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Original Article

Frequency of Hyperandrogenism in Young Women with Polycystic Ovarian Syndrome

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ABSTRACT

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is the communal disorder of endocrinology in females of reproductive age [1-2]. It is a clinical disorder of heterogeneous type categorized by chronic symptoms of oligo/anovulation and hyperandrogenism. Current variations in criteria of diagnostic methods may have additionally augmented the heterogeneity of the affected females [3-4]. Many females with diagnosis of PCOS in a gynecological department have amenorrhea and seek medical attention mainly for fear that

a menstrual disorder may affect their current or future productiveness. Other medical seeking reasons are overt infertility, anovulatory menometrorrhagia and hair growth. Many females identified later to 18-20 years of age because menstrual disorders and hyperandrogenism are communal signs in regular puberty [5-6]. Though, due to this syndrome heterogeneity, PCOS women may come across in a variety of clinical situations; dermatology, endocrinology and surgery [7]. The PCOS causes various health related

Polycystic ovary syndrome (PCOS) is the communal disorder of endocrinology in females of

reproductive age. Objective: The purpose of the study was to govern the incidence of

hyperandrogenism in young females with polycystic ovarian syndrome. Methods: Total 93

women of age 20 to 35 years with any parity and diagnosed patients of PCOS were included. All patients were assessed biochemically. Serum of testosterone and sex hormone binding globulin analysis was done randomly at any phase of menstrual cycle. Participants were followed in OPD.

Free androgen index was calculated. Score more than 5 labeled as Hyperandrogenemia. Data

were analyzed using SPSS version 21.0. Results: The mean age was 27.22±4.58 years, with range

of 15(20–35) years. Age of 46(49.5%) patients was \leq 27 years and age of 47(50.5%) patients was

>27 years. 41 patients were married and 52 patients were unmarried. The mean parity was

1.41±0.94 with range of 4(0-4). Results of free androgen index score (FAI) showed that overall

mean FAI was 7.80 \pm 5.82 with range of 32.60(0.80–33.40). Total 60 patients were found with hyperandrogenism. Among these patients the mean age was 26.93 \pm 4.68 years. Ages of 32(53.3%) patients were <27 years. participants it was observed that 18 patients were

nulliparous, 3 patients had 1-2 parity, and 2 patients had parity more than 2. Chi square results for

association of hyperandrogenism showed no significant association with age, marital status,

and parity with p>0.05. Conclusion: Hyperandrogenism is an important feature of PCOS. It

mainly comes from the ovaries of women diagnosed with PCOS. The best indicator of

hyperandrogenism is Serum testosterone levels.

risks and obesity is the utmost common than type II diabetes, insulin resistance, and lipid profile abnormalities. Probable health jeopardies comprise related risk factors and cardiovascular diseases. It is not known that all PCOS affected females have a comparable risk of cardiovascular disease and type 2 diabetes [8-9]. The PCOS prevalence in randomized people using the Rotterdam criteria shows that rates seen in young women in their 20s were 6.3% in Sri Lanka1, 217% in southern China, 518% in Thailand and 8% in the UK and the US [10-11]. Two researches from Southern Europe reflect an incidence of around 6.6% in Spain and Greece by means of the criteria of NIH. In Pakistan, Hag found the prevalence of PCOS is 17.6% in women visiting fertility clinics. So, existing data on epidemiology of PCOS support the diversity of ethnicity [12]. Diagnosis is usually grounded on 3 components: (i) ovarian dysfunction as demonstrated by anovulation and oligomenorrhea; (ii) ultrasound shows polycystic ovaries; and (iii) biochemical or clinical indication of hyperandrogenism. One of the most widely used definitions of the NIH from 1990 includes two of them: hyperandrogenemia and anovulatory menstrual cycles. The Rotterdam consensus recommends the exclusion of two of the three components mentioned above, as well as other etiologies. Hyperandrogenemia denotes to elevated androgens levels in the blood. At the consensus working group conference in Rotterdam in 2003, experts reviewed the diagnostic criteria for PCOS and concluded that 2 of the following 3 criteria should be present:[i]anovulation or oligomenorrhea[ii]biochemical factors or clinical signs of hyperandrogenism and [iii] PCOS. These criteria also take into account that other related disorders must be ruled out before making PCOS diagnosis [13]. It has also been reported that insulin resistance or the effects of insulin can lead to hyperandrogenemia in women with PCOS. In addition, there is proposition that the PCOS incidence is advanced in people at higher risk of metabolic diseases and insulin resistance [14]. Many factors associated with PCOS include hyperinsulinism, obesity, diabetes, dyslipidemia, and low birth weight history. In addition, available data on epidemiology of PCOS confirm the diversity of ethnicity on its occurrence [15]. Given the alterations in the prevalence of hyperandrogenism in different ethnic groups, it is important to understand the current extent of hyperandrogenism in our Pakistani population. If my test results show a high prevalence of hyperandrogenism in PCOS patients, these patients will be offered early intervention and future treatment.

