistan. RADS Journal of Biological Research & Applied Sciences. 2016 Jul; 7(2): 06-9.

[39] Khan AY, Ahmad SS, Avais M, Ashraf K. In-Vitro and In-Vivo Antimicrobial Activity of Five Medicinal Plants against Virulent *Escherichia coli* O157: H7 Strain Harboring Shiga Toxin Gene. Pakistan Journal of Zoology. 2023 Dec; 1-10. doi: 10.17582/journal.pjz/20221009171005.

[40] Phitaktim S, Chomnawang M, Sirichaiwetchakoon K, Dunkhunthod B, Hobbs G, Eumkeb G. Synergism and the mechanism of action of the combination of α-mangostin isolated from Garcinia mangostana L. and oxacillin against an oxacillin-resistant Staphylococcus saprophyticus. BMC Microbiology. 2016 Dec; 16: 1-4. doi: 10.1186/s12866-016-0814-4.

[41] Nawaz B, Ali A, Syed MN, Khan AB. Screening for toxigenic Escherichia coli in stool samples of diarrhoeal patients by polymerase chain reaction. Pakistan Journal of Pharmaceutical Sciences. 2014 Sep; 27(5): 1571-4.

[42] Dubreuil JD. Fruit extracts to control pathogenic Escherichia coli: A sweet solution. Heliyon. 2020 Feb; 6(2). doi: 10.1016/j.heliyon.2020.e03410.

[43] Siriwong S, Teethaisong Y, Thumanu K, Dunkhunthod B, Eumkeb G. The synergy and mode of action of quercetin plus amoxicillin against amoxicillin-resistant Staphylococcus epidermidis. BMC Pharmacology and Toxicology. 2016 Dec; 17:1-4. doi: 10.1186/s40360-016-0083-8.

[44] Chen JC, Chang YS, Wu SL, Chao DC, Chang CS, Li CC *et al.* Inhibition of Escherichia coli heat-labile enterotoxin-induced diarrhea by Chaenomeles speciosa. Journal of ethnopharmacology. 2007 Sep; 113(2): 233-9. doi: 10.1016/j.jep.2007.05.031.

[45] Coddens A, Loos M, Vanrompay D, Remon JP, Cox E. Cranberry extract inhibits in vitro adhesion of F4 and F18+ Escherichia coli to pig intestinal epithelium and reduces in vivo excretion of pigs orally challenged with F18+ verotoxigenic E. coli. Veterinary Microbiology. 2017 Apr; 202: 64-71. doi: 10.1016/j.vetmic.2017.01.019.

[46] Girennavar B, Cepeda ML, Soni KA, Vikram A, Jesudhasan P, Jayaprakasha GK *et al.* Grapefruit juice and its furocoumarins inhibits autoinducer signaling and biofilm formation in bacteria. International Journal of Food Microbiology. 2008 Jul; 125(2): 204-8. doi: 10.1016/j.ijfoodmicro.2008.03.028.

[47] Badar M, Khokhar I, Batool F, Iqbal R, Ch Y. Effect of boiling on removing of shiga toxins from drinking water samples. Journal of Entomology and Zoology Studies. 2017 Feb; 5(2): 672-676.

[48] Pastan I, Hassan R, FitzGerald DJ, Kreitman RJ. Immunotoxin therapy of cancer. Nature Reviews Cancer. 2006 Jul; 6(7): 559-65. doi: 10.1038/nrc1891.

[49] Melton-Celsa A, Mohawk K, Teel L, O'Brien A. Pathogenesis of Shiga-toxin producing Escherichia coli. Ricin and Shiga Toxins: Pathogenesis, Immunity, Vaccines and Therapeutics. 2012: 67-103. doi: 10.1007/82_2011_176.

DOI: https://doi.org/10.54393/pbmj.v7i07.1101

PAKISTAN BIOMEDICAL JOURNAL
https://www.pakistanbmj.com/journal/index.php/pbmj/index
ISSN (P): 2709-2798, (E): 2709-278X
Volume 7, Issue 7 (July 2024)

Original Article

OPEN ACCESS

Ultrasound for Identifying Gynecological and Obstetrical Etiologies of First-Trimester Pelvic Pain

Fatima Batool[1*], Mujahida[1], Asma Shakeel[1], Momina Shahid[1], Sayyam Jameel[1], Rida Aslam[1] and Asim Raza[1]

[1]School of Allied Health Sciences, Combined Military Hospital Lahore, Medical College and Institute of Dentistry, Lahore, Pakistan

ARTICLE INFO

Keywords:
Pelvic Pain, Pregnancy, First Trimester, Ultrasonography, Heterotopic

How to Cite:
Batool, F. ., Mujahida, ., Shakeel, A., Shahid, M., Jameel, S., Aslam, R., & Raza, A. (2024). Ultrasound for Identifying Gynecological and Obstetrical Etiologies of First-Trimester Pelvic Pain: Ultrasound and First-Trimester Pelvic Pain. Pakistan BioMedical Journal, 7(07). https://doi.org/10.54393/pbmj.v7i07.1101

***Corresponding Author:**
Fatima Batool
School of Allied Health Sciences, Combined Military Hospital Lahore, Medical College and Institute of Dentistry, Lahore, Pakistan
fatima-batool@cmhlahore.edu.pk

Received Date: 13th May, 2024
Acceptance Date: 27th July, 2024
Published Date: 31st July, 2024

ABSTRACT

For well-being of mother and fetus timely and accurate diagnosis is necessary. Pregnant patients frequently presented with pain and discomfort in the first trimester of pregnancy due to multiple gynaecological and obstetrical causes. **Objective:** To identify the gynecological and obstetrical causes of first-trimester pelvic pain using ultrasound. **Methods:** This retrospective, descriptive cross-sectional study was done after obtaining ethical approval from the Institutional Review Board (IRB). Data collection was done retrospectively from Al-Jannat Lab, Lahore. Patient's medical record of six-month period from April 2023 to September 2023 was reviewed. The data collection was done during time period of November 2023 to January 2024. Data analysis was done on SPSS version 26.0. **Results:** In this study, retrospective data were collected of 86 patients. Transvaginal Ultrasonography (TVUS) was performed on 43 patients (50.0%) Transabdominal Sonography (TAS) was done on 26 patients (30.2 percent), whereas both scanning techniques were used in 17 cases. Gynaecological causes of pelvic pain detected during first trimester of pregnancy were Pelvic Inflammatory Disease, Endometriosis, Ovarian Cyst, Fibroids and Adnexal Torsion whereas Obstetrical causes of pelvic pain were Ectopic Pregnancy, Sub chorionic Hemorrhage, Molar Pregnancy, Heterotopic Pregnancy and Miscarriage. **Conclusions:** Ultrasound identifies a variety of gynecological and obstetrical causes as a first-line diagnostic tool for pelvic pain in early pregnancy and helps in better patient management and avoids undue interventions

INTRODUCTION

Pelvic pain is pain in the lowest part of the torso, in the region below the abdomen and in the space between the hipbones (pelvis). The pain may come and go and be sharp or crampy (like menstrual cramps. Pregnant women frequently experience Pelvic Pain (PP), which can be caused by several diseases, including obstetric, gynaecological, gastrointestinal, genitourinary, and vascular disorders [1]. Lower back pain and pelvic pain are common pregnancy symptoms and have a wide range of reported incidences (24–90%) therefore; a "crampy" pelvic pain in early pregnancy is common and is caused by the uterus's quick growth, hormonal changes, and increased blood flow. Pregnant patients frequently express discomfort in the first trimester due to symptoms that are normal on diagnostic examinations [2]. Pregnancy-related pain can be caused by a wide range of disorders. Gynaecological (adnexal torsions, pelvic inflammatory disease, endometriosis, ruptured ovarian cysts) and obstetrical (miscarriage, ectopic pregnancy, subchorionic hematoma) conditions can be divided as the primary causes of pelvic pain in pregnancy [3]. Approximately 10-12% of known first trimester pregnancies undergo spontaneous abortions. Ectopic pregnancy is most commonly tubal (97%), although it can also be ovarian (1%), interstitial (3%), abdominal (<1%), or cervical (<1%) there are three kinds of placental hematoma: retro placental, sub chorionic and sub amniotic [3]. Retro placental hematomas, posterior to the placenta, form 43% of hematomas, whereas sub chorionic hematomas, between the chorion and the endometrium, represent roughly 57%.

DOI: https://doi.org/10.54393/pbmj.v7i07.1101

Sub amniotic ones, positioned between the amnion and the chorion, are uncommon around the world, uterine leiomyomas and uterine fibroids are the most prevalent gynecological tumors, affecting 20–50% of women [3, 4]. The safety of the mother and fetus should always come first when selecting the best diagnostic equipment for a pregnancy emergency disease assessment. Due to the known risks of ionizing radiation exposure to the developing fetus, Ultrasound (US) and Magnetic Resonance Imaging (MRI) are currently the preferred imaging techniques [5]. Ultrasound is quick, painless, produces extensive results, is widely accessible, and is regarded as safe. This modality is the first-line examination for the patients who are pregnant because it doesn't require for the administration of intravenous contrast material (agent) [5]. Pelvic scans are a general term for imaging tests used to examine the organs and structures within the pelvis [6]. There are two main ways an ultrasound can be performed for a pelvic scan: Transabdominal ultrasound: A probe is placed on abdomen to send sound waves through the tissues to pelvic organs. Transvaginal ultrasound: A thin probe is inserted into the vagina to get a closer look at the uterus, ovaries, and cervix [7, 4]. Ultrasonography is a non-invasive imaging method that has been shown to be beneficial in the diagnosis of a variety of gynecological and obstetric problems. Nevertheless, it is still uncertain if ultrasonography in evaluating the first trimester pelvic pain is completely feasible.

This study aimed to address this knowledge gap by employing strategic usage of ultrasonography to identify the underlying gynecological and obstetric reasons of pelvic pain in early pregnancy, and presenting evidence-based references for assessing and treating pregnant women. Moreover, this study may help in the elimination of unnecessary surgeries and therapies by accurately finding benign sources of pain

METHODS

This retrospective, descriptive cross-sectional study was done after obtaining ethical approval from the Institutional Review Board (IRB) with case number of 651/ERC/CMH/LMC. Data were collected retrospectively from Al-Jannat Lab, Lahore. Patient's medical record of six-month period from April 2023 to September 2023 was reviewed. The data collection was done during time period of November 2023 to January 2024. All the detailed history was collected including the age, duration of pain and associated symptoms. Informed consent was taken from each participant all possible benefits and expected risk were explained. Female with pelvic pain in first trimester of pregnancy and between ages of 18-35 years were included. Females with ggastrointestinal diseases, urinary tract infection and pelvic vascular diseases were excluded. Examination was done with Toshiba Xario and Logic 5 Ultrasound machine, Tran's abdominal transducer (2-5MHz), Tran's vaginal transducer (5-12MHz) of LOGIC 5 PRO. Both trans-abdominal and trans-vaginal scanning techniques were used for ultrasound examinations. Firstly, transabdominal scan was performed for all the participants , if the initial diagnosis were not clear, further Transvaginal Ultrasound (TVS) was performed. TVS was also done as a first line investigation in those patients prescribed by gynecologists. All the data were written on proforma and evaluated from SPSS version 26.0. Data were analyzed at 95% of confidence-interval. Mean and standard deviation were computed for quantitative variables in the descriptive analysis, whereas frequencies and percentages were computed for qualitative data.

