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ORIGINAL ARTICLE

Correlation of Clinical Features with Biochemical Status in Polycystic Ovarian Syndrome

Sandhya Agarwal

Professor, Department of Obstetrics & Gynaecology, Gold Field Institute of Medical Sciences & Research, Faridabad, Haryana, India

ABSTRACT:

Background: Polycystic Ovarian Syndrome (PCOS) stands out as the prevailing endocrine disorder among women in their reproductive years. PCOS is characterized by chronic anovulation, menstrual irregularities, hyperandrogenism, polycystic ovaries, and metabolic syndrome. The objectives of this study are to explore the clinical, biochemical, and hormonal profiles in individuals with PCOS and establish correlations with those of normal subjects.**Methods**: We are conducting a prospective case-control study involving 100 women aged 18-30 years. This study comprises two groups: 50 participants diagnosed with Polycystic Ovary Syndrome (PCOS) and an equal number of individuals in the control group.**Results**: Among individuals with Polycystic Ovary Syndrome (PCOS), 92% exhibited menstrual irregularities, with oligomenorrhea being the most prevalent presentation. Infertility was observed in 52%, and 53% displayed hirsutism. Comparatively, PCOS individuals showed statistically significant differences (P value <0.001) in mean BMI, waist-to-hip ratio, LH level, LH:FSH ratio, total testosterone, fasting insulin, and total cholesterol when compared to the control group. The mean LH was 15.44 ± 7.09 in the PCOS group and 9.92 ± 4.55 in the control group.**Conclusion**: The majority of individuals with Polycystic Ovary Syndrome (PCOS) exhibited characteristics such as oligomenorrhea, hirsutism, elevated BMI, and an increased waist-hip ratio. PCOS cases also demonstrated statistically significant elevations in mean LH, LH:FSH ratio, testosterone, and fasting insulin levels compared to non-PCOS individuals.

Keywords:Polycystic ovarian syndrome, luteinising hormone, total testosterone, biochemical status, body mass index

Corresponding author: Sandhya Agarwal, Professor, Department of Obstetrics & Gynaecology, Gold Field Institute of Medical Sciences & Research, Faridabad, Haryana, India

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INTRODUCTION

Polycystic Ovary Syndrome (PCOS) emerges as a prevalent endocrine disorder significantly impacting women during their reproductive years, presenting itself as a primary contributor to hyperandrogenism and oligoanovulation.[1] The repercussions of PCOS extend beyond the physiological realm, carrying considerable psychological, social, and economic implications for affected individuals. Various studies among adult women have reported a prevalence ranging from 4-12%, underscoring the significance of this condition.The historical roots of our understanding of PCOS trace back to 1935 when Stein and Leventhal provided the first comprehensive description of its classic form. PCOS encompasses a spectrum of manifestations, including chronic anovulation, menstrual irregularities, hyperandrogenism, polycystic ovaries, and metabolic syndrome.[2] These multifaceted aspects contribute to the complexity of the syndrome and its wide-ranging impact on affected individuals.To establish a standardized diagnostic framework, the Rotterdam consensus workshop in 2003, jointly sponsored by the European Society for Human Reproduction and Embryology (ESHRE) and the American Society for Reproductive Medicine (ASRM), introduced criteria for defining PCOS. According to these criteria, a diagnosis is confirmed when any two of the following three conditions are met: (1) oligo/anovulation, (2) the presence of clinical and/or biochemical signs of hyperandrogenism, such as acne or hirsutism, after ruling out alternative causes, and (3) ultrasound evidence of polycystic ovaries.[3] The latter is characterized by the presence of 12 or more follicles with a diameter ranging from 2 to 9 mm in one or both ovaries, or an ovarian volume exceeding 10 cm3.In summary, PCOS is a multifaceted syndrome with far-reaching implications for the well-being of affected individuals. The collaborative efforts of medical societies in defining and diagnosing PCOS underscore the ongoing commitment to understanding and addressing this complex condition.[4] Hyperandrogenism, a prevalent characteristic in Polycystic Ovary Syndrome (PCOS), primarily originates from ovarian sources and is clinically evident through common manifestations such as hirsutism and acne. Women diagnosed with PCOS often exhibit insulin resistance and hyperinsulinemia. The interplay of excessive insulin and elevated luteinizing hormone (LH) levels can result in heightened testosterone production in the ovaries, disrupting the follicle maturation process and impeding ovulation.[5]

