How to Cite:
Monika, Malik, N., Waqar, M., Naeem, N., Memon, E., & Abbas, H. Y. (2023). Clinical manifestations, hormonal profile and rationale of the polycystic ovary syndrome and infertility in Pakistani women. *International Journal of Health Sciences*, *6*(S10), 1550–1558. https://doi.org/10.53730/ijhs.v6nS10.14088

Clinical manifestations, hormonal profile and rationale of the polycystic ovary syndrome and infertility in Pakistani women

Monika
Woman Medical Officer, Population Welfare Department, Larkana Pakistan

Naushabah Malik
Specialist Trainee, West Midlands UK

Dr. Mehwish Waqar
Woman Medical Officer, Pak Red Crescent Teaching Hospital, Dina Nath Kasur Pakistan
Corresponding author email: mehwishwaqar4800@icloud.com

Dr. Nadeem Naeem
Consultant Endocrinologist and Physician, MMIH, Karachi Pakistan

Dr. Erum Memon
Assistant Professor Gynae & Obs, Jinnah Medical and Dental College, Karachi Pakistan

Dr. Hafiza Yasmeen Abbas
MBBS, FCPS, Specialist in OBG. Alkiyumi Medical Complex, Oman

Abstract---Introduction: Many women of reproductive age experience polycystic ovary syndrome (PCOS), characterized by growth of cysts on the ovaries that range in size from 2 to 10mm in antral measurement, oligomenorrhea, menorrhagia, acne and hyperandrogenism. Objective: The study aimed to correlate the rational of PCOS with infertility in women. Place and Duration: The study was conducted in different districts of Sindh in Pakistan during the period 2020-22. Methods: This cross-sectional study aimed to determine how common infertility was among women with PCOS who sought care at different gynecological clinics. Pathological investigation of the patient's hormonal profile, including serum insulin, serum prolactin, LH, FSH, and serum testosterone levels were also investigated. Results: 316 of infertile women (63.20%) were diagnosed with PCOS. Females had oligomenorrhea as the predominant ($p<0.05$) pattern of the PCOS-affected females. Acne, hirsutism, and hyperandrogenism were

significantly (P<0.05) more common among these women. In women with PCOS, the level of testosterone was significantly elevated (132+2.39 ng/dl; P<0.05). Conclusion: PCOS is the leading cause of infertility owing to anovulation, as affected women displayed severe clinical manifestations of oligomenorrhea, hirsutism, acne, hyperandrogenism, and elevated testosterone levels and thus can easily be diagnosed and treated accordingly.

Keywords---anovulation, endometrial cancer, female infertility, hyperandrogenism.

Introduction

As per Rotterdam reproductive medicine criteria, the patients with polycystic ovary syndrome (PCOS) experience two of these clinical manifestations; (a) oligo-anovulation, (b) biological or clinical hyperandrogenism, or (c) micro polycystic syndrome, characterized by >12 ovarian-follicles or >10ml ovarian-volume" [1,2]. It is a frequent disorder that has the potential to impede conception and is the most prevalent endocrine malfunction in fertile women, with a prevailing rate of 15-25%. It is regarded as a diverse and multidimensional illness with multiple reproductive and metabolic manifestations. Different phenotypes influence the risks of early and long-term syndromes. It predisposes the parturient to various poor pregnancy outcomes, including a significant risk of pregnancy-induced hypertension, spontaneous abortion, gestational diabetes, preeclampsia, and premature birth, which raise the risks of stillbirth and infant death [3].

It is thought that PCOS develops from androgen excess promoting the abdominal and visceral adipose tissue deposition, which increases insulin resistance and subsequent hyperinsulinemia, hence promoting androgen output by the ovaries and adrenal glands. This pathological association between insulin resistance, hyperinsulinemia and hyperandrogenism in conjunction with hypothalamic-pituitary dysfunction, results in infertility due to ovarian dysfunction [4]. PCOS is commonly associated with hormonal imbalances due to abnormalities in luteinizing hormone, prolactin, estrogen, and serum androgen levels. There is no solitary diagnostic criterion applicable to this illness. Rather, it is diagnosed using a combination of clinical, laboratory, and ultrasound ovarian morphologies [5].