RESULTS

The data were collected from total of 86 pregnant patients with 1st trimester. Table 1 displays the demographic characteristics of pregnant women during the first trimester, specifically focusing on two variables: Age Group (Years) and Weeks of Pregnancy. While frequencies of Obstetrical and gynaecological causes of pelvic pain in pregnant women of first trimester diagnosed on ultrasonography as shown in table 3 and table 4.

Table 1: Demographic Characteristics of Pregnant Women of First Trimester(n=86)

Variables	Categories	(%)
Age Group (Years)	18-23	17.44%
	24-29	44.18%
	30-35	38.37%
Weeks of Pregnancy	1-4	15.1%
	5 to 8	40.7%
	9 to 12	44.2%

Table 2 showed the various scanning techniques employed on pregnant women during the first trimester.

Table 2: Types of Scanning Techniques Performed on the Pregnant Women of First Trimester(n=86)

Scanning Technique	(%)
Trans-Abd US	30.23%
Tarns-Vaginal US	50%
Both	19.76%

While frequencies of Obstetrical and gynaecological causes of pelvic pain in pregnant women of first trimester diagnosed on ultrasonography, as shown in table 3.

Table 3: Frequency of Obstetrical Causes of Pelvic Pain in Pregnant Women (N=86) Of First Trimester Diagnosed On Ultrasonography

Variables	Responses	(%)	Types	(%)
Ectopic Pregnancy	Yes	93.02	-	-
	No	6.98	Tubal	4.7
			Ovarian	1.2

DOI: https://doi.org/10.54393/pbmj.v7i07.1101

			Previous Caesarean Scar	1.2
Sub chorionic Hemorrhage	Yes	88.37	-	-
	No	11.63	Mild	9.3
			Moderate	2.3
			Severe	0
Molar Pregnancy	Yes	98.8	-	-
	No	41.16	Complete	0
			Partial	1.2
Heterotopic Pregnancy	Yes	98.84	-	-
	No	1.16	Intrauterine and Tubal Ectopic	1.2
			Intrauterine and Ovarian Ectopic	0
			Intrauterine and Cervical Ectopic	0
			Intrauterine and Caesarean Scar	0
Miscarriage	Yes	75.58	-	-
	No	24.42	Incomplete	4.7
			Complete	1.2
			Missed	18.6

Table 4 presented the frequency of gynecological causes of pelvic pain in 86 pregnant women during their first trimester, as diagnosed through ultrasound examinations.

Table 4: Frequency of Gynaecological Causes of Pelvic Pain in Pregnant Women of First Trimester Diagnosed On Ultrasonography(n=86)

Variables	Responses	(%)	Types	(%)
Pelvic Inflammatory Disease	Yes	90.7	-	-
	No	9.3	Mild	0
			Moderate	5.8
			Severe	3.5
Endometriosis	Yes	96.51	-	-
	No	3.49	-	-
Ovarian Cyst	Yes	73.26	-	-
	No	26.74	Right	17.4
			Left	8.1
			Bilateral	1.2
Fibroids	Yes	75.58	-	-
	No	24.42	-	-
			Sub Mucosal	10.5
			Sub Serosal	8.1
			Pan Mural	2.3
			Pedunculated	3.5
Adnexal Torsion	Yes	100	-	-
	No	0	-	-

DISCUSSION

This study showed that ultrasound is effective in diagnosing a variety of conditions (e.g., pelvic inflammatory disease, ectopic pregnancy, miscarriage) that could be sources of pelvic pain. Our study population likely differed in age distribution compared to the research by Guena MN *et al.*, in 2019, where the average participant age was 30 years. This reinforces the importance of considering age when interpreting results, as pelvic pain presentations in pregnancy can vary across age groups. While our study identified a lower percentage of miscarriages (24.42%) compared to their 29.8%, the incidence of incomplete abortions (18.6%) aligned closely with their findings (22.3%). Notably, our study comparatively revealed a higher prevalence of ectopic pregnancies of which 6 were reported (4 tubal and 1 ovarian). This difference could be as a result of sample size differences or the pattern of referrals at the institution. One of the case (1. 2%) recalled having a scar on lower abdomen area as a result of a previous C-section, which was not stated in the mentioned study of Guena MN [8-13]. From the above findings, it can be noted that pelvic pain is complex in nature and a comprehensive diagnostic model is required for its analysis. In addition to the objective measurement of sonographic characteristics, patient's data such as history or age must also be considered [13]. Endometriomas during pregnancy were observed in 3 patients out of 86 of the studied group of women. Although their occurrence is relatively rare, several concerns are raised due to possible difficulties. It has been reported in a previous study that most endometriomas either diminish in size or become asymptomatic with time but, about 2. 8 % of pregnant women may experience a rupture of endometrioma. This is in concord with our focus on possible causes of pelvic pain, as endometrioma may get ruptured in the patient and might consequently be painful. In addition, they noticed that there is an increased chance of developing ovarian torsion due to larger endometriomas. Ovarian torsions are considered a serious complication that demand immediate medical procedures. However, no such case was identified in our study [14]. Different authors have also reported percentage prevalance of fibroids during the first trimester. When compared to a study by Tîrnovanu MC, where 68% cases of fibroids were found, our results indicated a significantly reduced figure of fibroids (24. 4%). This difference may correlate to differences in the demographic parameters, rates of diagnosis, or research methods. Further research should be carried out to determine the reasons that lead to this fluctuation and to have a refined first-trimester prevalence rate of fibroids [15]. The usage of ultrasonography has been described in several studies to provide excellent accuracy in diagnosing diverse causes of pelvic pain [16, 17]. These studies highlight the advantages of ultrasonography over other imaging techniques. Such benefits include safety for pregnant women and the ability to provide real-time image of the pelvic organs. Altogether, our results regarding the efficacy of transvaginal ultrasound in the acquisition of clearer images for particular conditions are confirmed by a previous study that emphasized its importance for evaluating complex cases [18-21]. This research underlines the significance of using ultrasonography for diagnosing the pelvic pain at the initial stage. By determining several gynecological and obstetrical aspects, this study will assist

DOI: https://doi.org/10.54393/pbmj.v7i07.1101

in the management of the patient so that unnecessary strategies are not applied. Data were obtained and recorded after the outcome variables were gathered so the impact of the confounder variables was not evaluated. Furthermore, the relatively small sample size might limit the generalizability of the findings. Future studies should be done prospectively with a larger sample size. Furthermore, investigating the relationship between certain ultrasound findings and pain intensity could provide significant information.

CONCLUSIONS

Ultrasound identifies a variety of gynecological and obstetrical causes as a first-line diagnostic tool for pelvic pain in early pregnancy and helps in better patient management and avoids undue interventions.

Authors Contribution

Conceptualization: FB
Methodology: MS, SJ
Formal analysis: AR
Writing, review and editing: M, AS, RA, AR

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Galan HL, Huguelet T, editors. Emergencies in Obstetrics and Gynecology, an Issue of Obstetrics and Gynecology Clinics, E-Book: Emergencies in Obstetrics and Gynecology, an Issue of Obstetrics and Gynecology Clinics, E-Book. Elsevier Health Sciences; 2022 Sep. doi: 10.1016/S0889-8545(22)00071-7.

[2] Caruso M, Dell'Aversano Orabona G, Di Serafino M, Iacobellis F, Verde F, Grimaldi D *et al.* Role of ultrasound in the assessment and differential diagnosis of pelvic pain in pregnancy. Diagnostics. 2022 Mar; 12(3): 640. doi: 10.3390/diagnostics12030640.

[3] Masselli G, Brunelli R, Monti R, Guida M, Laghi F, Casciani E *et al.* Imaging for acute pelvic pain in pregnancy. Insights into Imaging. 2014 Apr; 5: 165-81. doi: 10.1007/s13244-014-0314-8.

[4] Chai Y, Boudali AM, Walter WL. Correlations analysis of different pelvic tilt definitions: a preliminary study. HSS Journal®. 2023 May; 19(2): 187-92. doi: 10.1177/15563316221136128.

[5] Detti L, Francillon L, Christiansen ME, Peregrin-Alvarez I, Goedecke PJ, Bursac Z *et al.* Early pregnancy ultrasound measurements and prediction of first trimester pregnancy loss: A logistic model. Scientific Reports. 2020 Jan; 10(1): 1545. doi: 10.1038/s41598-020-58114-3.

[6] Flusberg M, Kobi M, Bahrami S, Glanc P, Palmer S, Chernyak V *et al.* Multimodality imaging of pelvic floor anatomy. Abdominal Radiology. 2021 Apr; 46: 1302-11. doi: 10.1007/s00261-019-02235-5.

[7] Collins SA, O'Shea M, Dykes N, Ramm O, Edenfield A, Shek KL *et al.* International Urogynecological Consultation: clinical definition of pelvic organ prolapse. International Urogynecology Journal. 2021 Aug; 32(8): 2011-9. doi: 10.1007/s00192-021-04875-y.

[8] Curry A, Williams T, Penny ML. Pelvic inflammatory disease: diagnosis, management, and prevention. American Family Physician. 2019 Sep; 100(6): 357-64.

[9] Marcinkowski KA, Mehta V, Mercier R, Berghella V. Pelvic inflammatory disease in pregnancy: a systematic review focusing on perinatal outcomes. American journal of obstetrics & gynecology MFM. 2022 Jul; 4(4): 100643. doi: 10.1016/j.ajogmf.2022.100643.

[10] Hasson J, Tsafrir Z, Azem F, Bar-On S, Almog B, Mashiach R *et al.* Comparison of adnexal torsion between pregnant and nonpregnant women. American Journal of Obstetrics and Gynecology. 2010 Jun; 202(6): 536-e1. doi: 10.1016/j.ajog.2009.11.028.

[11] Sasaki KJ and Miller CE. Adnexal torsion: review of the literature. Journal of Minimally Invasive Gynecology. 2014 Mar; 21(2): 196-202. doi: 10.1016/j.jmig.2013.09.010.

[12] Chill HH, Karavani G, Rachmani T, Dior U, Tadmor O, Shushan A. Growth pattern of uterine leiomyoma along pregnancy. BioMed Central Women's Health. 2019 Dec; 19: 1-5. doi: 10.1186/s12905-019-0803-5.

[13] Guena MN, Alapha FZ, Kemegne DC, Nana AN, Zeh OF, Fotsing JG. Ultrasound study of first trimester bleeding. Open Journal of Radiology. 2019 Jan; 9(1): 58-68. doi: 10.4236/ojrad.2019.91006.

[14] Woźniak A and Woźniak S. Ultrasonography of uterine leiomyomas. Menopause Review/Przegląd Menopauzalny.2017 Dec; 16(4): 113-7.doi: 10.5114/pm.2017.72754.

[15] Tîrnovanu MC, Lozneanu L, Tîrnovanu ŞD, Tîrnovanu VG, Onofriescu M, Ungureanu C *et al.* Uterine fibroids and pregnancy: a review of the challenges from a Romanian Tertiary Level Institution. InHealthcare. 2022 May; 10(5): 855. doi: 10.3390/healthcare10050855.