Insulin resistance plays a pivotal role in the late complications of PCOS, with over 40% of affected women demonstrating impaired glucose tolerance and

10% developing type 2 diabetes mellitus. The severity of insulin resistance manifests variably, ranging from slightly elevated fasting serum insulin levels in mild cases to the presence of acanthosis nigricans in more severe forms. While all women with PCOS exhibit evidence of insulin resistance, its prominence is particularly notable in those with chronic anovulation.PCOS is intricately linked to obesity, exacerbating hyperandrogenism and menstrual irregularities. Individuals with PCOS are more prone to accumulating excess adiposity in the central body region, a pattern associated with heightened insulin resistance. The association between central or visceral obesity and increased insulin resistance further underscores the complex interplay of metabolic factors in PCOS.Addressing PCOS in adolescents is crucial not only for alleviating immediate symptoms but also for mitigating long-term risks. Without intervention, there is an elevated risk of infertility, endometrial hyperplasia and carcinoma, type 2 diabetes mellitus, metabolic syndrome, and potentially cardiovascular diseases such as myocardial dysfunction, stroke, and hypertension.The primary objective of this study was to comprehensively investigate and correlate various clinical features, hormonal profiles, and biochemical changes in individuals diagnosed with PCOS compared to a normal control group.[6,7] Through this examination, we aim to enhance our understanding of the intricate dynamics involved in PCOS and contribute valuable insights for effective management and intervention strategies.

MATERIALS AND METHODS

In this thorough investigation, women within the age bracket of 18-30 years exhibiting irregular menstrual cycles, oligomenorrhea/amenorrhea, infertility, hirsutism, and excessive acne were meticulously examined. The primary objective was to diagnose Polycystic Ovary Syndrome (PCOS) based on the stringent criteria outlined by the Rotterdam guidelines. The study, conducted prospectively, enrolled 50 PCOS patients, stratified into 25 married and 25 unmarried individuals, alongside a control group of 50 women, similarly divided into married and unmarried categories. Ethical approval from the Institutional Ethics Committee underscored the commitment to ethical research practices.To ensure the robustness of the study, stringent exclusion criteria were applied. Individuals with a history of oral contraceptive, glucocorticoid, antiandrogen, ovulation induction agent, antidiabetic, antiobesity, or other hormonal drug usage were excluded. Similarly, those with pregnancy, breastfeeding, diabetes mellitus, chronic illness, or hyperandrogenism due to other endocrinopathies were not included. Prior to participation, written informed consent was obtained from all study participants.Anthropometric measurements, including height, weight, waist and hip circumference, were meticulously recorded. Essential parameters such as Body Mass Index (BMI) and waist-to-hip ratios were calculated to provide a comprehensive overview of the participants' physical profiles. The degree of hirsutism was quantified using the Ferriman & Gallwey score, with a score exceeding 8 indicating significance. Additionally, ultrasound examinations of the lower abdomen were performed for each participant to assess ovarian morphology.

The hormonal assessment constituted a critical aspect of the study, involving morning blood samples for the analysis of serum LH, FSH, total testosterone, fasting insulin, FT3, FT4, TSH, and Prolactin levels. Timing of sample collection was meticulous, with samples taken on specific days of the menstrual cycle for menstruating women and randomly for those with oligomenorrhea. Normal values were defined for key hormonal markers, including FSH (3-4.3 mIU/ml), LH (4.2-6.3 mIU/ml), and total testosterone (8-60 ng/dl). The LH: FSH ratio was considered significant if it reached 2:1, and fasting insulin levels were deemed significant if they exceeded 25 mIU/L.The thyroid profile was evaluated with normal ranges set for FT3 (3.1-6.8 pmol/L), FT4 (12-22 pmol/L), and TSH (0.27-4.2 μIU/ml). Serum Prolactin levels within the range of 2-29 ng/ml were considered normal. This meticulous and comprehensive approach aimed to uncover nuanced insights into the clinical, hormonal, and biochemical profiles of women with PCOS compared to the control group, thereby contributing substantively to the broader understanding of this intricate syndrome.

