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ORIGINAL ARTICLE

Exploring Polycystic Ovarian Disease and Its Clinical and Biochemical Characteristics in Young Females

Tayyaba Batool[1], Sabahat Fatima [2], Jazib Andleeb[3], Khadija Kiran[4], Zahid Mahmood[5], Adnan Riaz[6]

[1]*Department of Biochemistry, Quaid-E-Azam Medical College Bahawalpur, Pakistan*
[2]*Department of Biochemistry, Gujranwala Medical College, Pakistan*
[3]*Department of Physiology, CIMS Bahawalpur, Pakistan*
[4]*Department of Physiology, Gujranwala Medical College, Pakistan*
[5]*Department of Biochemistry, Wah Medical College, Pakistan*
[6]*Department of Biochemistry, M Islam Medical College, Gujranwala, Pakistan*

Correspondence:
Tayyaba Batool
drtayyababatool@yahoo.com

Abstract

Background: The most contentious endocrine disorder affecting women worldwide is called PCOS, or polycystic ovarian syndrome. Compared to women in the UK, where the incidence of PCOS is between 20% and 25%, Pakistani females had a higher prevalence of 52%. One major limitation of previous community studies was the lack of biochemical and clinical screening.

Objective: To investigate the clinical and biochemical characteristics of polycystic ovaries (PCO) and associated factors, such as insulin, LH, FSH, oestradiol, testosterone, free testosterone, and SHBG in young women.

Material and Methods: This prospective study was conducted at the Department of Biochemistry, Central Park Medical College, Lahore, from August 1, 2023, to February 1, 2024. Women attending hospitals were informed about the study and underwent ultrasonography to identify PCO. The study included 201 women diagnosed with PCO as the case group and 233 healthy women as the comparison group. After obtaining consent, participants completed questionnaires and underwent hormonal and biochemical analysis. Data were analyzed using SPSS version 26.

Results: The average age of the control group was 25.83 ± 4.6 years, while the PCO group had an average age of 27.12 ± 5.52 years, with a significantly higher BMI ($p = 0.001$). Women with PCO showed increased insulin resistance, higher LH, and oestradiol levels, and reduced FSH. Testosterone levels and free testosterone index did not differ significantly between groups.

Conclusion: A significant proportion of women with infertility issues in Pakistan exhibit PCO. Insulin resistance is a key factor in PCO, and effective management of insulin levels may reduce the risk of developing PCOS.

Keywords: PCOS, Insulin resistance, oestradiol, HOMA-IR

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Introduction

Although polycystic ovaries (PCO) are the most commonly occurring endocrine condition affecting women of reproductive ages, their etiology remains unclear [1]. The most contentious endocrine disorder affecting women worldwide is called PCOS, or polycystic ovarian syndrome. Compared to women in

In the UK, where the incidence of PCOS is between 20% and 25%, Pakistani females had a higher prevalence of 52%[2]. This disorder manifests as irregular menstruation, cystic acne, hirsutism, hair loss, seborrhea, and obesity. Clinical features include hyperandrogenism, obesity, irregular menstruation,

and ovular infertility, however individual patient presentation may vary 3. The primary cause of hirsutism (excessive hair growth) and ovulation (infertility) in women is PCOS. Women with PCO are more likely to