METHODS

This cross-sectional study held at department of Obstetrics & Gynae of teaching hospital affiliated with Dow

University of Health Sciences, Karachi. It was conducted for the duration of one Year from 7th May 2017 to 6th May 2018. Total 93 diagnosed patients of PCOS were enrolled. Patients' ages were ranging between 20 to 35 years. Detailed demographics of all subjects were recorded after attaining informed consent in written form. Pregnant women, lactating, history of miscarriage, women taking oral contraceptive pills, hyperprolactinemia, thyroid disorder (confirmed by history), late onset-CAH, testosterone secreting ovarian tumor or adrenal tumor, Cushing's syndrome and women with no other endocrine disorder e.g. adrenal enzymatic deficiency were excluded. Serum analyses for serum testosterone and sex hormone binding globulin was done randomly at any phase of menstrual cycle. Participants of this study were followed along with the reports of advised investigation by the researcher in OPD under the supervision of consultant who has more than 5 years' clinical experience. The following formula was used to determine the free androgen index by dividing serum testosterone with serum sex hormone binding globulin and was labeled as operational definition. All these information was entered on specified fields in the proforma. All statistical calculations were done by using SPSS version 21. The standard deviation and mean were determined for serum testosterone, age and sex hormone binding globulin. Frequency and percentage were calculated for marital status, parity and hyperandrogenism. Stratification with respect to age, parity and marital status was completed. The chi-square test was pragmatic later to post stratification and p-value < 0.05 was deliberated significant.

RESULTS

The mean age was 27.22 ± 4.58 years, with range of 15(20-35) years. The results showed that among study subjects, 41 were married and 52 were unmarried. The descriptive statistics of parity was also evaluated. Results showed that overall mean parity was 1.41 ± 0.94 with range of 4(0-4). The descriptive statistics of free androgen index score (FAI) was also evaluated. Results showed that overall mean FAI was 7.80 ± 5.82 with range of 32.60(0.80-33.40). The results showed that among all study subjects, 60 women were found with hyperandrogenism, and 33 had no findings of hyperandrogenism. The percentages are presented in Figure 1.



Figure 1: Frequency of Hyperandrogenism Post stratification it was observed that among 60 patients

who were found with hyperandrogenism, ages of 32 patients were \leq 27 years and age of 28 patients were >27 years, also presented in Table No 2. The chi square test results presented no substantial relation amid hyperandrogenism and age with p>0.05.

Age (Years)	Hyperandrogenism		Total	P-Value
	Yes (n=60)	No(n=33)	Total	P-value
≤ 27 years (n=46)	32	14	46	
> 27 years (n=47)	28	19	47	0.314*
TOTAL	60	33	93	

Table 1: Association and Frequency of HyperandrogenismConferring to Age Groups

Marital status showed that among patients who were found with hyperandrogenism, 23 patients were married and 37 patients were unmarried. The chi square test results presented no substantial relation amid hyperandrogenism and marital status with p>0.05 as shown in Table 2.

Marital Status	Hyperandrogenism		Total	P-Value
	Yes (n=60)	No(n=33)	Total	P-value
Married (n=41)	23	18	41	
Unmarried (n=52)	37	15	52	0.132*
TOTAL	60	33	93]

Table 2: Frequency and Association of HyperandrogenismAccording to Marital Status

As far as parity is concerned, it was observed that among patients who were found with hyperandrogenism, 18 patients had 0 parity, 3 patients had 1-2 parity, 2 patients had parity more than 2 and rest of the 37 patients had no parity because they were unmarried. Chi square results for association of hyperandrogenism with parity showed no significant association with p>0.05. The results are given in Table 4.

