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ORIGINAL ARTICLE

Polycystic Ovaries and Associated Clinical and Biochemical Features in Young Women

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ABSTRACT

Background: The aetiology of polycystic ovarian syndrome (PCOS) is unknown, even though it is the most frequent endocrine disorder in women of reproductive age. Previous community-based studies were unable to directly estimate the prevalence of PCOS in these communities since they did not conduct comprehensive biochemical and clinical screening.

Objective: This research focused on polycystic ovaries and associated clinical and biochemical features in young women.

Study Design: Cross-sectional study

Study Setting: This study was conducted in Department of Biochemistry Central Park Medical College, Lahore from 1st August 2022 1st February 2023.

Methodology: During the study period, volunteers were recruited from hospitals and requested their consent. While women were informed specifically that ovaries scan (ultrasound) would be used to detect polycystic ovaries. After the confirmation of polycystic ovaries, they were taken 201 as a case group. To compare the data, we also recruited 233 healthy participants as a control group. After taking consent and filling the questionnaire both cases and controls participants were requested for biochemical and hormonal analysis. SPSS version 20 was used for data analysis.

Results: The mean age of control 25.83 ± 4.6 years and 27.12 ± 5.52 years of with significantly increased BMI in the women with PCO as compared to controls (p = 0.001). Insulin and resistance are significantly increased in those women suffering from PCO. LH, oestradiol are significantly increased and FSH is significantly decreased in cases as compared to control. The level of testosterone is not significant in this cohort. SHBG and also free testosterone index are also not significantly different.

Practical implication: Even though many women in rural areas experience signs of a disease, they are hesitant to see a gynecologist or endocrinologist for treatment due to a lack of disease awareness, management, and medical therapy that conforms to criteria. Most patients don't get treatment because of this hesitation, which can cause a host of problems down the road. This study was done to better understand the clinical and biochemical characteristics of polycystic ovary syndrome in young women.

Conclusion: Most women with infertility in Pakistan's leading medical centers have polycystic ovaries. Women with polycystic ovaries may not always experience the symptoms of polycystic ovarian syndrome. However, 26 percent of women in this research had PCOS. Women with polycystic ovaries often have hyperinsulinemia and high levels of insulin resistance. While LH and FSH are both considerably higher in cases than in controls, they are unrelated. The results of this investigation showed that although testosterone levels did not influence PCO, a negative correlation between insulin levels and SHBG hormone was seen in individuals with elevated insulin. Hence, the management of insulin can reduce the risk of PCO.

Keywords: PCO, PCOS, LH, FSH, oestradiole, hyperinsulinemia, HOMA-IR

INTRODUCTION

The aetiology of polycystic ovaries (PCO) is unknown, even though it is the most frequent endocrine disorder in women of reproductive age.[1] The polycystic ovarian syndrome (PCOS) is the most controversial female endocrine illness in the world. Pakistani women had a greater prevalence of PCOS of 52% as compared to the UK with a 20%-25% prevalence.[2] Menstrual abnormalities, hirsutism, cystic acne, seborrhea, hair loss, and obesity are all symptoms of this condition. Hyperandrogenism, obesity, menstrual irregularity, and ovular infertility are some of its clinical characteristics, however, each patient may present differently.[3]

In women, polycystic ovary syndrome (PCOS) is the leading cause of anovulation (infertility) and hirsutism (excess hair growth). There is a higher risk of glucose intolerance and insulin resistance in women with polycystic ovary syndrome. The insulin resistance associated with PCOS is more pronounced in ovular women than in hyperandrogenemia women who have regular menstrual cycles.[4] Both overweight and normal-weight women with PCOS have excessive insulin production in response to a glucose load, which is out of proportion to their insulin resistance.[5] Androgen excess leads to "android obesity" in women with polycystic ovary syndrome, defined as an excess of fat in the middle and upper parts of the body (a waist-hip ratio of 0.85 or higher). Independent of BMI, an increased waist-hip ratio is associated with dyslipidemia and insulin resistance.[2, 6] Insulin resistance and changes in ovarian function have been linked to PCOS more often than to any other condition. Insulin stimulates steroidogenesis in the normal ovary via a receptor-mediated mechanism. Women with diabetes mellitus, obesity, syndromes of high insulin resistance, and polycystic ovary syndrome (PCOS) are studied to characterize the consequences of elevated insulin on the ovaries.[7] Metformin's success as an insulin sensitizer in the management of polycystic ovary syndrome lends credence to this theory.[8] Ovarian androgen hypersecretion in women with polycystic ovary syndrome is caused by excess insulin due to peripheral insulin resistance affecting skeletal muscle and adipose tissue but not the ovary.[8, 9] Insulin resistance is increased in obese women with polycystic ovary syndrome (PCOS) compared to lean controls. Nevertheless, only in certain people does weight reduction restore insulin sensitivity, and insulin resistance has also been documented in non-obese PCOS participants. Nevertheless, a diagnosis of polycystic ovarian syndrome cannot be made only on the basis of an ultrasound showing polycystic ovaries (PCOS).[7] Menstrual irregularities, infertility, obesity, hirsutism, acne, and abnormal biochemistry (such as increased serum testosterone, androstenedione, luteinizing hormone (LH), and insulin) are only some of the symptoms of PCOS, which is a very variable illness.[10] Women with polycystic ovaries on ultrasonography may exhibit any one of these symptoms or a combination of symptoms throughout the range of the illness. Yet, estimates from community-based research put the frequency of polycystic ovaries in the general population anywhere between 17 and 22 percent.[11] Previous community studies' primary

shortcoming were unable to directly estimate the prevalence of PCOS in these communities since they did not conduct comprehensive biochemical and clinical screening. We thus planned a cross-sectional study of women aged 20-30 years evaluated based on their BMI, insulin resistance, and hormonal analysis. Using the collected information, we were able to investigate any possible connections between the existence of PCO and other PCOS features.