[16] Shaamash AH, Aly HA, Abdel-Aleem M, Akhnowkh SN. Clinical and ultrasound evaluation of early threatened miscarriage to predict pregnancy continuation up to

DOI: https://doi.org/10.54393/pbmj.v7i07.1101

28 weeks: a prospective cohort study. Journal of Ultrasound in Medicine. 2020 Sep; 39(9): 1777-85. doi: 10.1002/jum.15282.

[17] Takami M, Kajiyama R, Miyagi E, Aoki S. Characteri stics of ovarian endometrioma during pregnancy. Journal of Obstetrics and Gynaecology Research. 2021 Sep; 47(9): 3250-6. doi: 10.1111/jog.14862.

[18] Nawrocka-Rutkowska J, Szydłowska I, Rył A, Ciećwież S, Ptak M, Starczewski A. Evaluation of the diagnostic accuracy of the interview and physical examination in the diagnosis of endometriosis as the cause of chronic pelvic pain. International Journal of Environmental Research and Public Health. 2021 Jun; 18(12): 6606. doi: 10.3390/ijerph18126606.

[19] Roditis A, Florin M, Rousset P, Touboul C, Bendifallah S, Bazot M *et al.* Accuracy of combined physical examination, transvaginal ultrasonography, and magnetic resonance imaging to diagnose deep endometriosis. Fertility and Sterility. 2023 Apr; 119(4): 634-43. doi: 10.1016/j.fertnstert.2022.12.025.

[20] Liu L, Li W, Leonardi M, Condous G, Da Silva Costa F, Mol BW *et al.* Diagnostic accuracy of transvaginal ultrasound and magnetic resonance imaging for adenomyosis: systematic review and meta-analysis and review of sonographic diagnostic criteria. Journal of Ultrasound in Medicine. 2021 Nov; 40(11): 2289-306. doi: 10.1002/jum.15635.

[21] Huang CC, Huang CC, Lin SY, Chang CY, Lin WC, Chung CH *et al.* Association of pelvic inflammatory disease (PID) with ectopic pregnancy and preterm labor in Taiwan: a nationwide population-based retrospec tive cohort study. PLOS One. 2019 Aug; 14(8): e02193 51. doi: 10.1371/journal.pone.0219351.

DOI: https://doi.org/10.54393/pbmj.v7i07.1118

PAKISTAN BIOMEDICAL JOURNAL

https://www.pakistanbmj.com/journal/index.php/pbmj/index

ISSN (P): 2709-2798, (E): 2709-278X

Volume 7, Issue 7 (July 2024)

Original Article

OPEN ACCESS

Assessing Knowledge and Practice Among Nurses Regarding Postoperative Wound Care in Public Sector Teaching Hospitals of Peshawar

Muhammad Huzaifa[1], Imran Waheed Ahmad[2*], Ibn-e-Amin[2], Kashif Raheem[1], Komal Gul[2] and Shaista Aziz[1]

[1]Department of Nursing Education and Training, Hayat Abad Medical Complex, Peshawar, Pakistan
[2]Institute of Nursing Sciences, Khyber Medical University, Peshawar, Pakistan

ARTICLE INFO

Keywords:
Wound Management, Nursing Knowledge, Post-Operative Wound Care

How to Cite:
Huzaifa, M., Ahmad, I. W., Amin, I. e, Raheem, K., Gul, K., & Aziz, S. (2024). Assessing Knowledge and Practice Among Nurses Regarding Postoperative Wound Care in Public Sector Teaching Hospitals of Peshawar: Nurse Practices and Knowledge in Postoperative Wound Care. Pakistan BioMedical Journal, 7(07). https://doi.org/10.54393/pbmj.v7i07.1118

***Corresponding Author:**
Imran Waheed Ahmad
Institute of Nursing Sciences, Khyber Medical University, Peshawar, Pakistan
imran.ins@kmu.edu.pk

Received Date: 11th June, 2024
Acceptance Date: 26th July, 2024
Published Date: 31st July, 2024

ABSTRACT

Wound management, or the expert practice carried out by healthcare professionals in a hospital context, poses a significant challenge to patient care. Because the whole expense of wound management was covered by health insurance in various care settings, the impact of wound complications on people and healthcare institutions was typically underestimated or even ignored. **Objective:** To assess the knowledge and to determine practices among nurses regarding post-operative wound care. **Methods:** A cross-sectional study design was used among 209 nurses, having at least 1-year experience, of Khyber Teaching Hospital and Hayatabad Medical Complex (KTH and HMC). Data were collected through self-administered questionnaire via convenient sampling. Descriptive statistics and variable were computed using SPSS version 23.0 and correlation and significance was determined among variables. **Results:** The study showed that 60.8 % nurses had good knowledge while 82.3% had good practices regarding post-operative wound care. Educational level and experience of nurse were significant and positively correlated to the knowledge and practice of nurse regarding wound care. The greater the educational level and experience of nurse, greater is the knowledge and practice of that nurse regarding wound care. **Conclusions:** Nurses displayed good wound care knowledge and practice. Education and work experience were recognized as key factors impacting nurses' knowledge and practices in the study.

INTRODUCTION

Pathogenic organisms that invade the healthy tissue close to a localized injury, fissure or laceration in the skin or underlying soft tissue result in wound infection. Bacterial wound infections can be brought on by antibiotic-resistant bacteria and are associated with increased morbidity and medical expenses [1]. If correct wound care is not given, the wound-healing process may be delayed, prolonged hospital stays, production of scars, and hernias spurred on by wound dehiscence, all of which raise expenditures. Postoperative wound care negligence contributes to global high mortality rate, global research indicates the wound care can is an insidious and result in measurable deaths [2]. Moreover, they are the main cause of illness and death in developing nations [1, 3]. The duration of wound healing process varies depending on the type of wound, ranging from a few days to several weeks or even months [4]. Numerous factors may lead to erroneous or inefficient tissue restoration, resulting in delayed wound healing. Wound care procedure is also influenced by local circumstances like resources readily accessible, skill mix, healthcare provider preferences, patient behavior, and duration of hospital stay [5]. In cancer patients, wounds may exhibit atypical symptoms and fail to heal in the usual manner [6, 7]. According to published studies, surgical site infections are common in Africa after a variety of surgical operations, with rates ranging from 2.5% to 34.6 [8, 9]. The total surgical site infection rate in Ethiopia ranges from 9.1% to 75% [8-10]. According to 131 nurses who participated in a study in Pakistan, 58% of staff nurses had effective practices for avoiding and controlling surgical

DOI: https://doi.org/10.54393/pbmj.v7i07.1118

wound infections [11]. According to a research done in the Ethiopian city of Mekele, 58.2% of nurses practiced effective postoperative wound care [12]. The primary goal of wound care is to facilitate the healing process, prevent infection, and promote optimal tissue regeneration [13]. Wound management, or the expert practice carried out by healthcare professionals in a hospital context, poses a significant challenge to patient care. Because the whole expense of wound management was covered by health insurance in various care settings, the impact of wound complications on people and healthcare institutions was typically underestimated or even ignored [14]. In order to properly care for a wound, wash the wound with normal saline solution and, if necessary, use hydrogen peroxide solution or povidone-iodine solution to remove discharges, slough, dead particles, infectious pathogens, and dressing leftovers without harming cellular activity, which helps the wound heal and prevents further damage Gizaw *et al.*, in 2022 [12]. The usage of goods like honey, butter, coffee beans, herbs, and fragrances as well as other medicines derived from plants, like myrrh, can be used into traditional medical practices [14, 15]. Although a diverse team performs wound care, it is essentially a nurse-led task [5]. In fact, nursing interventions and understanding of the physiology and process of wound healing are both essential for wound healing [12]. A nurse who is well-versed in wound healing techniques may conduct a comprehensive, all-encompassing patient evaluation and spot potential wound issues early on [1].

To reduce wound infection, wound care knowledge and practice must be improved. A person's quality of life is improved and wound-related problems and frequent hospitalizations are reduced with better knowledge and use of wound care.

METHODS

A cross-sectional research method was used in this study to evaluate nurses' postoperative wound care practices and knowledge in tertiary care hospitals of Peshawar, Khyber Teaching Hospital and Hayatabad Medical Complex (KTH and HMC). Ethical approval letter was obtained from Institute of nursing sciences, Khyber medical university (Reference Number: KMU/INS/6167). Non-probability convenience sampling technique had been used in the study to choose registered nurses employed in tertiary care hospitals (KTH and HMC) with at least 1-year clinical experience. Sample size was 209 and calculated using online software. The research includes all nurses who are actively involved in providing patients with post-operative wound care and who hold at least a diploma in nursing. Those who did not want to participate were excluded from the study. An official letter was written from the institute of nursing sciences, Khyber medical university to the public sector tertiary care hospitals (HMC and KTH) of Peshawar region to obtain their approval for participation in the study. Ensuring participant confidentiality and anonymity through the assignment of unique identifiers to questionnaires and secure data storage were the ethical considerations. Informed consent was given by participants, who were also made aware of their freedom to leave the study at any moment without facing repercussions. The research complied with ethical standards and laws that govern studies involving human subjects in order to safeguard the subjects' welfare and rights. The questionnaire was developed by reviewing the literature comprising of three parts; demographic details of participants, fourteen yes-or-no questions in Section 2 related to knowledge of nurses regarding wound care and fifteen Likert scale questions (ranging from "never" to "always") in Section 3 are practice-related items. Four BSN students and one MSN supervisor collected the data. The mean knowledge score of participants was 11.42 with standard deviation of 1.87, with minimum score of 1 and maximum score of 14. Using the cutoff point as 12, 60.8% of the participant have good knowledge score and 39.2% have poor knowledge. Mean practice score was 29.82 with standard deviation of 7.57. Using 22.5 score as cutoff point, 82.3% of respondents had good practice of wound care while 17.7% had poor practice. To ensure the validity and usefulness of the questionnaire, its preparation considers established wound care recommendations, prior research, and expert advice. The questionnaire was reviewed by experts in wound care and research methodology to ensure it was appropriate, relevant, and clear. Collected data were analyzed in SPSS 23.0 version. Frequency, percentage, mean, standard deviations and other statistical test were applied and calculated for all three sections of the questionnaire. Later, correlational tests were used to identify the association between different variables affecting the knowledge and practices regarding post-operative wound care.

RESULTS

Of the sample (Table 1 showed demographic characteristics), 23% (48) were between the ages of 31 and 40, and 72.2% (151) were between the ages of 20 and 30. There were just 4.8% (10) participants that were older than 40. 124 were male nurses and 85 were females. Among them, 43.1% (90) were married and 56.9% (119) were unmarried. More than half of nurses were BSN qualified i.e., 55% (115), diploma holders were 12.4% (26), and the number of post RN nurses was 32.5% (68). The research sample comprises 46.4% nurses from HMC and 53.6% nurses from the KTH. Regarding experience of nurses, 137 nurses experience ranges from 1-5 years, 35 nurses have 6-10 years of experience, 23 nurses have 11-15 years and 14 nurses have more than 15 years of experience (Table 1).