Despite being one of the most populous countries in the world (at 5th ranking), with a population growth rate of approximately 2% (per annum), Pakistan also has a higher frequency of infertility (21.9%); the incidence of infertility in Pakistan is 21.9 percent, and 70% of the cases are directly correlated with PCOS. Therefore, this research was executed to assess the incidence as well as the association of infertility in Pakistani women along with the investigation of their hormonal profile.

Material and Methods

This retrospective cross-sectional study was carried out in different districts of Sindh, Pakistan from July 2020 to June 2022. Females from age ranging 18 to 45

years, with irregular menstruation like amenorrhea, polymenorrhea, oligomenorrhea and menometrorrhagia were included in the study. The exclusion criteria set for the participants was a known history of PCOS, oral contraceptive therapy, insulin, thyroxin, or other hormonal therapy. A total of 500 women (n=500) were included as per the above-set inclusion criteria, from various gynecological clinics in the government run and private hospitals, 100 patients from each district of Sindh (n=100). A pre-designed approved questionnaire was used to collect and analyze the metadata, including their age, menstrual irregularity, genetic history, gynecological history, and manifesting clinical signs recorded. The Hirsutism and acne were scored using Ferriman Gallwey and Global Acne Grading methods, respectively [6]. PCOS was diagnosed using Rotterdam criteria, 2003 (Rotterdam, 2004). As per Rotterdam Reproductive Medicine Criteria, the patients were diagnosed with PCOS, manifesting two of the following three clinical presentations and were confirmed through trans-vaginal ultrasonography.

- Oligo-anovulation,
- Biological or clinical hyperandrogenism,
- Micropolycystic syndrome is characterized by >12 ovarian follicles or >10ml ovarian volume.

The blood samples were collected from the PCOS-diagnosed women for further laboratory investigation of the following endocrine parameters for the determination of the association of the hormones with PCOS [7].

- Serum testosterone level
- Serum follicle-stimulating hormone
- Serum luteinizing hormone
- Serum insulin
- Serum prolactin

The research was conducted in compliance with the 1964 Helsinki Declaration's ethical guidelines and all the participants were included on their willingness through acquiring informed consent from all the Cohorts [8]. SPSS version 20 was used to conduct the statistical analysis of the collected data. The Chi-square test was the tool used in the statistical analysis between the treatment groups at the p-value of less than 0.05 as the significance cut-off value. The data was also analyzed by mean with a standard deviation of frequency and percentages of continuous variables [7].

Results

All the participants willingly participated in the study with 100% response and out of 500 infertile participants included in the study, 316 were diagnosed with PCOS using Rotterdam criteria, with a prevalence of 63.20% and patients had mean age of 32.71+2.34. The infertile females presented at the gynecology clinics of 05 districts of Pakistan were significantly affected ($p<0.05$) with PCOS. The rest of the infertile patients with complaints of menstrual irregularities were comparatively investigated with PCOS. The number of ovarian follicles (on both ovaries) in PCOS women was determined through trans-vaginal ultrasonography,

and the mean follicular number was 18.78+1.20, which was significantly higher ($p<0.05$) than in non-PCOS patients. Forty-seven patients had a family history of PCOS and 23 participants had gynecological history. The clinical manifestation revealed the highest incidence ($p<0.05$) of acne and hyperandrogenism in PCOS-affected females (Table 1).