Parity	Hyperandrogenism		Total	P-Value
	Yes (n=43)	No (n=50)	Total	r-value
0 (n=5)	18	12	30	
1-2(n=30)	3	3	6	
> 2 (n=6)	2	3	5	0.346*
NO (n=52)	37	15	52	
TOTAL	60	33	93	

Table 3: Association and Frequency of HyperandrogenismConferring to Parity

DISCUSSION

Polycystic ovary syndrome (PCOS) is the communal disorder of endocrinology in females of reproductive age, with a prevalence of 4-12%, reaching 25% in some populations. PCOS is measured to be the leading cause of androgen excess and ovulation disorders. Conferring to the British Medical Journal, a study published the PCOS definition as hyperandrogenism (biochemical and clinical) and the presence of polycystic ovaries or ovarian dysfunction (oligo-anovulation) and related disorders [16]. The cutaneous manifestations of hyperandrogenism in

PCOS include acne, hirsutism, androgenetic alopecia, seborrhea and actinic keratosis (AN). Though insulin resistance and androgen excess play an important role in the advancement of skin lesions, the particular cause of these features is unknown. AN is directly caused by insulin resistance [17-18]. Since insulin increases level of androgens through and direct mechanisms, it also associated with other skin characteristics. Abnormal changes in carbohydrate metabolism in some skin features have also been reported [19]. The incidence of an augmented incidence of hyperandrogenism amongst PCOS in the present study was comparable with the large study series results of females identified with PCOS by Aziz, as there was evidence of clinical hyperandrogenism in approximately 75-85% of PCOS affected women. Females with PCOS exhibited hirsutism, one of the skin symptoms of hyperandrogenism. Markopoulos reported that hyperandrogenism is a vital pathophysiological polycystic ovary syndrome (PCOS) feature, with an incidence of 60-80% [20]. While increased androgen production in the ovaries by the sheath cells is a main sponsor to the excess of androgens in PCOS affected females of childbearing age, 20-65% of females with classic non-ovulatory PCOS have an excess of androgens in their adrenal glands, which is determined by high levels of dehydroepiandrosterone sulfate (DHEAS). The later comes chiefly from the reticular zone of the adrenal cortex [21]. Excessive secretion of adrenal androgens is also observed following adrenal stimulation in women with PCOS of childbearing age. The degree and incidence of hirsutism also be contingent on the patient's ethnicity. Hirsutism is less common in PCOS women of Pacific Island or East Asian descent, but much common in females in the subcontinent [22]. Although age is the vital determinant of fertility in females, Pedersen and Monga found that postponing marriage till age 30 will affect fertility rates as fertility drops sharply after age 35. Polycystic ovary syndrome has been reported to occur more frequently in young women (<35 years old) than in older females [23]. This is likely due to a physiological decline in the follicular cohort result in normalized ultrasound picture of the ovaries with age. In our study, all study participants were 35 years of age or younger. This study results are in line with those of Al-Taee and Alnakash as they found that 88.2% of the PCOS affected females enrolled in our study were under the age of 35 [24]. In one Pakistan study, the women mean age with PCOS was 27.1± 34.3 years, which is comparable to this study. Although a female may be predisposed genetically to progress towards PCOS, only in the environmental factor (obesity) interaction with genetic factors results in PCOS clinical expressions. The age and marital status of women were also associated with hyperandrogenism. In determining

hyperandrogenism, the true state of androgens can be measured by calculating the free androgen index (FAI) and gauging free testosterone. Multiple studies have formerly assessed the efficacy of FAI and serum total testosterone in detecting hyperandrogenism. The specific ethnic changes in the PCOS phenotype are recognized well. There are no reports of this characteristic of the PCOS analysis among women of South Asian region. In vitro or in vivo studies by means of cultured capsular cells have dependably shown that in PCOS affected females, the ovarian capsular cells are more effective at converting androgen precursors to testosterone than normal capsular cells. Insulin plays indirect or direct role in the hyperandrogenemia pathogenesis in PCOS. Our results are comparable and in line with previously published studies. The mean age was 27.22 ± 4.58 years, most patients were over 27 years of age, but all were 35 years or younger. Most of the patients were lonely. The mean free androgen index (FAI) score was 7.80 ± 5.82 with a range of 32.60 (0.80-33.40). In our study, 60 (64.5%) patients with hyperandrogenism were observed. The age of these patients was 26.93 ± 4.68 years, 32 of them were ≤ 27 years of age, 28 of them were> 27 years of age. 23 patients were married and 37 patients were unmarried. Among patients with hyperandrogenism in terms of the number of deliveries, the delivery was greater than 0 in 81 patients, 1-2 in 3 patients, and greater than 2 in 2 patients [25].