DOI: https://doi.org/10.54393/pbmj.v7i07.1118

Table 1: Demographic Data of study participants

Variables	Category	N (%)
Age	20-30	151 (72.2)
	31-40	48 (23.0)
	>40	10 (4.8)
Gender	Female	124 (59.3)
	Male	85 (40.7)
Marital Status	Married	90 (43.1)
	Single	119 (56.9)
Educational Level	Diploma	26 (12.4)
	Post RN	68 (32.5)
	BSN	115 (55.0)
	MSN	0 (0.0)
Area of work	HMC	97 (46.4)
	KTH	112 (53.6)
Experience	1-5	137 (65.6)
	6-10	35 (16.7)
	11-15	23 (11.0)
	>15	14 (6.7)

Table 2 showed the mean and standard deviation of knowledge and practice score and Table 3 shows frequency and percentage of knowledge in four different categories.

Table 2: Knowledge and Practice Score

Knowledge and Practice Score (Mean ± SD)/n		
Variables	**Knowledge**	**Practice**
Total Score	14	45
	11.42 ± 1.87	29.82 ± 7.57

Table 3 illustrated the distribution of nurses' knowledge and practice levels regarding postoperative wound care. According to the table, 60.8% of nurses had good knowledge about postoperative wound care, while 39.2% had poor knowledge. In terms of practices, a majority of 82.3% demonstrated good practices, whereas 17.7% had poor practices. This indicated that while most nurses had a strong understanding of wound care, a high proportion also effectively applied this knowledge in their practice (Table 3).

Table 3: Knowledge and Practice Level

Variables	N (%)
Poor Knowledge	127 (39.2)
Good Knowledge	92 (60.8)
Poor Practice	37 (17.7)
Good Practice	172 (82.3)

Educational level is positively correlated to the knowledge level regarding wound care. It means that the knowledge level will increase as the qualifications of the nurse increases. The percentage of poor knowledge at diploma level is 61.5 percent. The knowledge level gradually starts increasing and reaches the total of 71.3% at the BSN level. Both Post RN and BSN have greater percentage of nurses with good knowledge as it is a degree program compared to the diploma level (Table 4).

Table 4: Educational Level Correlation to the Knowledge Level

Educational Level	Knowledge Level
Pearson Correlation	0.250**
Significant (2-tailed)	0.000

Table 5 percentage presented the distribution of knowledge levels among nurses based on their educational qualifications. For those with a diploma, 61.5% had poor knowledge and 38.5% had good knowledge. Among nurses with Post RN qualifications, 48.5% had poor knowledge and 51.5% had good knowledge. In contrast, nurses with a BSN showed a higher proportion of good knowledge, with 71.3%, while 28.7% had poor knowledge. This indicated that higher educational levels were associated with better knowledge of wound care.

Table 5: Educational Level and Knowledge Level Frequency and Percentage

Knowledge Level		
Educational Level		**Frequency (%)**
Diploma	Poor Knowledge	16 (61.5)
	Good Knowledge	10 (38.5)
Post RN	Poor Knowledge	33 (48.5)
	Good Knowledge	35 (51.5)
BSN	Poor Knowledge	33 (28.7)
	Good Knowledge	82 (71.3)

The working experience was positively correlated with the knowledge and practice levels regarding wound care. As the number of years of working experience increased, both the knowledge level and practice level of the nurses also increased (Table 6).

Table 6: Working Experience Correlation to the Knowledge Level and Practice Level

Experience	Knowledge Level	Practice Level
Pearson Correlation	0.182**	0.253
Significant (2-tailed)	0.008	0.000

DISCUSSION

The study sought to investigate post-operative wound care behaviors and knowledge among nurses at two tertiary care facilities in Peshawar, Pakistan: Khyber Teaching Hospital (KTH) and Hayatabad Medical Complex (HMC). The researchers recognized that nurses' wound care proficiency is frequently influenced by their educational background and job experience. According to the study's findings, 82.3% of nurses at HMC and KTH displayed good wound care procedures. Furthermore, the survey discovered that 60.8% of nurses had strong wound treatment knowledge. Compared to the studies in the South Wollo Zone of Ethiopia, only 40.3% of nurses were found to have good knowledge of wound care, while 51% demonstrated good wound care practices [1]. Similarly, in the Public hospitals of West Showa Zone, Ethiopia, the percentages were 44.3% for good knowledge and 48% for good practices among nurses [12]. But the research

DOI: https://doi.org/10.54393/pbmj.v7i07.1118

findings regarding knowledge of wound care was almost same as the knowledge of the nurses in Mekelle city of Ethiopia, where 55% of nurses had good knowledge of wound care [15]. The disparity in the results between the Peshawar study and the Ethiopian studies may be attributed to several factors, including differences in the educational level of the participants and their working experience in wound care. The variation could also be influenced by the differences in the healthcare systems and resources available in the respective regions. Moreover, the finding was higher than the research conducted in Nigeria where only 32% of nurses had good knowledge of wound care [16]. The results of our study are far better as compared to the Lahore and Faisalabad. According to the research conducted in Lahore 31% of nurses were performing good practices [17]. In Allied Hospital Faisalabad, 13.5% always wash their hands before and after changing wound dressings, indicating hand hygiene practices. 35.7% nurses use aseptic technique and 10.5% uses facemask during surgical wound dressing [18]. While in this research, 42.6% nurses always wash their hands, 60.3% nurses use aseptic technique and 64% always wear facial mask. This research implies that when nurses gain experience and spend more time in wound care settings, their expertise in this area improves. The current study's findings are congruent with similar research conducted in Oromia, Bahirdar, and Amhara regional states, indicating that the association between years of experience and expertise in wound care is constant throughout geographical locations [12, 19, 20]. The cumulative effect of experience, in which nurses continually gain and perfect their knowledge and abilities over time, may be linked to this consistency. These statements also coincide with the study conducted in the South Wollo Ethiopia [1].

CONCLUSIONS

According to the study's findings, nurses displayed good wound care knowledge and practice. Education and work experience were recognized as key factors impacting nurses' knowledge and practices in the study. Based on these findings, it is recommended that nurses take steps to improve their education and receive basic wound care knowledge and practices. This is especially important in postoperative wound care to prevent infections and improve patient outcomes.

Authors Contribution

Conceptualization: MH
Methodology: IA
Formal analysis: IWA
Writing, review and editing: IWA, KR, KG, SA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Tegegne B, Yimam F, Mengesha Yalew Z, Wuhib M, Mekonnen L, Asmamaw Yitayew Y *et al.* Knowledge and practice of wound care and associated factors among nurses working in South Wollo Zone Government Hospitals, Ethiopia. Chronic Wound Care Management and Research. 2022 Dec: 1-1. doi: 10.2147/CWCMR.S366322.

[2] Macefield RC, Blazeby JM, Reeves BC, King A, Rees J, Pullyblank A *et al.* Remote assessment of surgical site infection (SSI) using patient-taken wound images: development and evaluation of a method for research and routine practice. Journal of Tissue Viability. 2023 Feb; 32(1): 94-101. doi: 10.1016/j.jtv.2023.01.001.

[3] Gould D. Causes, prevention and management of surgical site infection. Nursing Standard (through 2013). 2012 Jul; 26(47): 47. doi: 10.7748/ns.26.47.47.s51.

[4] Whitby M, McLaws ML, Collopy B, Looke DF, Doidge S, Henderson B *et al.* Post-discharge surveillance: can patients reliably diagnose surgical wound infections?. Journal of Hospital Infection. 2002 Nov; 52(3): 155-60. doi: 10.1053/jhin.2002.1275.

[5] Gillespie BM, Walker R, Lin F, Roberts S, Eskes A, Perry J *et al.* Wound care practices across two acute care settings: A comparative study. Journal of Clinical Nursing. 2020 Mar; 29(5-6): 831-9. doi: 10.1111/jocn.15135.

[6] Chhabra S, Chhabra N, Kaur A, Gupta N. Wound healing concepts in clinical practice of OMFS. Journal of Maxillofacial and Oral Surgery. 2017 Dec; 16: 403-23. doi: 10.1007/s12663-016-0880-z.

[7] Niculescu AG, Georgescu M, Marinas IC, Ustundag CB, Bertesteanu G, Pinteală M *et al.* Therapeutic Management of Malignant Wounds: An Update. Current Treatment Options in Oncology. 2024 Jan; 25(1): 97-126. doi: 10.1007/s11864-023-01172-2.

[8] Mukagendaneza MJ, Munyaneza E, Muhawenayo E, Nyirasebura D, Abahuje E, Nyirigira J *et al.* Incidence, root causes, and outcomes of surgical site infections in a tertiary care hospital in Rwanda: a prospective observational cohort study. Patient Safety in Surgery. 2019 Dec; 13: 1-8. doi: 10.1186/s13037-019-0190-8.

[9] Seid MA, Mengstie MA, Teshome AA, Abdu K, Abtew YD. Post-operative site infections among surgical

DOI: https://doi.org/10.54393/pbmj.v7i07.1118

patients at Southern Ethiopia: A prospective cohort study. Heliyon. 2024 Apr; 10(7). doi: 10.1016/j.heliyon.2024.e28650.

[10] Shiferaw WS, Aynalem YA, Akalu TY, Petrucka PM. Surgical site infection and its associated factors in Ethiopia: a systematic review and meta-analysis. BioMed Central Surgery. 2020 Dec; 20: 1-5. doi: 10.1186/s12893-020-00764-1.

[11] Shaheen SR and Hawash MA. Assessment of Nurses' Knowledge and Practices Regarding Prevention of Surgical Site Infection. Egyptian Journal of Nursing and Health Sciences. 2021 Sep; 2(2): 176-97. doi: 10.21608/ejnhs.2021.234371.

[12] Gizaw MA, Negawo MK, Bala ET, Daba DB. Knowledge, practice, and associated factors towards postoperative wound care among nurses working in public hospitals in Ethiopia: A multicenter cross-sectional study in low resource setting area. Health Science Reports. 2022 Jul; 5(4): e677. doi: 10.1002/hsr2.677.

[13] Choi JS, Jo S, Park S. Awareness and Practice of Wound Disinfection among Wound Care Nurses in Korea. Journal of Wound Ostomy & Continence Nursing. 2013 Sep; 40(5): 475-80. doi: 10.1097/WON.0b013e3182a21e26.

[14] Heerschap C, Nicholas A, Whitehead M. Wound management: investigating the interprofessional decision-making process. International Wound Journal. 2019 Feb; 16(1): 233-42. doi: 10.1111/iwj.13017.

[15] Berhe H, Abebe YT, Brhan HT, Ibrahim S, Tesfay K. Knowledge, Practice and Associated Factors Regarding Postoperative Wound Care of Hospitalized Pediatric Patients in Public Hospitals of Mekelle. International Journal of Development Research. 2018 Sep; 08(10): 23592-603.

[16] Famakinwa TT, Bello BG, Oyeniran YA, Okhiah O, Nwadike RN. Knowledge and practice of post-operative wound infection prevention among nurses in the surgical unit of a teaching hospital in Nigeria. International Journal of Basic, Applied and Innovative Research. 2014 Jun; 3(1): 23-8.

[17] Javed S, Parveen K, Afzal M, Gillani SA. Awareness, Behavior, and Practices of Nurses related to Nursing Ethics, in tertiary care Hospitals of Lahore, Pakistan. International Journal of Health Medicine and Nursing Practice. 2021 Jun; 3(3): 1-12. doi:10.47941/ijhmnp.597.

[18] Sadaf S, Inayat S, Afzal M, Hussain M. Nurse's knowledge and practice regarding prevention of surgical site infection at allied hospital Faisalabad. International Journal of Scientific & Engineering Research. 2018 May; 9(5): 351-69.