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have insulin resistance and glucose intolerance. PCOS females exhibit a greater degree of insulin resistance in comparison to hyperandrogenemia[4]. In response to a glucose load, PCOS patients who are overweight or normal weight produce excessive amounts of insulin that are out of scale due to their insulin resistance[5].In women with PCOS, increased testosterone causes "android obesity," which is characterized by an excess of fatty depositions in the upper and central regions of the body including a waist-to-hip ratio of about 0.85 or greater. An elevated waist-hip ratio is linked to insulin resistance and dyslipidemia regardless of BMI[6]. More commonly than any other disorder, PCOS has been associated with insulin resistance and alterations in ovarian function. Insulin acts through a receptor-mediated method to induce steroid genesis in a normal ovary. The effects of increased insulin on the ovaries are researched in women with obesity, diabetes mellitus, high insulin resistance, and polycystic ovarian syndrome (PCOS)[7]. This notion is supported by the fact that metformin works well as an insulin-sensitizing drug in the treatment of polycystic ovarian conditions[8]. In PCO patients, extra insulin is brought on by insulin resistance, which affects the skeletal muscle and the adipose tissues but not the ovaries. This results in ovarian androgen hypersecretion[9-10]. Compared to lean controls, obese PCOS patients had higher levels of insulin resistance. However, weight loss only improves insulin sensitivity in a small percentage of individuals, and non-obese PCOS sufferers have also been shown to have insulin resistance. However, an ultrasound demonstrating polycystic ovaries (PCOS) alone cannot be used to diagnose PCOS[7]. PCOS is a very varied condition characterized by a variety of symptoms, including irregular menstruation, infertility, acne, hirsutism, weight gain issues, and abnormal biochemical variables (such as elevated androstenedione, testosterone, LH, and insulin)[10]. Throughout the disease, women with polycystic ovaries on ultrasound may present with any one of the above symptoms or a combination of more than one. However, estimates from community-based studies place the whole population's incidence of polycystic ovarian syndrome anywhere from 17 to 22 percent[11]. One major limitation of previous community studies was that they did not do thorough biochemical and clinical screening, which made it impossible to determine the prevalence of PCOS in these areas directly. Thus, we designed prospective research in which women in their 35 to 50 years were assessed for insulin resistance, BMI, and hormonal imbalance. We had the opportunity to look at any potential relationships between PCO and additional PCOS characteristics using the data that was gathered.

Material and Method:

Study design: This prospective study was conducted at the Department of Biochemistry, Central Park Medical College, Lahore, from August 1, 2023, to February 1, 2024. Institutional Review Board approval was obtained before the initiation of the study.

Study population: Women attending the hospital were informed about the study and underwent ultrasonography to identify polycystic ovaries (PCO). A total of 201 women diagnosed with PCO were included as the case group, while 233 healthy women without PCO served as the control group.

Inclusion and Exclusion Criteria

Inclusion Criteria: Women with PCO confirmed by ultrasonography and healthy women without PCO.

Exclusion Criteria: Women with other causes of ovulation/oligomenorrhea, such as Cushing syndrome, androgen hormone-secreting tumors, non-classical congenital adrenal hyperplasia (NC-CAH), thyroid disorders, hyperprolactinemia, or drug-induced androgen excess.

Sample size calculation: The sample size was calculated using a 52% prevalence rate, with a total of 160 participants determined via the WHO sampling size calculator. A prevalence of two polycystic ovaries was assumed, with a 95% confidence interval and a 5% margin of error.

Data Collection

Demographic and Anthropometric Data:

Demographic details such as age, marital status, height, weight, and socioeconomic status were collected using a structured questionnaire. Body Mass Index (BMI) was calculated using the formula: BMI=weight(kg)height(m)2 BMI values of ≥25 were classified as overweight. Skinfold thickness was measured at four different sites, and the waist-to-hip ratio was calculated to assess body fat distribution.

Biochemical Analysis:

Fasting blood samples were collected during the first five days of the menstrual cycle.

The following parameters were measured:

Glucose: Using the automated analyzer Mindray BS-240.

Insulin: Using the IMMULITE 1000 Analyzer.

Follicle-stimulating hormone (FSH) and Luteinizing Hormone (LH): Enzyme assay performed using the Roche Cobas e411 Analyzer.

Estradiol: Measured using a double-antibody kit (Elecsys Estradiol II by Roche).

Sex Hormone-Binding Globulin (SHBG) and Testosterone: Measured using the Abbott Architect i1000SR Analyzer.

Calculated Indices:

The free Testosterone Index (FTI) was calculated as:

FTI=Testosterone concentration in bloodSHBG concentration in serum×100\{FTI} = \frac\ {Testosterone concentration in blood} {SHBG concentration in serum}/times 100

Insulin Resistance: Assessed using the Homeostatic Model Assessment (HOMA-IR) software (version 2), provided by the Diabetes Research Center at the Radcliffe Institute, Oxford.

Statistical analysis: Data analysis was performed using IBM SPSS version 26.0. Descriptive statistics were applied for demographic variables. The independent t-test was used to determine the mean and standard deviation for anthropometric and biochemical parameters. A p-value <0.05 was considered statistically significant.

Results:

In all, 201 women with PCO and 233 women without PCO were included in this study. Table I, provides a frequency and percentage summary of the marital, socioeconomic, and level of education of all females, including cases (PCO) and controls (non-PCO). As per the table, the highest proportion of married women with low economic status and greatest education were found to be married. As shown in Table 2, the mean age of the subjects was 27.12 ± 5.52 years while that of the subjects in the control group was 25.83 ± 4.6 years. When comparing PCO-afflicted women to control groups, their BMI increased dramatically (p= 0.001).