Table 1
Metadata of Cohort variables of PCOS vs Non-PCOS patients

Cohort Variables	PCOS n (%)	Non-PCOS n (%)	x2	p-value
Infertile patients	316 (63.20)	184 (36.80)	22.884	0.00001*
Mean age (years) Mean+SD	32.71+2.34	25.66+1.89	-	-
No. of follicles on both ovaries (Mean+SD)	18.78+1.20	7.1+0.3	-	-
Family history	47 (14.87)	76 (41.30)	24.3322	0.00001*
Gynecological history	23 (7.27)	18 (9.78)	0.3547	0.5514
Acne	72 (22.78)	09 (4.89)	19.5945	0.00001*
Hyperandrogenism	156 (49.36)	06 (3.26)	63.8874	0.00001*

The cohort variables pertaining to menstrual irregularities were also studied. It was found that the infertile females diagnosed with PCOS had significantly ($p<0.05$) higher percentages of menstrual irregularities (81.01%). And among these, oligomenorrhea was significantly predominant ($p<0.05$), followed by polymenorrhea, menometrorrhagia and amenorrhea with the prevalence percentage of 36.07, 18.03, 14.55 and 12.34%, respectively (Table 2).

Table 2
Cohort variables pertaining to the menstrual irregularities

Parameters	PCOS (%)	Non-PCOS (%)	x2	p-value
Infertility	316 (63.2)	184 (36.80)	22.88	0.00001*
Menstrual irregularities	256 (81.01)	102 (55.43)	6.4805	0.0134*
Amenorrhea	39 (12.34)	18 (9.78)	0.398	0.5277
Oligomenorrhea	114 (36.07)	33 (17.93)	9.8622	0.001687*
Polymenorrhea	57 (18.03)	36 (19.56)	0.0544	0.8156
Menometrorrhagia	46 (14.55)	15 (8.15)	3.0276	0.0818

The PCOS-suffering females were sorted into three categories of hirsutism based on the Ferriman Gallwey scoring criteria and among these categories, 85% of PCOS patients ($p<0.05$) were placed on over 25 hirsutism scores (Figure 1). The acne was scored using the Global Acne Grading method (Figure 2) and the significantly highest population of 148 patients showed an acne score of 1-18 points (mild acne) as per the above criteria.