[19] Woldegioris T, Bantie G, Getachew H. Nurses' knowledge and practice regarding prevention of surgical site infection in Bahir Dar, Northwest Ethiopia. Surgical Infections. 2019 Jan; 20(1): 71-7. doi: 10.1089/sur.2018.081.

[20] Teshager FA, Engeda EH, Worku WZ. Knowledge, practice, and associated factors towards prevention of surgical site infection among nurses working in Amhara regional state referral hospitals, Northwest Ethiopia. Surgery Research and Practice. 2015 Dec; 2015(1): 736175. doi: 10.1155/2015/736175.

DOI: https://doi.org/10.54393/pbmj.v7i07.1042

PAKISTAN BIOMEDICAL JOURNAL

https://www.pakistanbmj.com/journal/index.php/pbmj/index

ISSN (P): 2709-2798, (E): 2709-278X

Volume 7, Issue 7 (July 2024)

Original Article

OPEN ACCESS

Prevalence of Carpal Tunnel Syndrome among Tailors

Somiya Asif[1*], Ayesha Firdous[2], Rabiya Tahir[2], Amna Shabbir[2], Abdul Rehman[2] and Muhammad Ali Qasim[2]

[1]Department of Physiotherapy, Ibadat International University, Islamabad, Pakistan

[2]Department of Physiotherapy, Margalla Institute of Health Sciences, Rawalpindi, Pakistan

ARTICLE INFO

Keywords:

Boston Carpal Tunnel Syndrome Questionnaire, Carpal Tunnel Syndrome, Median Nerve, Tailors

How to Cite:

Asif, S., Firdous, A., Tahir, R., Shabbir, A., Rehman, A., & Qasim, M. A. (2024). Prevalence of Carpal Tunnel Syndrome among Tailors: Prevalence of Carpal Tunnel Syndrome. Pakistan BioMedical Journal, 7(07). https://doi.org/10.54393/pbmj.v7i07.1042

***Corresponding Author:**

Somiya Asif

Department of Physiotherapy, Ibadat International University, Islamabad, Pakistan

sumaiya.asif@gmail.com

Received Date: 15th February, 2024

Acceptance Date: 14th July, 2024

Published Date: 31st July, 2024

ABSTRACT

Carpal tunnel syndrome is the most prevalent musculoskeletal disorder and a common neuropathic illness. This condition is because of long-term median nerve compression due to repetitive hand movements. Some occupations have a higher risk of acquiring Carpal tunnel syndrome given that they call for continuous wrist use during work hours. Tailors are far more likely to develop Carpal tunnel syndrome as they repeatedly perform motions that applies continuous vibration, repetitive stress and force on the wrist. **Objective:** To determine prevalence of carpal tunnel syndrome among tailors. **Methods:** Cross- sectional study design and non-probability convenience sampling technique was used to collect data from twin cities (Rawalpindi and Islamabad). After synopsis approval, the duration of the study was 6 months. 377 tailors from twin cities were selected. Self-structured and Boston Carpal Tunnel Syndrome Questionnaire (BCTQ) were used. Assessment of symptoms severity and functional limitations of tailors with carpal tunnel syndrome was also done. **Results:** The prevalence of carpal tunnel syndrome among tailors in twin cities was 24.9%. There were (94.8%) males and (5.2%) were females. The tailors having age between 26-30 years were mostly affected with working experience of 15.99 ± 10.81 years. Most of the participants 207 (59.3) worked 6 days in a week. According to Boston Carpal Tunnel Syndrome Questionnaire (BCTQ), there was mild level of symptoms severity and functional limitations were present in tailors suffering from carpal tunnel syndrome. **Conclusions:** This study concluded that prevalence of carpal tunnel syndrome was found in tailors. There was mild level of functional limitations as well as symptom severity among tailors in twin cities.

INTRODUCTION

Carpal Tunnel Syndrome is a common neuropathic disorder in the hand caused by increased pressure on the median nerve exhibiting symptoms like pain, numbness, or tingling on the volar surface of the thumb, index finger, middle finger, and half of the ring finger with difficulty in hand movements. It commonly coincides with symptoms that occur at night, such as hand numbness and pain. It also can cause weakness and loss of grip strength [1]. Carpal tunnel syndrome is diagnosed on both subjective and objective assessment based on symptoms such as numbness, tingling, and pain in the fingers within a minute [2]. EMG electromyograms, which are used as the Gold Standard test to evaluate muscle injury, capture the electrical activity of the afflicted muscles both when they are tensed and at rest. Due to its great specificity in measuring electrical impulses through nerves, nerve conduction studies (NCS) are a confirmatory test. In addition, Tinel's sign and Phalen's test, which involves flexing the wrist forcefully, are used to confirm the presence of carpal tunnel syndrome [2]. The Phalen test's specificity ranges from 40% to 98%, while its sensitivity is 67% to 83%. Tinel's test has a range of 48% to 73% for sensitivity and 30% to 94% for specificity [3]. Needle EMG can also be used to document axon loss in CTS, but it is also typically required to diagnose polyneuropathy, proximate median nerve damage, and radiculopathy of the cervical spine. These conditions can occur instead of or in addition to CTS. To document axonal loss, patients with lowered amplitude of the median compound muscle action potential (CMAP), atrophy of the thenar eminence, or weakening of the Androgen binding protein (APB) may benefit from a needle examination. Neural EMG of the median-innervated thenar muscles is the only method available in certain circumstances to record axonal loss [4]. Although, CTS

DOI: https://doi.org/10.54393/pbmj.v7i07.1042

diagnosis is primarily associated with clinical signs, its confirmation is eased by multiple methods including magnetic resonance imaging and ultrasonography. In conservative approach to management of CTS symptoms there exists few measures that could be easily implemented [5]. Van Meir and De Smet extended this work by conducting a meta-analysis of 163 patient data from 35 reported articles, many of which are small case series or individual case reports. In adults, CTS is usually diagnosed clinically and ELECTRODIAGNOSIS can be performed to show the presence of CTS. Clinical indicators of adult CTS are uncommon in CTS secondary to MPS, with difficulty with fine motor tasks being the most common finding [6]. Two kinds of CTS management are used. The first is Conservative and the second one is surgical treatments. Usually, the first treatment is received by patients with mild to moderate symptoms. nonsteroidal anti-inflammatory drugs (NSAIDs), vitamins B6 and B12, the mobilizations of carpal bone, hand splints, corticosteroids and yoga are few potential treatments. Exercise, magnetic therapy, chiropractic and splint treatment are some more conservative therapeutic approaches that haven't substantially decreased symptomatology when compared to controls [3]. The nonsurgical CTS treatment may be provided by a number of different physicians, such as primary care providers, physiatrists, neurologists, and surgeons, which provides a potential for providing nonevidence-based care. The nonsurgical treatment of carpal tunnel syndrome (CTS) consists of multiple modalities: Other treatments were splitting, cortisone injections, hand therapy, and systemic medications [7]. The carpal tunnel area is increased using gradual stretching exercises in conjunction with the special pneumatic and dynamic hand traction tool known as C-TRAC. The hand experiences a "3-point" force of action when the air bladder of the device is inflated, and the apparatus is on the hand. Transverse attachment of carpal ligament is subsequently stretched as a result. The distance between the trapezium and the hook of hamate, as well as the distance between the scaphoid and the pisiform bones, increased by as much as 3 mm according to X-rays are taken with C-TRAC and as well as without the C-TRAC in place [7]. A surgical treatment called a carpal tunnel release (CTR) is performed to treat CTS. The transverse attachment of carpal ligament (TCL) is cut during this treatment, so the carpel tunnel is widened and pressure is released. Between 70 and 90 percent long term success is seen in patients who receives CTR. CTR is a suitable therapy option for diabetic people with CTS and peripheral neuropathy [3]. The UK Royal College of Surgeons provides patient information and advice on returning to work after carpal tunnel release surgery [8]. Thus, the underlying structure of the BCTQ may include, at least, three factors that may be labeled as Functionality, Paresthesia and Pain domains. Two log-linear subscales may be proposed: subscale 1 consists of the Factor-Functionality and the second subscale which includes the Factor-Paresthesia and Factor-Pain under a bifactor model. The degree of correlation between Neurophysiologic and clinical severity classification system is extremely low [9]. The prevalence in normal adult general population is about 5% in women and 2% in men [2]. The aims of managing CTS are to reduce symptoms and restore normal usage of the hand and fingers. At present, the most widely used nonsurgical management everywhere is the use of a rigid wrist brace at night sometimes with other interventions [10]. There are considerable possibilities to find the connection with systemic, anatomical, idiopathic, and ergonomic factors since age, sex, and even BMI could be the risk factors of CTS in certain patients [11]. Another condition that has been associated with CTS is BMI, where the excess of 30 is referred to as obesity; Several studies have however found a connection between BMI and CTS; still, its correlation with other anthropometric factors such as the waist size and size of the wrist remain unknown According to a study 3% to 6% of CTS prevalence was found in general population [12]. According to a previous study conducted in Riyadh, Saudi Arabia, 20% of diabetic patients experience CTS, compared to nearly 62% of pregnant women [13]. A global prevalence of about 4% and 5% of the population is affected by CTS people and the most vulnerable are those in the 40-60 years age bracket [14]. Higher rates of CTS events are also related to the longevity of workers, and with more instances of factors for risk such as diabetes and pregnancies too [15]. As per existing literature, previous international studies have been done to find out the relationship between types of workers and CTS, but no study has been done on tailors. Due to nature of their job, repetitive hand movements cause an increase pressure on the wrist which ultimately could result in median nerve entrapment. Improving knowledge of prophylaxis and raising awareness could reduce the occurrence of CTS.

The study aimed to find out prevalence of CTS among tailors.

METHODS

Descriptive cross-sectional study and convenience (non-probability) sampling technique was employed to collect data from twin cities i.e., Islamabad and Rawalpindi. The duration of study was from February 2023 to June 2023. Ethical approval was issued by the ethical committee of Margalla Institute of Health Sciences, Rawalpindi (Ref No: AF/183/23). A total of 377 participants with CTS were taken into consideration by using Raosoft. Data were collected after taking written informed consent from all participants. Participants were secured regarding confidentiality and were granted the right to seek any detail about the study. Both male and female tailors with age 18 years or above and

DOI: https://doi.org/10.54393/pbmj.v7i07.1042

having working experience of minimum one year and working at least 3 days per week were included in the study while participants were excluded if they have any wrist trauma i.e. wrist fracture in the last 3 months, systemic diseases, pregnancy at that time, wrist arthritis, diabetes, thyroid gland disease. Study subjects were interviewed through a self-structure questionnaire that included information regarding demographics, presence of CTS, working experience and working days. The English version of Boston Carpal Tunnel Syndrome Questionnaire (BCTQ) was used. The severity of CTS symptoms and functional limitations was evaluated by Boston Carpal Tunnel Syndrome Questionnaire BCTQ. The BCTQ form consist of 2 parts, Symptom Severity Scale SSS with 11 items which is scored on a Likert measure of 1-5 and the Functional Status Scale FSS with 8 items which is scored from 1-5 with 1 as no trouble and 5 as troublesome. Data were entered and analyzed using SPSS-26.0. Frequency and percentages were calculated for qualitative data. Descriptive analysis was conducted.