CONCLUSION

Hyperandrogenism is an important feature of PCOS. It mainly comes from the ovaries of women diagnosed with PCOS. The best indicator of hyperandrogenism are Serum testosterone levels. Hyperinsulinemia seems to be one of the main factors responsible for steroidogenesis deregulation. It was also concluded that in our study hyperandrogenism was mostly prevalent among PCO women which was identified by FAI Score. It also observed in younger aged and unmarried women

REFERENCES

- [1] Pinola P, Puukka K, Piltonen TT, Puurunen J, Vanky E, Sundström-Poromaa I, et al. Normo- and hyperandrogenic women with polycystic ovary syndrome exhibit an adverse metabolic profile through life. Fertility and Sterility. 2017 Mar; 107(3):788-795.e2. doi: 10.1016/j.fertnstert.2016.12. 017.
- [2] Kim JJ, Kim D, Yim JY, Kang JH, Han KH, Kim SM, et al. Polycystic ovary syndrome with hyperandrogenism as a risk factor for non-obese non-alcoholic fatty liver disease. Alimentary Pharmacology & Therapeutics. 2017 Jun; 45(11):1403-1412. doi: 10.1111/apt.14058.
- [3] Chang RJ, Dumesic DA. Polycystic ovary syndrome

and hyperandrogenic states. InYen and Jaffe's reproductive endocrinology. Elsevier. 2019 Jan: 520-55.

- [4] Hachul H, Polesel DN, Tock L, Carneiro G, Pereira AZ, Zanella MT, et al. Sleep disorders in polycystic ovary syndrome: influence of obesity and hyperandrogenism. Revista da Associacao Medica Brasileira (1992). 2019 Mar; 65(3):375-383. doi: 10.1590/1806-9282.65.3.375.
- [5] Cutler DA, Pride SM, Cheung AP. Low intakes of dietary fiber and magnesium are associated with insulin resistance and hyperandrogenism in polycystic ovary syndrome: A cohort study. Food Science and Nutrition. 2019 Feb; 7(4):1426-1437. doi: 10.1002/fsn3.977.
- [6] Kogure GS, Silva RC, Miranda-Furtado CL, Ribeiro VB, Pedroso DC, Melo AS, et al. Hyperandrogenism enhances muscle strength after progressive resistance training, independent of body composition, in women with polycystic ovary syndrome. The Journal of Strength & Conditioning Research. 2018 Sep; 32(9):2642-2651. doi: 10.1519/ JSC.000000000002714.
- [7] Pasquali R, Gambineri A. New perspectives on the definition and management of polycystic ovary syndrome. Journal of Endocrinological Investigation.
 2018 Oct; 41(10):1123-1135. doi: 10.1007/s40618-018-0832-1.
- [8] Copp T, Jansen J, Doust J, Mol BW, Dokras A, McCaffery K. Are expanding disease definitions unnecessarily labelling women with polycystic ovary syndrome? British medical journal BMJ. 2017 Aug; 358: j3694. doi: 10.1136/bmj. j3694.
- [9] Amiri M, Tehrani FR, Bidhendi-Yarandi R, Behboudi-Gandevani S, Azizi F, Carmina E. Relationships between biochemical markers of hyperandrogenism and metabolic parameters in women with polycystic ovary syndrome: A systematic review and metaanalysis. Hormone and Metabolic Research. 2019 Jan; 51(1):22-34. doi: 10.1055/a-0806-8281.
- [10] Fenichel P, Rougier C, Hieronimus S, Chevalier N. Which origin for polycystic ovaries syndrome: Genetic, environmental or both? Annales d'Endocrinologie (Paris). 2017 Jul; 78(3):176-185. doi: 10.1016/ j.ando.2017.04.024.
- [11] O'Brien B, Dahiya R, Kimble R. Hyperandrogenism, insulin resistance and acanthosis nigricans (HAIR-AN syndrome): an extreme subphenotype of polycystic ovary syndrome. BMJ Case Reports. 2020 Apr; 13(4): e231749. doi: 10.1136/bcr-2019-231749.
- [12] Chan JL, Kar S, Vanky E, Morin-Papunen L, Piltonen T, Puurunen J, et al. Racial and ethnic differences in the

prevalence of metabolic syndrome and its components of metabolic syndrome in women with polycystic ovary syndrome: a regional crosssectional study. American journal of obstetrics and gynecology. 2017 Aug; 217(2): 189.e1-189.e8. doi: 10. 1016/j.ajog.2017.04.007.