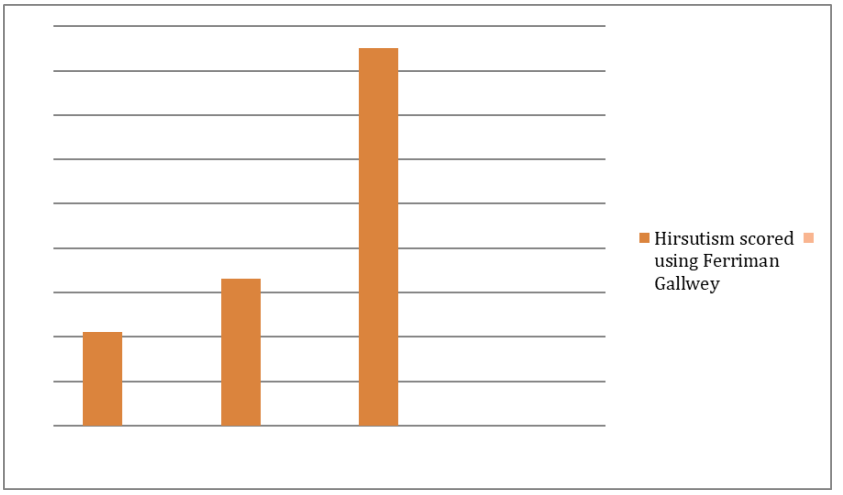

Figure 1. Hirsutism scores in PCOS patients on Ferriman Gallwey scoring criteria

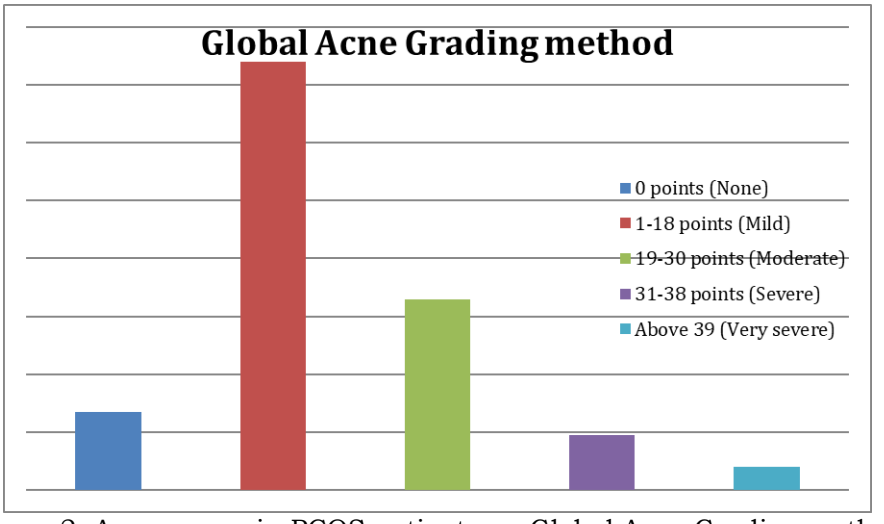

Figure 2. Acne scores in PCOS patients on Global Acne Grading method

The hormonal status of the participants in the PCOS group was comparatively studied with the normal endocrine values, which showed a statistically significant difference ($p<0.05$) in their serum testosterone, serum insulin and serum prolactin levels (Table 3).

Table 3
Comparative study of Endocrine parameters of PCOS and Non-PCOS female patients

S. No	Endocrine parameters	PCOS Mean+SD	Normal (Control)
1	Serum testosterone level (ng/dl)	132+2.39	15-70
2	Serum follicle-stimulating hormone (mIU/ml)	4.27+0.89	1.5-12.4
3	Serum luteinizing hormone	9.01+2.31	0.7-7.9

	(mIU/ml)		
4	Serum insulin (µIU/L)	15.3+2.1	5-10
5	Serum prolactin (ng/ml)	27.41+3.65	<20

Discussion

Multiple psychological, ethnic, medical and gynecological complications resulted due to PCOS in women with serious concerns and put a significant economic burden on the economy of developing countries like Pakistan [9]. Our findings revealed 63.20% incidence in the presented infertile women. Our results were also in agreement with the study conducted in Hyderabad Pakistan in which the incidence of PCOS was found 48.5% using Rotterdam reproductive medicine criteria [6]. Our findings were supported by an Indian cohort study reporting a 46.8% prevalence of PCOS [9, 10]. Another study revealed a 41% incidence of PCOS in Indian women with menstrual irregularities, diagnosed using criteria laid down by NIH [11]. The highest incidence was found by Zandi et al. who found a 60.2% incidence of PCOS by NIH criteria [12]. Spontaneous abortions and miscarriages were also caused by PCOS [13]. A study in Nigeria reported a 55.2% incidence of PCOS in infertile women [14,15]. Different incidence rates in Iraq, Iran, Denmark and Tanzania (74.6, 69.7, 68 and 32%, respectively) were reported, which might be due to using different validation criteria for PCOS determination [16-18].

In our research, the number of ovarian follicles was significantly increased ($p<0.05$) to 18.78+1.20 (Mean+SD) in the PCOS patients. Our findings were in close liaison with Lentscher et al. [13]. The results of our study were also supported by a study in which ≥12 follicles on the ovaries were found [6]. Similar results were revealed in which more than 12 Graffian follicles of size 2-10mm were seen in the polycystic ovaries [19]. As PCOS is an oligogenic disorder in which genetic and environmental factors interact to define the diverse, clinical, and biochemical phenotype, the genetic etiology of PCOS in the form of family history cannot be ignored and the genetic predisposition played a vital role in the PCOS incidence [20]. Another study reported a 24.5% association between family history with PCOS [6].