RESULTS

In our study, the mean age of participants within the PCOS group was 22.50 ± 2.937 years, while in the control group, it was slightly higher at 23.47 ± 2.696 years. However, this observed difference did not reach statistical significance, as indicated by a P value of 0.055. Notably, the majority of participants in both the PCOS group (80%) and the control group (75%) fell below the age of 25. Despite a numerical discrepancy, this age distribution did not demonstrate a statistically significant difference, with a P value of 0.397.Furthermore, we ensured an equitable distribution of marital status among participants in both groups. Married and unmarried individuals were equally represented in both the PCOS and control groups, reinforcing the comparability of the two cohorts in terms of marital demographics. This meticulous balance in participant characteristics enhances the reliability and validity of our study findings, allowing for a more robust examination of the specific parameters under investigation.

Table 1: Comparison of age and marital status a between the PCOS and control group

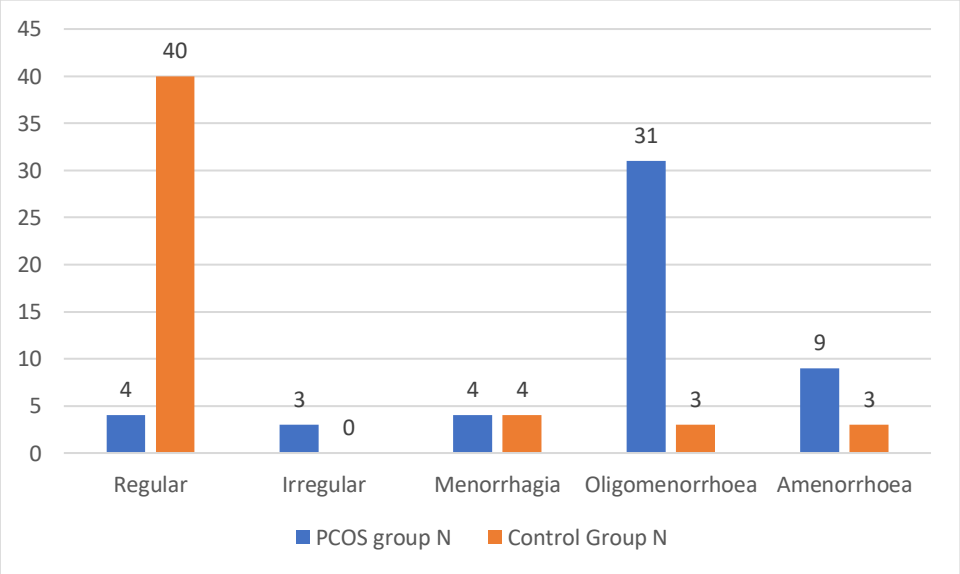
Variables	PCOS group N (%)	Control Group N (%)	P value
Age			
< 25 years	40 (80%)	35 (75%)	0.397
≥ 25 Years	10 (20%)	15 (25%)	
Marital status			
Unmarried	25 (50%)	25 (50%)	1.00
Married	25 (50%)	25 (50%)	

In our study, a striking 92% of individuals with Polycystic Ovary Syndrome (PCOS) experienced menstrual irregularities, presenting a stark contrast to the control group where only 15% encountered such irregularities.[8] This discrepancy in proportions was not only evident but also statistically significant, as indicated by a P value less than 0.001.Among the PCOS group, the most prevalent form of menstrual irregularity was oligomenorrhea, affecting 61% of cases, followed by amenorrhea, observed in 18% of individuals. This pattern underscored the complexity and diversity of menstrual disturbances within the PCOS cohort. In contrast, the control group exhibited a notably higher prevalence of regular menstrual cycles, with 80% of participants falling into this category.These findings illuminate the significant association between PCOS and menstrual irregularities, emphasizing the clinical relevance of such disturbances in individuals with PCOS compared to those in the control group. The detailed breakdown of specific irregularities further contributes to our understanding of the varied nature of menstrual patterns in the context of PCOS.