- [13] Saleem F, Rizvi SW. New Therapeutic Approaches in Obesity and Metabolic Syndrome Associated with Polycystic Ovary Syndrome. Cureus. 2017 Nov; 9(11): e1844. doi: 10.7759/cureus.1844.
- [14] González F, Considine RV, Abdelhadi OA, Acton AJ. Inflammation Triggered by Saturated Fat Ingestion Is Linked to Insulin Resistance and Hyperandrogenism in Polycystic Ovary Syndrome. The Journal of Clinical Endocrinology & Metabolism. 2020 Jun; 105(6): e2152-67. doi: 10.1210/clinem/dgaa108.
- [15] Amiri M, Ramezani Tehrani F, Nahidi F, Bidhendi Yarandi R, Behboudi-Gandevani S, Azizi F. Association between biochemical hyperandrogenism parameters and Ferriman-Gallwey score in patients with polycystic ovary syndrome: A systematic review and meta-regression analysis. Clinical Endocrinology (Oxf). 2017 Sep; 87(3):217-230. doi: 10.1111/cen.13389.
- [16] Pasquali R, Pignatelli D, editors. Hyperandrogenism in women: Beyond polycystic ovary syndrome. Karger Medical and Scientific Publishers; 2019 Sep.
- [17] Çoban ÖG, Tulacı ÖD, Adanır AS, Önder A. Psychiatric Disorders, Self-Esteem, and Quality of Life in Adolescents with Polycystic Ovary Syndrome. Journal of Pediatric and Adolescent Gynecology 2019 Dec; 32(6):600-604. doi: 10.1016/j.jpag.2019.07.008.
- [18] Shengir M, Krishnamurthy S, Ghali P, Deschenes M, Wong P, Chen T, et al. Prevalence and predictors of nonalcoholic fatty liver disease in South Asian women with polycystic ovary syndrome. World Journal of Gastroenterology. 2020 Nov; 26(44):7046-7060. doi: 10.3748/wjg.v26.i44.7046.
- [19] Al Nofal A, Viers LD, Javed A. Can the source of hyperandrogenism in adolescents with polycystic ovary syndrome predict metabolic phenotype? Gynecological Endocrinology. 2017 Nov; 33(11):882-887. doi: 10.1080/09513590.2017.1342236.
- [20] Paixão L, Ramos RB, Lavarda A, Morsh DM, Spritzer PM. Animal models of hyperandrogenism and ovarian morphology changes as features of polycystic ovary syndrome: a systematic review. Reproductive Biology and Endocrinology. 2017 Feb; 15(1):12. doi: 10.1186/s12958-017-0231-z.
- [21] Hansen SL, Bojsen-Møller KN, Lundsgaard AM, Hendrich FL, Nilas L, Sjøberg KA. Mechanisms underlying absent training-induced improvement in

insulin action in lean, hyperandrogenic women with polycystic ovary syndrome. Diabetes. 2020 Nov; 69(11):2267-2280.doi:10.2337/db20-0062.

- [22] Choudhary A, Jain S, Chaudhari P. Prevalence and symptomatology of polycystic ovarian syndrome in Indian women: is there a rising incidence? International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2017 Nov; 6(11):4971-6.
- [23] Otto-Buczkowska E, Grzyb K, Jainta N. Polycystic ovary syndrome (PCOS) and the accompanying disorders of glucose homeostasis among girls at the time of puberty. Pediatric Endocrinology Diabetes and Metabolism. 2018; 24(1):40-44. doi: 10.18544/ PEDM-24.01.0101.
- [24] Gupta M, Singh D, Toppo M, Priya A, Sethia S, Gupta P. A cross sectional study of polycystic ovarian syndrome among young women in Bhopal, Central India. The International Journal of Community Medicine and Public Health 2018 Jan; 5(1):95-100.
- [25] Sørensen AE, Udesen PB, Maciag G, Geiger J, Saliani N, Januszewski AS, et al. Hyperandrogenism and metabolic syndrome are associated with changes in serum-derived microRNAs in women with polycystic ovary syndrome. Frontiers in medicine (Lausanne). 2019 Nov; 6:242. doi: 10.3389/fmed.2019.00242.