Tables 1 show the Participants' Demography.

Table 1: Demographic Characteristics of Participants

Category	Subcategory	Frequency	Percentage (%)
Marital Status	Single	86	19.8
	Married	348	80.1
Socioeconomic Status	Low income	262	60.4
	Middle income	137	31.6
	High income	35	8.1
Educational Status	Under matriculation	49	11.5
	Matriculation	37	8.4
	Intermediate	40	9.5
	Bachelors	125	29.0
	Masters	189	43.5

Table 2: Age, Body Mass Index, Hormonal and biochemical Comparison of Case and Control group

Variable	Unit	Group	Mean ± SD	p-value	Odds Ratio (OR)	95% Confidence Interval (CI)
Age	Years	Cases	27.12 ± 5.52	0.010	Referent	Referent
	Cases	Controls	25.83 ± 4,65		1.12	(1.03 -1.22)
BMI	Kg/m²		24.72 ± 4.93	0.001	Referent	Referent
		Controls	22.30 ± 3.79		1.18	(1.08-1.28)
Insulin	IU/ml	Cases	36.92 ± 7.28	0.000	Referent	Referent
		Controls	12.31 ± 1.85		4.02	(3.01-5.36)

LH	IU/L	Cases	5.12± 0.31		Referent	Referent
		Controls	3.83 ± 0.29		1.34	(1.01-1.78)
FSH	IU/L	Cases	4.08 ± 0.36	0.000	Referent	Referent
		Controls	5.90 ± 0.93		0.62	(0.48-0.80)
Oestradiol	pmol/L	Cases	105.88 ± 0.36	0.000	Referent	Referent
		Controls	78.53 ± 0.93		1.41	(1.12-1.78)
Testosterone	nmol/L	Cases	6.44± 2.90	0.057	Referent	Referent
		Controls	6.25 ± 2.68		1.03	(0.99 -1.07)
Free Testosterone	nmol/L	Cases	4.53 ± 0.07	0.562	Referent	Referent
			4.17± 0.047		1.08	(0.82 -1.42)
SHBG	nmol/L	Cases	16.84 ± 15.19	0.965	Referent	Referent
		Controls	16.31 ± 15.26		1.03	(0.82 -1.42)

This table provides an overview of the hormonal and biochemical exhibit of markedly elevated insulin and insulin resistance. When comparing the cases to the control, there is a large increase in LH and estradiol and a significant drop in FSH. In this group, the testosterone level is not substantial. The free testosterone index and SHBG do not differ substantially either. The mean as well as the standard deviation (SD) of the data are displayed. To examine the outcome, an independent t-test was used. P < 0.05 indicates significance. Thirty-three of the twenty-one women—or 26 percent of all women with PCO and 12.1 percent of all 434 women—met the criteria for polycystic ovarian syndrome. Meeting these criteria, 201 women with PCO were included in the cases group, and 233 healthy women were picked as the control group. In pairing, only characteristics of women's instances were correlated. Table III indicates that there was little difference between LH and FSH. However, insulin and SHBG have a negative correlation (r2 = -0.015, p = 0.040).

Table 3 Correlation of insulin and hormonal parameters on Pearson's test

Correlation	r2	P value
FSH x LH	0.027	0.780
Insulin X SBHG	0.015	0.040

Pearson's correlation analysis was used to examine the outcome. There is significance ($p<0.05$).

Discussion:

The prevalence rates of PCOS have increased to 26% in cases, which is a considerable rise from the 17 to 22% found in other community-based research[12]. In this study, women having PCOS were compared to healthy women based on clinical observations. Although the association between the condition and irregular monthly periods was not statistically significant in this cohort of women, it was in women with normal ovaries. Studies conducted in hospitals have revealed a direct link between irregular menstruation and polycystic ovaries. In contrast to the studies by Yilei Hi et al., Jeena Nobles et al., and A; rates of irregularity According to Marina Sakiba and her colleagues, the females without PCO had
significantly higher irregularity frequencies under the given circumstances[13-15]. Given that the research population was young when they underwent menarche and began having menstrual periods regularly over five years later, this discrepancy might be explained as was already indicated in the research that Anagnostis, Panagiotis, and colleagues undertook[16]. Merely 20% of the participants in this research had progressed five years or more past menarche. It's also critical to keep in mind that various research may use varying definitions of

what qualifies as an "irregular" cycle as well as various approaches to obtain this information. Yet, the high frequency of irregular cycles is most likely due to selection bias. Individuals with menstrual problems could be more inclined to take part in research if it involves a pelvic ultrasound [17].