Table 2: Comparison of menstrual cycle pattern between the PCOS and control group

Menstrual cycle	PCOS group N	Control Group N	P value
Regular	4	40	< 0.001
Irregular	3	0	
Menorrhagia	4	4	
Oligomenorrhoea	31	3	
Amenorrhoea	9	3	

Figure1: Comparison of menstrual cycle pattern between the PCOS and control group



DISCUSSION

In our comprehensive study targeting individuals aged 18-30 years, the mean age of participants diagnosed with Polycystic Ovary Syndrome (PCOS) was 22.70 ± 2.937 years, whereas the control group had a slightly higher mean age of 23.47 ± 2.696 years. Comparing our findings with other studies, Kumar AN[9], who included subjects aged 19-35 years, reported a mean age of 25.6 ± 3.9 in PCOS and 26.7 ± 3.4 in the control group. Meanwhile, Spandana and Shetty found a mean age of 27 ± 5.0 years in PCOS, with a significant proportion falling within the 26-30 years age group (43%).Examining menstrual irregularities, our study revealed that oligomenorrhea was the predominant irregularity, affecting 61% of PCOS cases, a noteworthy contrast to the 6% observed in the control group. This aligns with the findings of Spandana and Shetty, who reported a similar

prevalence of 59% for oligomenorrhea in PCOS cases.Infertility emerged as a substantial concern in our study, with 52% of PCOS cases experiencing fertility challenges compared to 10% in the control group, a highly significant difference (P value <0.001).[10] These findings parallel those of Panda et al, who reported 16% infertility in PCOS compared to 6% in the control group, and Himabindu and Neelima, who found infertility in 40% of PCOS cases. Arain et al highlighted PCOS as the second most common cause of female factor-related infertility, accounting for 36.5%.Hirsutism, a common clinical presentation of androgen excess in young women, was notably prevalent in our PCOS group, with 53% exhibiting this condition compared to 13% in the control group. This aligns with findings by Abdulrazzak et al and Pache TD et al, who reported hirsutism in 64.49% and 63% of PCOS cases, respectively.Examining measures of obesity, both BMI and waist-hip ratio were significantly higher in the PCOS group compared to the control group. The mean BMI in our study was 26.08 ± 2.97 in PCOS and 23.44 ± 1.93 in the control group, echoing similar findings by Hahn S et al, Dipankar et al, and Begum et al. Mean waist-hip ratio was also higher in PCOS (0.74 ± 0.10) compared to the control group (0.63 ± 0.06), a trend supported by Codner E et al's study.In terms of hormonal markers, elevated LH levels were prominent in our PCOS group, with Nasr et al reporting 86.7% of PCOS cases having elevated LH. Yousouf et al found raised LH in 63% of PCOS patients and 32% of controls.[11] Our study further substantiated these findings, reporting a statistically significant mean LH level of 15.44 ± 7.09 mIU/ml in PCOS compared to 9.92 ± 4.55 mIU/ml in the control group (P value <0.001).

The intricate relationship between testosterone levels and various aspects of Polycystic Ovary Syndrome (PCOS) underscores the multifaceted nature of this endocrine disorder. Elevated testosterone levels have been consistently linked to an increase in the LH/FSH ratio, antral follicular count, and the manifestation of hirsutism. This surge in androgen levels not only contributes to the characteristic symptoms of PCOS but also fosters insulin resistance, culminating in heightened insulin levels.[12] This intricate interplay between androgens and insulin resistance not only exacerbates PCOS symptoms but also elevates the risk of diabetes, obesity, and cardiovascular complications among affected individuals.In our study, the mean testosterone level was notably elevated in the PCOS group, measuring at 70.69 ± 25.67 ng/dl, in stark contrast to the control group where it was 30.41 ± 14.43 ng/dl. This difference was not only substantial but also statistically significant (P value <0.001). These findings align with the study by Maheswari et al, where a high mean total testosterone level of 71.58 was reported in the PCOS group compared to 28.7 in the control group. Robinson et al similarly identified total testosterone concentration as significantly higher in PCOS, serving as the most frequently abnormal biochemical marker, observed in 70% of cases.