RESULTS

Total 377 participants were included in this cross-sectional study. Out of which 28 participants were excluded as they were not fulfilling eligibility criteria. As 16 were having diabetes, 5 having wrist fracture in last three months and 1 was diagnosed with wrist arthritis, 2 female were pregnant, 2 participants were suffering from systemic disease and 2 were suffering from thyroid gland disease. So, final data were analyzed from 349 participants. The demographics and the participant`s characteristics have been mentioned (Table 1).

Table 1: Demographic Characteristics of Participants

Characteristics	Frequency (%)
Age Range	
Up to 20	4 (1.1)
21 to 25	32 (9.2)
26 to 30	82 (23.5)
31 to 35	55 (15.8)
36 to 40	57 (16.3)
41 to 45	46 (13.2)
46 to 50	30 (8.6)
50 above	43 (12.3)
Gender	
Male	331 (94.8)
Female	18 (5.2)
Working Days	
3	8 (2.3)
4	16 (4.6)
5	30 (8.6)
6	207 (59.3)
7	88 (25.2)
Marital Status	
Single	50 (14.3)
Married	299 (85.7)
Extremity Involved	
Right	86 (24.6)
Left	2 (0.6)

Out of 349 participants 87 (24.9%) participants had carpal tunnel syndrome and 262 (75.1%) had no carpal tunnel syndrome (Table 2).

Table 2: Prevalence of CTS among Tailors

Variables	Frequency (%)
With CTS	87 (24.9%)
Without CTS	262 (75.1%)
Total	349

Out of 349 participants 262 (75.1%) were asymptomatic, 51 (14.6%) were with mild symptoms, 28 (8.0%) were with moderate symptoms, 7 (2.0%) were with severe symptoms and 1 (0.3%) was with very severe symptoms (Figure 1).

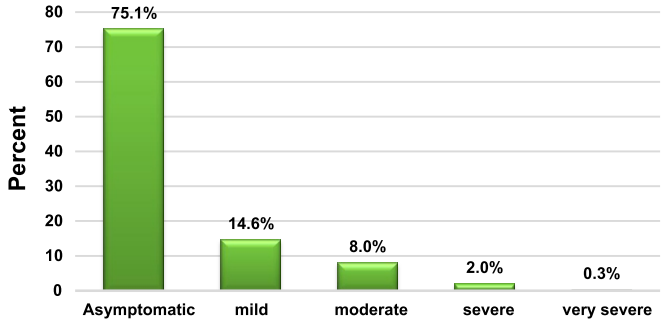

Figure 1: Graphic representation of Boston Symptom Severity Scale.

According to Functional status scoring, out of 349 participants 264 (75.6%) were asymptomatic, 64 (18.3%) were with mild functional limitation, 15 (4.3%) were with moderate functional limitation and 6 (1.7%) were with severe functional limitation. So, our result shows that most of the participants having CTS were with mild functional limitations (Figure 2).

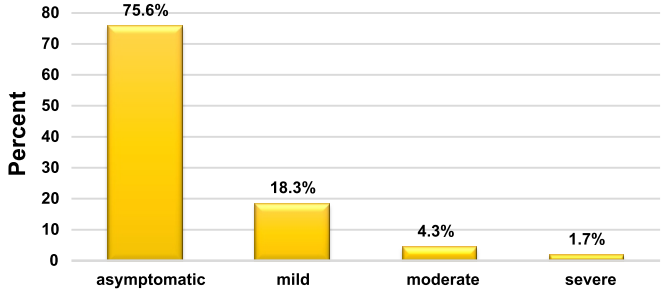

Figure 2: Graphic representation of Boston Functional Status Scale

DOI: https://doi.org/10.54393/pbmj.v7i07.1042

DISCUSSION

Carpal Tunnel Syndrome (CTS) is the utmost widespread musculoskeletal pathology caused by compression of the median nerve as it travels through the carpal tunnel at the wrist. Mechanical injury, increased pressure, and ischemia of the median nerve in the carpal tunnel are all contributing factors to carpal tunnel syndrome. 90% of all neuropathy occurrences are CTS, making it the most frequent entrapment of neuropathy. A history of repeated wrist activities, such as typing, vibrating force and sewing, are the most frequent cause of CTS [16]. According to research, the risk of CTS is higher for a number of vocations, especially those that demand constant or repeated hand motion. Worker productivity is lost as a result of carpal tunnel syndrome and other musculoskeletal system problems that can arise from a variety of vocations. The current study showed prevalence of CTS in tailors among twin cities of Pakistan was (24.9%), in contrast to other labor workers as a study conducted in Bangkok on Motorcycle taxi drivers by Danaisawat and Jiamjarasrangsi, had a 20.1% CTS prevalence rate [17]. Among other professions, the most influential factors correlating with CTS development were grocery store workers, hairdressers, telephone operators, and blue-collar workers [18]. The Tool used in current study BCTQ showed most of participants with CTS had mild symptoms severity (8.02%) and functional limitation (18.33%). In 2015, Banerjee *et al.*, conducted research on musculoskeletal morbidity among tailors working in a Kolkata slum. The purpose of this study was to ascertain the prevalence of musculoskeletal disorders among tailors and the factors that are linked to these disorders. In a cross-sectional study, 110 out of the 383 local tailors were selected through simple random sampling, and the tailors were approached at their place of employment to participate in interviews. 65.45% of tailors have musculoskeletal conditions. In this study, disorders affecting people over 45 years of age were discovered, and women were more likely than men to experience musculoskeletal morbidity [19]. This study indicates prevalence of CTS in tailors with minimum working experience of 1 year. The present study shows common age group of participants having age between 26 to 30 years (15.7%), contrast to a previous study conducted by Sitompul in North Jakarta common age group was 35 to 40 years of participants (53.7%) [20]. Due to non-probability convenience sampling, there is male gender dominancy (94.8%) in this study in contrast to previous study in which female gender was more dominant (68.5%). In our study among all the respondents, (94.8%) were male and (5.2%) were female.

CONCLUSIONS

This study concluded the prevalence of CTS was found among tailors with mild level of symptom severity and functional limitations. Moreover, there was a higher proportion of males.

Authors Contribution

Conceptualization: AF, MAQ
Methodology: RT, AF
Formal analysis: SA
Writing, review and editing: AR, AS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Demiryurek BE and Aksoy Gündoğdu A. Prevalence of Carpal Tunnel Syndrome and Its Correlation with Pain amongst Female Hairdressers. International Journal of Occupational Medicine and Environmental Health. 2017 Jul; 31(3): 333-9. doi: 10.13075/ijomeh.1896.01068.

[2] Nadiger R, Shaikh S, Abichandani S. Carpal tunnel syndrome: An Occupational Hazard. Indian Journal of Oral Sciences. 2012 Sep; 3(3): 138. doi: 10.4103/0976-6944.111175.

[3] Zamborsky R, Kokavec M, Simko L, Bohac M. Carpal Tunnel Syndrome: Symptoms, Causes and Treatment Options. Literature Review. Ortopedia Traumatologia Rehabilitacja. 2017 Jan; 19(1): 1-8. doi: 10.5604/15093492.1232629.

[4] Werner RA and Andary M. Electrodiagnostic Evaluation of Carpal Tunnel Syndrome. Muscle & nerve. 2011 Oct; 44(4): 597-607. doi: 10.1002/mus.22208.

[5] Malakootian M, Soveizi M, Gholipour A, Oveisee M. Pathophysiology, Diagnosis, Treatment, and Genetics of Carpal Tunnel Syndrome: A Review. Cellular And Molecular Neurobiology. 2023 Jul; 43(5): 1817-31. doi: 10.1007/s10571-022-01297-2.

[6] Billakota S and Hobson-Webb LD. Standard Median Nerve Ultrasound in Carpal Tunnel Syndrome: A Retrospective Review of 1,021 Cases. Clinical Neurophysiology Practice. 2017 Jan; 2: 188-91. doi: 10.1016/j.cnp.2017.07.004.

[7] Billig JI and Sears ED. Nonsurgical Treatment of Carpal Tunnel Syndrome: A Survey of Hand Surgeons. Plastic And Reconstructive Surgery-Global. 2022 Apr; 10(4): 1-6. doi: 10.1097/GOX.0000000000004189.

[8] Newington L, Harris EC, Walker-Bone K. Carpal Tunnel Syndrome and Work. Best Practice &

DOI: https://doi.org/10.54393/pbmj.v7i07.1042

Research Clinical Rheumatology. 2015 Jun; 29(3): 440-53. doi: 10.1016/j.berh.2015.04.026.

[9] Mendoza-Pulido C and Ortiz-Corredor F. Measurement Properties of The Boston Carpal Tunnel Questionnaire in Subjects with Neurophysiological Confirmation of Carpal Tunnel Syndrome: A Rasch Analysis Perspective. Quality of Life Research. 2021 Sep; 30(9): 2697-710. doi: 10.1007/s11136-021-02860-y.

[10] Atroshi I, Tadjerbashi K, McCabe SJ, Ranstam J. Treatment of Carpal Tunnel Syndrome with Wrist Splinting: Study Protocol for A Randomized Placebo-Controlled Trial. Trials. 2019 Dec; 20: 1-1. doi: 10.1186/s13063-019-3635-6.

[11] Cazares-Manríquez MA, Wilson CC, Vardasca R, García-Alcaraz JL, Olguín-Tiznado JE, López-Barreras JA *et al.* A Review of Carpal Tunnel Syndrome and Its Association with Age, Body Mass Index, Cardiovascular Risk Factors, Hand Dominance, And Sex. Applied Sciences. 2020 May; 10(10): 2-31. doi: 10.3390/app10103488.

[12] Komurcu HF, Kilic S, Anlar O. Relationship of Age, Body Mass Index, Wrist and Waist Circumferences to Carpal Tunnel Syndrome Severity. Neurologia Medico-Chirurgica. 2014; 54(5): 395-400. doi: 10.2176/nmc.oa2013-0028.

[13] Alhusain FA, Almohrij M, Althukeir F, Alshater A, Alghamdi B, Masuadi E et al. Prevalence of Carpal Tunnel Syndrome Symptoms Among Dentists Working in Riyadh. Annals of Saudi Medicine. 2019 Mar; 39(2): 104-11. doi: 10.5144/0256-4947.2019.07.03.1405.

[14] Genova A, Dix O, Saefan A, Thakur M, Hassan A. Carpal Tunnel Syndrome: A Review of Literature. Cureus. 2020 Mar; 12(3). doi: 10.7759/cureus.7333.

[15] Chammas M, Boretto J, Burmann LM, Ramos RM, Santos Neto FC, Silva JB. Carpal Tunnel Syndrome-Part I (Anatomy, Physiology, Etiology and Diagnosis). Revista Brasileira De Ortopedia. 2014 Oct; 49(5): 429-36. doi: 10.1016/j.rboe.2014.08.001.

[16] Lalchanzani JA and Rosita R. Women with Carpal Tunnel Syndrome Caused by being Overweight and Her Occupation as a Tailor. Jurnal Ilmu Kedokteran Keluarga. 2022 Dec; 1(2): 55-63.doi: 10.56674/altera.v1i2.11.

[17] Danaisawat T and Jiamjarasrangsi W. Prevalence Survey of Carpal Tunnel Syndrome and Its Related Factors by Using CTS-6 Evaluation Tools among Motorcycle Taxi Drivers in Bangkok Area. Royal Thai Army Medical Journal. 2019 Dec; 72(4): 217.