According to Stephanie S. Rothenberg et al., the biochemical characteristic that most clearly distinguished PCOS women from those with a pair of normal and healthy ovaries who were not taking hormonal contraceptives was serum testosterone levels. Serum testosterone levels are frequently elevated in individuals with polycystic ovaries[18]. There was no statistically noteworthy difference in the free testosterone index between women with PCO and those with normal ovarian development. It was previously thought that women having polycystic ovaries would have better testosterone bioavailability due to decreased amounts of circulating SHBG. Research by Diamanti-Kandarakis E states that this study supports the results of other studies that indicate there is no difference in levels of SHBG between women with healthy ovaries and those with PCO[19-20]. According to Narinx N et al., there is an inverse relationship between serum concentrations of SHBG and body mass index. Therefore, the absence of significant differences in BMI between both groups may be the reason for the absence of significance in SHBG levels[21-22]. It is generally known that women having polycystic ovarian syndrome, regardless of weight, have higher fasting blood insulin levels and decreased insulin sensitivity by tissues. Our research revealed a significant difference between women with polycystic ovaries and those with normal ovaries in terms of fasting insulin and HOMA-IR. A more thorough study is anticipated to take into consideration the impacts of fat mass and the consumption of hormonal contraceptives since obesity is recognized to be a significant factor in the onset of insulin resistance in women, as stated by Rashidi, and Homeira[21]. When the data were split down by ovarian status, women with PCOS and polycystic ovaries showed better insulin sensitivity and lower fasting insulin concentrations, in contrast to the previously described results[22]. These findings suggest that poor insulin sensitivity and hyperinsulinism are not often signs of polycystic ovarian syndrome in young women (PCOS). We accept that this may be the result of chance, but the limited sample numbers in each group prevent us from making any solid conclusions about the relationship between PCOS and a more gradual or rapid change in biochemical characteristics. It is challenging to diagnose PCOS using stricter criteria, including hirsutism, elevated blood testosterone, as well as anovulation/ oligo-ovulation. Because we did not track the blood progesterone levels of the women in our study during the luteal phase, we are unable to determine the exact number of women who ovulated [23]. These results demonstrated that although polycystic ovaries, as determined by ultrasonography, are rather common in the 20–30 age group, they are not invariably associated with additional symptoms. This brings up the question once again of whether the appearance of polycystic ovaries on ultrasonography represents a "common" variety" of ovarian forms or is pathological.

In many instances, those with polycystic ovaries exhibited far higher amounts of LH than others with PCOS or even simply oligo anovulation. Thus, oligoanovulation and PCO combined indicate the existence of PCOS [24]. Similar to our research, there is a connection between serious reproductive issues and elevated LH levels. Midway through the follicular phase, a rise in LH may negatively impact oocyte development, resulting in the release of an "old" egg. This research was beset by several issues; first, because FSH and LH levels vary during a menstruation cycle, it was unable to precisely account for the day of the menstrual cycle on which the blood was drawn. As mentioned before, Check, JH, and Choe, JK have shown that the therapeutic usefulness of circulating androgens is not significantly affected by any of these variables. The study's drawback was that only total testosterone was evaluated, which resulted in a lack of diagnostic analysis and the absence of testing for important blood androgens such as dehydroepiandrosterone sulfate and androstenedione. Consequently, it's possible that the actual incidence of PCOS was underestimated. Lastly, because of the limitations of a cross-sectional research design, it is difficult to estimate the number of these young females with polycystic ovaries who may experience symptoms in the future. To learn more about the possibility of long-term risk, extensive future research on women with polycystic ovaries is required.

Conclusion:

In conclusion, polycystic ovaries are a common feature among infertile women in Pakistani tertiary care facilities. Women having polycystic ovaries do not necessarily exhibit the signs of PCOS. Nonetheless, 26% of the study group women had PCOS. Women having polycystic ovaries experience substantial resistance and hyperinsulinemia. Nonetheless, there is a considerable rise and drop in LH and FSH in cases compared to controls, although there is no meaningful correlation between them. In this investigation, testosterone levels did not alter PCO; however, individuals with high insulin levels showed a negative correlation with SHBG hormone. Therefore, controlling insulin can lower the chance of PCO.

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Conflict Of Interest: None

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