The association between hyperandrogenic phenotypes of PCOS and metabolic complications has been emphasized by Kar S, highlighting the increased susceptibility of this subgroup to metabolic disturbances compared to phenotypes with normal androgen levels.[13]Further supporting the significance of elevated testosterone levels in PCOS, Nahar et al reported a mean total testosterone value of 70.40 ± 27.9 in PCOS cases, with 30% exhibiting total testosterone levels above the reference range of 30-95 ng/dl. This collective evidence reinforces the pivotal role of androgen excess in the pathophysiology of PCOS and its implications for metabolic health in affected individuals.

The association between Polycystic Ovary Syndrome (PCOS) and thyroid dysfunction has been explored in various studies, revealing noteworthy insights into the prevalence and characteristics of hypothyroidism among individuals with PCOS. Islam et al reported a prevalence of hypothyroidism in 11.4% of PCOS cases, while Sinha et al detected subclinical hypothyroidism in 22.5% of cases, with 2.5% exhibiting overt hypothyroidism. In the study by Sinha et al, PCOS cases demonstrated higher mean TSH levels compared to the control group (4.547 ± 2.66 vs. 2.67 ± 3.11, $p < 0.05$). Similarly, the present study found a mean TSH level of 3.47 ± 2.40 in PCOS patients, consistent with the findings of Timpatanapong and Rojanasakul, who reported a mean TSH of 3.53 ± 3.28.Contrastingly, Karakose et al reported lower mean TSH levels in both PCOS (1.90 ± 1.16) and the control group (1.76 ± 0.90), indicating some variability in TSH levels among different studies. Importantly, the present study did not find a statistically significant correlation of TSH levels between PCOS and the control group (P value 0.921).Regarding glucose metabolism, mean Fasting Blood Sugar (FBS) and Postprandial Blood Sugar (PPBS) values were comparable between PCOS and control groups, both falling within normal ranges. Similarly, Karakose et al[14] reported normal FBS levels in both PCOS and control groups. The lack of significant differences in these parameters suggests that glucose metabolism may not be substantially altered in the PCOS cohort under investigation.In the lipid profile analysis, the present study revealed significantly higher mean total cholesterol levels in PCOS compared to the control group (198 ± 20.54 mg/dl vs. 178.94 ± 17.93, P value < 0.001). This finding aligns with studies by Silfen et al and Leustean et al, which reported mean total cholesterol levels of 164.0 ± 32.10 mg/dl and 214 ± 40.08 mg/dl, respectively, in PCOS cases. Additionally, the mean Low-Density Lipoprotein (LDL) level in the current PCOS cases was 93.02 ± 9.21 mg/dl, whereas Christodoulopoulou et al observed a higher mean LDL of 110.7 ± 33.5 mg/dl in their study.

These results collectively contribute to our understanding of the metabolic implications associated with PCOS, emphasizing the need for comprehensive evaluation and management of associated conditions such as thyroid dysfunction and dyslipidemia in individuals with PCOS.

CONCLUSION

The study identified oligomenorrhea as the predominant presenting symptom among individuals with Polycystic Ovary Syndrome (PCOS). This observation was found to be correlated with significantly elevated levels of Luteinizing Hormone (LH) and an increased LH: Follicle-Stimulating Hormone (FSH) ratio in PCOS cases. These hormonal imbalances contribute to the disrupted menstrual patterns characteristic of PCOS.The study also highlighted that individuals with PCOS exhibited higher mean Body Mass Index (BMI) and waist-to-hip ratio, both of which are indicators of obesity, compared to the control group. This aligns with existing evidence linking PCOS with metabolic disturbances and obesity.Importantly, the study revealed that mean fasting insulin and total cholesterol levels were significantly higher in the PCOS group compared to the control group. These findings suggest a potential increased risk for the future development of type 2 Diabetes Mellitus and cardiovascular disease in individuals with PCOS. Insulin resistance, often present in PCOS, can lead to elevated insulin levels, contributing to both hyperandrogenism and metabolic complications.In summary, the study provides a comprehensive overview of the clinical, hormonal, and metabolic features associated with PCOS. The identification of key markers, such as elevated total testosterone, fasting insulin, and total cholesterol levels, emphasizes the importance of a multidimensional approach in the diagnosis and management of PCOS, taking into account both reproductive and metabolic aspects of the condition.

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