[18] Nowak W, Znamirowska P, Szmigielska N, Zemsta K, Miśkiewicz J, Plata H *et al.* Risk factors for Carpal Tunnel Syndrome. Journal of Pre-Clinical & Clinical Research. 2023 Jul; 17(3). doi: 10.26444/jpccr/168559.

[19] Banerjee S, Bandyopadhyay L, Dasgupta A, Paul B, Chattopadhyay O. Work Related Musculoskeletal Morbidity among Tailors: A Cross-Sectional Study in a Slum of Kolkata. Kathmandu University Medical Journal. 2016 Oct; 14(56): 305-10.

[20] Sitompul YR. The Relationship between Types of Workers and Incidence of Carpal Tunnel Syndrome in Tailors at the Garment Factory North Jakarta. International Journal of Health Sciences and Research. 2022 May; 12(5): 282-9. doi: 10.52403/ijhsr.20220529.

DOI: https://doi.org/10.54393/pbmj.v7i07.1098

PAKISTAN BIOMEDICAL JOURNAL
https://www.pakistanbmj.com/journal/index.php/pbmj/index
ISSN (P): 2709-2798, (E): 2709-278X
Volume 7, Issue 7 (July 2024)

Original Article

OPEN ACCESS

The Association of Anti-CCP Positivity with Extra-Articular Manifestations in Patients with Rheumatoid Arthritis

Najib Ullah[1], Abdul Waris[2], Alam Zeb[1*], Muheebur Rehman[3], Shawkat Ali[4] Muhammad Imran[1] and Zahid Muhammad Wazir[5]

[1]Department of Rheumatology, Khyber Teaching Hospital Peshawar, Peshawar, Pakistan
[2]Department of Rheumatology, Lady Reading Hospital Peshawar, Peshawar, Pakistan
[3]Department of Allied Health and Biological Science, Abasyn University Peshawar, Peshawar, Pakistan
[4]Department of Pathology, Khyber Teaching Hospital Peshawar, Peshawar, Pakistan
[5]Department of Medicine, Khyber Teaching Hospital Peshawar, Peshawar, Pakistan

ARTICLE INFO

Keywords:
Rheumatoid Arthritis, Anti-Cyclic Citrullinated Peptide Positivity, Autoimmune Diseases, RA Disease Activity Score

How to Cite:
Ullah, N., Waris, A., Zeb, A., Rehman, M., Ali, S., Imran, M., & Muhammad wazir, Z. (2024). The Association of Anti-CCP Positivity with Extra-Articular Manifestations in Patients with Rheumatoid Arthritis: Anti-Cyclic Citrullinated Peptide Positivity and Extra-Articular Rheumatoid Arthritis. Pakistan BioMedical Journal, 7(07). https://doi.org/10.54393/pbmj.v7i07.1098

***Corresponding Author:**
Alam Zeb
Department of Rheumatology, Khyber Teaching Hospital Peshawar, Peshawar, Pakistan
dralamzeba111197@gmail.com

Received Date: 3rd May, 2024
Acceptance Date: 27th July, 2024
Published Date: 31st July, 2024

ABSTRACT

Rheumatoid Arthritis (RA) is an autoimmune inflammatory disorder that primarily affects the joints. **Objective:** To examine association between anti-cyclic citrullinated peptide and extra-articular manifestation of Rheumatoid arthritis. **Methods:** It was a descriptive cross-sectional study in the Department of Rheumatology outpatient Khyber Teaching Hospital in Peshawar from 13th April 2023 to 13th September 2023. A descriptive cross-sectional study was conducted on 100 patients diagnosed with rheumatoid arthritis according to ACR/EULAR 2010 criteria at the Rheumatology outpatient department of Khyber teaching hospital in Peshawar from 13th April 2023 to 13th September 2023. Sampling technique was non probability consecutive. Statistical analysis was performed using SPSS version 23.0. **Results:** Our study involved 100 patients diagnosed with rheumatoid arthritis. Majority of the patients were female (90%) with overall mean age was 42.3 ± 10.06 years. The average duration of the disease was 5.9 years, with a mean RA disease activity score of 2.8. Extra-articular manifestations were observed in 84% of the patients, encompassing various symptoms such as anemia, subcutaneous nodules, episcleritis, and interstitial lung disease. Most patients (94%) tested positive for Rheumatoid Arthritis Factor, while 84% tested positive for anti-CCP antibodies. Our analysis revealed significant associations between the presence of extra-articular manifestations and factors such gender distribution, disease activity score and anti-CCP antibody positivity while no significance was noted for factors such as age, Rheumatoid Arthritis Factor and duration of disease. **Conclusions:** Our study concludes that anti-CCP was positively associated with the presence of extra-articular manifestation of Rheumatoid Arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is commonly associated with the presence of rheumatoid factor (RF), a chronic autoimmune illness that affects both the joints and other regions of the body. Early diagnosis and treatment with disease modifying ant rheumatic drugs (DMARDs) are essential for controlling the disease and preventing joint damage. Finding a trustworthy serological marker or markers is therefore essential for an early and precise diagnosis. Although RF can be positive for a number of viral and autoimmune disorders, its sensitivity for diagnosing RA is only moderate [1]. Rheumatoid arthritis (RA) is a serious health concern; research indicates that it affects 0.5% to 1% of the world's population. Following osteoarthritis and gout as the top causes of disability, RA is listed as well [2]. According to earlier data from Pakistan, Karachi has a 0.142% prevalence of rheumatoid arthritis (RA), with a higher incidence rate in women [3]. One of the classification criteria recommended by the American College of Rheumatology (ACR) is the IgM rheumatoid factor (RF), which is frequently used to diagnose

DOI: https://doi.org/10.54393/pbmj.v7i07.1098

rheumatoid arthritis (RA) [4]. Research has demonstrated that autoantibody positivity can be detected up to twenty years before the clinical manifestations of rheumatoid arthritis (RA). Additionally, studies have shown that anti-cyclic citrullinated peptide (anti-CCP) might be positive even in patients with. RA who do not have an RF test. Anti-CCP may therefore be regarded as the recommended course of action for patients who are suspected of having RA [5]. The happening of Reports has indicated that between 17.8% and 40.9% of patients with rheumatoid arthritis (RA) experience extra-articular symptoms (ExRA) [6]. Male gender, certain genetic markers such the HLA-DRB1*04 subtype, antinuclear antibodies (ANA), positive rheumatoid factor (RF), and anti-CCP antibodies, as well as various environmental variables, particularly smoking, are all linked to exaggerated RA (ExRA) in people with RA [7]. In clinical practice, it is essential to recognize and acknowledge the existence of ExRA because it is linked to increased rates of morbidity and mortality [8]. Research findings indicated that patients with ExRA had a 2.5-fold worse mortality rate than those with RA without ExRA [8]. Along with antinuclear antibodies (ANA) and rheumatoid factor (RF), other factors that may be related to ExRA have also been studied: anti-cyclic citrullinated peptide (anti-CCP) antibodies. With frequencies ranging from 55% to 69%, these antibodies are commonly detected in the serum of RA patients [9]. Even more reliable than rheumatoid factor, anti-CCP antibodies are highly specific for RA and indicate the severity of the illness [10]. ExRA, such as serositis and pulmonary fibrosis, has been associated with elevated levels of anti-CCP2 antibodies [11]. A study conducted on menopausal women diagnosed with RA showed that patients with ExRA had a significantly higher frequency of osteoporosis compared to RA patients without these manifestations. This was determined through a retrospective analysis of patient data [12]. SE (Shared Epitope) alleles have been found to be associated with an increased risk for RA, and studies have shown that the presence of SE alleles in RA patients is associated with the presence of anti-CCP antibodies. Interestingly, anti-CCP antibodies have been detected in both SE-positive and SE-negative RA patients, indicating that the presence of SE alleles is not a prerequisite for the development of anti-CCP antibodies [5]. To examine association between anti-cyclic citrullinated peptide and extra-articular manifestation of Rheumatoid arthritis.

METHODS

Descriptive cross sectional study was conducted on patients diagnosed with RA at outpatient department, Rheumatology, Khyber teaching hospital Peshawar, from 13th April 2023 to 13th Sep 2023 and data collection letter was obtained with Reference Number: 5146-5/CRD/KTH. Total of 100 patients were included in the study. 33 patients were excluded based on exclusion criteria. The sampling technique was nonprobability consecutive. Sample size was calculated by WHO sample size calculator. Informed verbal and written consent were taken from every patient. Age, gender, disease duration, and rheumatoid arthritis Disease activity scores 28 (DAS-28) were among the clinical and demographic information gathered from each patient after a thorough assessment. A rheumatologist's clinical evaluations and medical imaging were used to gather information on the existence of ExRA. A pre-made questionnaire was used to collect the data, which was then stored in a safe database for analysis. The inclusion criteria include: 1) individuals diagnosed with rheumatoid arthritis as adults (older than 16 years) based on 2010 selection criteria of the American College of Rheumatology/ European League against Rheumatism (ACR/EULAR); patients tested with anti-CCP antibodies; individuals with history of cardiovascular conditions, interstitial lung disease, and rheumatoid nodules undergo assessment for extra-articular rheumatoid arthritis (ExRA). The exclusion criteria include individuals with medical history of autoimmune diseases, lung conditions like COPD or asthma and patients refused to take part in study. Software for statistical analysis was SPSS version 23.0. In addition to Descriptive statistics, to investigate the relationship between gender, Anti-CCP positivity, and DAS 28, bivariate analysis was employed, and ExRA using appropriate statistical tests, such as chi-square tests or t-tests. A P-value of less than 0.05 will be considered statistically significant for all analyses.

RESULTS

The 100 patients, n=90(90%) were female while n=10(10%) were male. The patients' average age was 42.3 (SD±10.06). The patient's mean illness duration was 5.9 (SD±3.2). The mean RA disease activity score was 2.8(SD±0.54). According to Table 1, patients were divided into age categories, with 55% of patients falling in the 16-40 years range and the remaining 45% being 41 years or above. 84% of patients exhibited ExRA manifestations, while the remaining 16% did not. Further details regarding the type of extra articular manifestations are provided, with varying frequencies such as anemia (6%), anemia with subcutaneous nodules (11%), episcleritis (5%), interstitial lung disease (12%), and others. The table also includes information on the Rheumatoid Arthritis Factor, where 94% were positive and 6% were negative for it. Lastly, the Anti-CCP results indicate that 84% tested positive, while 16% tested negative (Table 1).