Hyperandrogenism is the hallmark characteristic of PCOS-affected women. It is caused by the disturbance of normal ovarian or adrenal function, which resulted in an overabundance of androgens. In the early gonadotropin-independent stage, increased androgens encouraged the production of primordial follicles and increased the number of antral follicles. The clinical manifestation in our research revealed the highest incidence ($p<0.05$) of acne and hyperandrogenism in PCOS-affected females [21]. Our study was supported by a study in which 32.21% patients of with PCOS were suffering from acne and 63.08% from hyperandrogenism [22]. Similar conclusions were produced by a study that acne vulgaris is the most important clinical feature of PCOS [23]. It was also reported that PCOS created hirsutism and acne which were drug-resistant [2]. Significantly ($p<0.05$) elevated concentrations of testosterone were reported to be 78, 78.2 and 85.6% [24].

Severe menstrual irregularities ($p<0.05$) of 81.01% were seen in our cohort studies with oligomenorrhea being the most predominant pattern of menstruation in PCOS. Our findings were strongly supported by the study in which oligomenorrhea was a common pattern of menstruation in PCOS [22]. Our findings were in an agreement with the study in which 56.7% of cases of irregular menstruation were seen in PCOS women [6]. However, in another study, a lower incidence of uterine bleeding at 33.7% was seen [25].

Conclusion

It was concluded from our study that PCOS is the predominant cause of infertility in Pakistani women of Sindh Province and they bear the highest incidence of 63.20%. The clinical manifestations of PCOS are irregular menstruation most probably oligomenorrhea, drug-resistant acne vulgaris, hyperandrogenism, elevated testosterone levels, hairy patches on the skin and a significantly increased number of ovarian follicles. PCOS is mainly an endocrine and curable illness if properly recognized. Therefore, all the presented infertile women with such clinical manifestations should be investigated for PCOS and the research activity about PCOS should be strengthened by the government organizations to decrease the socioeconomic load on this nation.

References

1. Collee J, Mawet M, Tebache L, Nisolle M and Brichant G. Review: Polycystic ovarian syndrome and infertility: overview and insights of the putative treatments. Gynecological Endocrinology. 2021;37(10): 869–874.
2. Rotterdam Eshre/ASRM-Sponsored PCOS consensus Workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Human Reproduction. 2004;19:41–7.
3. Mirza FG, Tahlak MA, Rjeili RB, Hazari K, Ennab F, Hodgman C, Khamis AH and Atiomo W. Polycystic ovarian syndrome (PCOS): Does the challenge end at conception? International Journal of Envrionmental Research and Public Health. 2022;19(22): 14914.
4. Cunha A and Povoa AM. Infertility management in women with polycystic ovary syndrome: a review. Porto Biomedical Journal. 2021;26:6(1):e116.
5. Yousaf J, Khadija S, Arshad N, Amjad MR, Gulzar J and Ullah S. The Chances of Infertility in a Patient Presenting with PCOS in Childbearing Age, Review Article. Saudi Journal of Medicine. 2022;7(1):15-21.
6. Memon TF, Meghji KA, Rajar AB, Khowaja S, Azam A and Khatoon S. Clinical, hormonal and metabolic factors associated with polycystic ovary syndrome among Pakistani women. Rawal Medical Journal. 2020;45(4):817-821.
7. Saadia Z. 2020. Follicle Stimulating Hormone (LH: FSH) Ratio in Polycystic Ovary Syndrome (PCOS) - Obese vs. Non- Obese Women. Medical Archives. 2020;74(4):289-293.
8. Declaration of Helsinki. In clinical research Adopted by the 18th World Medical Assembly, Helsinki, Finland, June 1964.