Table 1: Clinicodemographic Characteristics among study participants

Variables	Categories	N (%)
Gender of Patient	Male	10 (10.0)
	Female	90 (90.0)
	Total	100 (100.0)

DOI: https://doi.org/10.54393/pbmj.v7i07.1098

Age (Years)	16-40yrs	55 (55.0)
	41 or above	45 (45.0)
	Total	100 (100.0)
Presence Extra	Yes	84 (84.0)
	No	16 (16.0)
	Total	100 (100.0)
Type of Extra Articular Manifestation	Anemia	6 (6.0)
	Anemia	22 (22.0)
	Anemia, Subcutaneous Nodule	11 (11.0)
	Anemia, Pleural Effusion	5 (5.0)
	Anemia, Subcutaneous Nodule	6 (6.0)
	Episcleritis	5 (5.0)
	ILD	12 (12.0)
	None	16 (16.0)
	Pericarditis	5 (5.0)
	Scleritis	6 (6.0)
	Subcutaneous Nodule	6 (6.0)
	Total	100 (100.0)
Rheumatoid Arthritis Factor	1	94 (94.0)
	2	6 (6.0)
	Total	100 (100.0)
Anti CCP Results	Positive	84 (84.0)
	Negative	16 (16.0)
	Total	100 (100.0)

The table 2 provided a detailed summary of the variables and their relationships within the study. In the context of the existence of non-articular symptoms, in which 84 patients had these manifestations and 16 did not. In age categories, out of the 55 patients aged 16-40 years, 44 had extra-articular manifestations while 11 did not. In the 41 years or above category, 40 patients had manifestations and 5 did not with the value of 0.176. In gender distribution, out of the 10 male patients, 5 had extra-articular manifestations, while out of the 90 female patients, 79 had them with p value of 0.009. Within the group of patients with extra-articular manifestations, 78 patients tested positive for the RA factor, and 6 patients tested negative. On the other hand, among the patients without extra-articular manifestations, none of them had a positive RA factor result with p value of 0.341. Within the group of patients with extra-articular manifestations, 79 patients tested positive for Anti-CCP, indicating anti-CCP antibodies, whereas five patients had negative test results. On the other hand, among the patients without extra-articular manifestations, 11 patients did not have anti-CCP antibodies, and 5 patients tested positive for Anti*CCP. According to duration of disease, patients with shorter disease durations of 1.5 and 2 years exhibited a 100% prevalence of extra-articular manifestations. Further more, patients with disease durations of 5, 7, and 10 years also showed a high occurrence of these manifestations, ranging from 66.7% to 100% (p value 0.14). Among the total 100 patients, varying scores were observed, with 12 patients (12.0%) having a score of 2.00, 33 patients (33.0%) having a score of 2.50, 27 patients (27.0%) having a score of 3.00, 23 patients (23.0%) having a score of 3.50, and 5 patients (5.0%) having a score of 4.00. Notably, for scores of 3.50 and 4.00, no patients without disease activity were observed (P value=0.001).

Table 2: Comparison of Presence of Extra and Different Variables

Variables	Categories	Presence Extra Articular Manifestation		Total	P-Value
		Yes	No		
Age	16-40 Years	44	11	55	0.176
	41 or above	40	5	45	
Total		84	16	100	
Gender	Male	5	5	10	0.009
	Female	79	11	90	
Total		84	16	100	
Rheumatoid Arthritis Factor	Positive	78	16	94	0.341
	Negative	6	0	6	
Total		84	16	100	
Anti CCP Results		Postive	79	5	<0.001
		Negative	5	11	
Total		84	16	100	
Duration of Disease		1.5 years	11	0	0.14
		2	6	0	
		3.00	17	5	
		5.00	12	0	
		7.00	16	0	
		10.00	22	11	
Total		84	16	100	
RA Disease Activity Score		2.00	6	6	0.001
		2.50	28	5	
		3.00	22	5	
		3.50	23	0	
		4.00	5	0	
		2.00	6	6	
Total		84	16	100	

DISCUSSION

Rheumatology has advanced significantly with the addition of the complementary component of the anti-cyclic citrullinated peptide (anti-CCP) antibody assay ACR/EULAR RA classification criteria [1]. The importance the use of the anti-CCP antibody test in the preliminary identification of ExRA has been the subject of debate in the literature [13]. In this study, the majority of patients diagnosed were in the middle age group, with a higher prevalence among females, which is consistent with similar studies [13-16]. The mean disease activity score in our study was 2.8 (SD 0.53), while Sulaiman FN reported a mean disease activity score of 4.74 [13] Another study reported a mean DAS28 of 6 [14]. It was observed a positive association between gender and ExRA in our study, which differs from the findings of ElSharbini DA, who reported no statistical significance [14]. The frequency of ExRA in our

DOI: https://doi.org/10.54393/pbmj.v7i07.1098

study was 84%, whereas other studies reported frequencies of 40.6% and 42.6%, respectively [7, 17]. Anti-CCP antibodies and ExRA were found to be related (p value <0.001). the results of our study differ from the study conducted by De Rycke *et al* [18]. It was found positive association between presence of ExRA and disease activity score, which is line with the finding of Rehman M *et al* [19]. It did not find any significant relationship between the duration of disease and ExRA with a p-value of 0.14. However, a study by Cojocaru M *et al.*, reported a significant association between longer disease duration and the presence of extra-articular manifestations [20]. The study is subjected to few limitations worth mention. First it was cross sectional study. Second, the sample size may be low make a generalize statement. Third, we didn't measure the association between different types of ExRA and antiCCP. Fourth, the consecutive nature of sampling technique might introduce bias in the results. Despite limitations, our study highlights the importance of anti CCP in the management of RA with ExRA.

CONCLUSIONS

This study revealed significant associations between the presence of ExRA and anti-CCP antibody positivity. Furthermore, gender was also positively associated with ExRA along with disease activity score while no association was between duration of disease and presence of extra articular manifestation.

Authors Contribution

Conceptualization: NU, AZ
Methodology: NU, AW, AZ, MR, SA, MI, ZMW
Formal analysis: NU, AZ
Writing, review and editing: NU, AW, AZ

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Mun S, Lee J, Park M, Shin J, Lim MK, Kang HG. Serum biomarker panel for the diagnosis of rheumatoid arthritis. Arthritis Research & Therapy. 2021 Dec; 23:1-0. doi: 10.1186/s13075-020-02405-7.

[2] Goma SH, Razek MR, Abdelbary NM. Impact of rheumatoid arthritis on the quality of life and its relation to disease activity. Egyptian Rheumatology and Rehabilitation. 2019 Oct; 46:304-12. doi: 10.4103/err.err_39_19.

[3] Naqvi AA, Hassali MA, Aftab MT. Epidemiology of rheumatoid arthritis, clinical aspects and socio-economic determinants in Pakistani patients: A systematic review and meta-analysis. The Journal of the Pakistan Medical Association. 2019 Mar; 69(3): 389-98.

[4] Motta F, Bizzaro N, Giavarina D, Franceschini F, Infantino M, Palterer B, Sebastiani GD, Selmi C. Rheumatoid factor isotypes in rheumatoid arthritis diagnosis and prognosis: a systematic review and meta-analysis. RMD open. 2023 Aug 1;9(3):e002817. doi: 10.1136/rmdopen-2022-002817

[5] Iyengar KP, Vaish A, Nune A. Anti-cyclic citrullinated peptide antibody (ACPA) and Rheumatoid arthritis: Clinical relevance. Journal of Clinical Orthopaedics and Trauma. 2022 Jan 1;24: 101729. doi: 10.1016/j.jcot.2021.101729.

[6] Ljung L, Jönsson E, Franklin J, Berglin E, Lundquist A, Rantapää-Dahlqvist S. Incidence and predisposing factors of extra-articular manifestations in contemporary rheumatoid arthritis. European journal of internal medicine. 2024 May 4. doi: 10.1016/j.ejim.2024.04.026

[7] Cheng Q, Chen X, Wu H, Du Y. Three hematologic/immune system-specific expressed genes are considered as the potential biomarkers for the diagnosis of early rheumatoid arthritis through bioinformatics analysis. Journal of translational medicine. 2021 Dec; 19:1-5. doi.org/10.1186/s12967-020-02689-y

[8] Díaz Cuña C, Consani S, Rostan S, Fernández L, Moreira E, Sanmartí R. Rheumatoid arthritis: Extra articular manifestations and comorbidities. Revista Colombiana de Reumatología. 2022 Sep; 29(3): 196-204. doi: 10.1016/j.rcreue.2021.03.003.

[9] Taylor P, Gartemann J, Hsieh J, Creeden J. A systematic review of serum biomarkers anti-cyclic citrullinated peptide and rheumatoid factor as tests for rheumatoid arthritis. Autoimmune diseases. 2011 Sep; 2011(1): 815038. doi: 10.4061/2011/815038.

[10] Yasmin R, Sarker HN. Anti-CCP antibody in rheumatoid arthritis patients and its relation with severity of the disease. BIRDEM Medical Journal. 2022; 12(1): 36-40. doi: 10.3329/birdem.v12i1.57223.

[11] Birtane M, Yavuz S, Taştekin N. Laboratory evaluation in rheumatic diseases. World Journal of Methodology . 2017 Mar 3; 7(1):1. doi: 10.5662/wjm.v7.i1.1

[12] Mitroi A, Ionescu AM. Extra-Articular Manifestations in Rheumatoid Arthritis-Predictors of Osteoporosis. Acta Medica Transilvanica. 2021 Dec; 26(4): 50-2. doi: 10.2478/amtsb-2021-0073.

[13] Sulaiman FN, Wong KK, Ahmad WA, Ghazali WS. Anti-cyclic citrullinated peptide antibody is highly

DOI: https://doi.org/10.54393/pbmj.v7i07.1098

associated with rheumatoid factor and radiological defects in rheumatoid arthritis patients. Medicine. 2019 Mar; 98(12): e14945. doi: 10.1097/MD.0000000000014945.

[14] ElSherbiny DA. Frequency and predictors of extra-articular manifestations in patients with rheumatoid arthritis. The Egyptian Journal of Hospital Medicine. 2019 Jul; 76(5): 4062-7. doi: 10.21608/ejhm.2019.42300.

[15] Shakiba Y, Koopah S, Jamshidi AR, Amirzargar AA, Masoud A, Kiani A *et al* . Anti-cyclic citrullinated peptide antibody and rheumatoid factor isotypes in Iranian patients with rheumatoid arthritis: evaluation of clinical value and association with disease activity. Iranian Journal of Allergy, Asthma and Immunology. 2014 Jun; 13(3): 147-56.

[16] van der Woude D, van der Helm-van AH. Update on the epidemiology, risk factors, and disease outcomes of rheumatoid arthritis. Best Practice & Research Clinical Rheumatology. 2018 Apr; 32(2): 174-87. doi: 10.1016/j.berh.2018.10.005.

[17] Turesson C, O'fallon WM, Crowson CS, Gabriel SE, Matteson EL. Extra-articular disease manifestations in rheumatoid arthritis: incidence trends and risk factors over 46 years. Annals of The Rheumatic Diseases. 2003 Aug; 62(8): 722-7. doi: 10.1136/ard.62.8.722.

[18] De Rycke L, Peene I, Hoffman IE, Kruithof E, Union A, Meheus L *et al*. Rheumatoid factor and anticitrullinated protein antibodies in rheumatoid arthritis: diagnostic value, associations with radiological progression rate, and extra-articular manifestations. Annals Of The Rheumatic Diseases. 2004 Dec; 63(12): 1587-93. doi: 10.1136/ard.2003.017574.

[19] Rehman M, Ahmad U, Waseem M, Ali B, Tariq MI. Effects of exercise training in patients with lung cancer during chemotherapy treatment. The Malaysian Journal of Medical Sciences. 2023 Apr; 30(2): 141. doi: 10.21315/mjms2023.30.2.13.

[20] Cojocaru M, Cojocaru IM, Silosi I, Vrabie CD, Tanasescu R. Extra-articular manifestations in rheumatoid arthritis. Maedica. 2010 Dec; 5(4): 286.