9. Deswal R, Narwal V, Dang A and Pundir CS. The Prevalence of Polycystic Ovary Syndrome: A Brief Systematic Review. Journal of Human Reproductive Sciences. 2020;13(4):261-271.
10. Ganie MA, Marwaha RK, Aggarwal R and Singh S. High prevalence of polycystic ovary syndrome characteristics in girls with euthyroid chronic lymphocytic thyroiditis: A case-control study. European Journal of Endocrinology. 2010;162:1117–22.
11. Joshi B, Mukherjee S, Patil A, Purandare A, Chauhan S and Vaidya R. A cross-sectional study of polycystic ovarian syndrome among adolescent and young girls in Mumbai, India. Indian Journal of Endocrinology and Metabolism. 2014;18:317–24.
12. Zandi S, Farajzadeh S and Safari H. Prevalence of polycystic ovary syndrome in women with acne: hormone profiles and clinical findings. Journal of Pakistan Association of Dermatologists. 2016;20:194-8.
13. Lentscher JA, Slocum B and Torrealday S. Polycystic ovarian syndrome and fertility. Clinical Obstetrics and Gynecology. 2020;64(1):65-75.
14. Oriji VK and Onwuegbulam C. Prevalence of Polycystic Ovary Syndrome (PCOS) among Infertile Women Attending Fertility Clinic at a University Teaching Hospital in Nigeria. Journal of Gynecology and Women's Health. 2020;15(5):555922.
15. Obuna JA, Ndukwe EO, Ugboma HAA, Ejikeme BN, Ugboma EW. Clinical presentation of infertility in an outpatient clinic of a resource poor setting, South East Nigeria. International Journal of Tropical Disease and Health. 2012;2(2):123-131.
16. Hussein B and Alalaf S. prevalence and characteristics of polycystic ovary syndrome in a sample of infertile Kurdish women attending IVF infertility centre in Mternity Teaching Hospital of Erbil City. Open Journal of Obstetrics and Gynecology. 2013;3:577- 585.
17. Kristensen SL, Ramiau-Hansen CH, Ernst E, Olsen SF and Bonde JP. A very large population of young Danish women have polycystic ovaries: is a revision of the Rotterdam criteria needed? Hum Reproduction. 2010;25(12):3117-3122.
18. Kousta E, White DM, Cela E, McCarthy MI and Frank S. The prevalence of polycystic ovaries in women with infertility. Human Reproduction. 1999;14(11):2720-2723.
19. Martins WP, Kollmann M and Fenning NR. Counting ovarian follicles: updated threshold for diagnosis of hyperandrogenic anovulation. Ultrasound in Obstetrics and Gynecology. 2014;44(2):131-134.
20. Ndefo UA, Eaton A, Green MR. Polycystic ovary syndrome: a review of treatment options with a focus on pharmacological approaches. Physical Therapy. 2013;38(6):336-55.
21. Ashraf S, Nabi M, Rasool SA, Rashid F and Amin S. Hyperandrogenism in polycystic ovarian syndrome and role of CYP gene variants: a review. Egyptian Journal of Medical Human Genetics. 2019;20(25):1-10.
22. Akram M and Roohi N. Endocrine Correlates of Polycystic Ovary Syndrome in Pakistani Women. Journal of the College of Physicians and Surgeons Pakistan. 2015;25(1):22-26.
23. Frank G, Bizan A, Wloch S, Kowalczik K, Bartnik AB and Madej P. Hormonal and metabolic aspects of acne vulgaris in women with polycystic

ovary syndrome. European Review for Medical and Pharmacological Sciences. 2018;22:4411-4448.
24. Khan TU, Memon NN, Riaz A, Khan ZH, Haroon SM and Khan KH. Serum free testosterone levels in polycystic ovarian syndrome patients and its correlation with clinical hyperandrogenism in Pakistan. Journal of Fatima Jinnah Medical University. 2020;14(3):132-135.
25. Zafar U, Memon Z, Moin K, Agha S, Hassan JA and Zehra D. Prevalence of PCOS with associated symptoms and complications at Tertiary Care Hospital of Karachi. Journal of Advanced Medicine and Medical Research. 2019;30:1-9.