METHODS

Study Design and Setting: This cross-sectional study was completed in the Department of Biochemistry Central Park Medical College, Lahore from 1st August 2022 1st February 2023. This study was approved by the Ethical review committee. In this case-control study, the demographic details were recorded on a questionnaire. For biochemical analysis, laboratory data were noted.

Inclusion and Exclusion Criteria: All women who were diagnosed with and without polycystic ovaries were included as cases and control. It is important to rule out other causes of oligomenorrhea or anovulation, such as NC-CAH, Cushing's syndrome, androgen-secreting tumors, hyperprolactinemia, thyroid illnesses, drug-induced androgen excess, and so on were excluded from the study.[28,29]

Sample Size Calculation: On the WHO sample size calculator, a total of 160 subjects were chosen based on a prevalence of 52% [2] polycystic ovaries prevalence with 95% confidence interval and margin of error was 5%.

Study Participants: During the study period, volunteers were recruited from hospitals and requested their consent. While women were informed specifically that ovaries scan (ultrasound) would be used to detect polycystic ovaries. After the confirmation of polycystic ovaries, they were taken 201 as a case group. To compare the data, we also recruited 233 healthy participants as a control group. After taking consent and filling the questionnaire both cases and controls participants were requested for biochemical analysis.

Demographic details: Age, marital status, social economic status, education and body mass index was determined by recording the subjects' height and weight. "Overweight" was defined as a body mass index (BMI) of 25 or above. Body fat was evaluated by measuring skinfold thickness in four locations and calculating the waist-to-hip ratio.

Biochemical Parameters: To determine levels of glucose (mg/dl), insulin (uIU/ml), oestradiol (pmol/L), sex hormone binding globulin (SHBG, nmol/L), testosterone (nmol/L), follicle stimulating hormone (FSH, IU/L) luteinizing hormone (LH, IU/L) a fasting blood sample was taken in the 5 days of the menstrual cycle.

An automatic analyzer was used to determine blood sugar levels (machine name). Serum was tested using a (machine name) to determine insulin levels. The (machine name) Analyzer was used for the enzyme immunoassay for LH and FSH. To measure oestradiol in the blood, a double-antibody (kit name). On the analyzer (machine name), were used to determine testosterone and and SHBG was determined. The formula for the calculation of free testosterone index was xtestosterone blood concentrations/SHBG serum concentrations x 100. The Diabetes Research Center at the Radcliffe Infimary Oxford provided the Homeostatic Model Assessment (HOMA) software, version 2.

Statistical Analysis: The data analysis for this study was carried out using version 20.0 of the IBM-SPSS. Descriptive analysis was performed on demographic factors. Independent t test was used to determine the mean and standard deviation of anatomical parameters. If the p-value was lower than 0.05, the data were statistically significant.

RESULTS

Total 233 women of without PCO and 201 with PCO were enrolled in this study. The marital, socio economic and educational status of all women including cases (PCO) and control (non-PCO) summarizes in Table I as frequency and percentage. According to the table the maximum percentage of women were married, with low-income status with maximum education. The mean age of control 25.83 ± 4.6 years and 27.12 ± 5.52 years of cases as summarized in table II. The BMI was significantly increased in the women with PCO as compared to controls (p= 0.001).

Table 1: Demographics status of study participants.

Marital Status	Frequency	Percent
Single	85	19.6
Married	349	80.4
Socioeconomic Status		
Low income status	262	60.4
Middle income status	137	31.6
High income status	35	8.1
Educational Status		
Non-Matriculated	48	11.1
Matriculated	36	8.3
Intermediate	39	9.0
Bachelors	123	28.3
Masters	188	43.3

Further table II summarizes the biochemical and hormonal analysis. Insulin and its resistance is significantly increased in those women suffering from PCO. LH, oestradiol are significantly increased and FSH is significantly decreased in cases as compared to control. The level of testosterone is not significant in this cohort. SHBG and also free testosterone index are also not significantly different.

Table 2: Age, BMI, Biochemical and Hormonal Comparison of Cases and Controls

Variables		Mean	Std. Deviation	p Value
Age (years)	Control	25.83	4.638	.010
	Cases	27.12	5.521	
BMI (Kg/m2)	Control	22.30	3.794	.001
	Cases	24.72	4.926	
Insulin (uIU/ml)	Control	12.13	1.846	.00
	Cases	36.92	7.780	
HOMAIRI	Control	2.37	0.46	.00
	Cases	9.69	3.02	
LH (IU/L)	Control	3.83	0.29	.047
	Cases	5.12	0.31	
FSH (IU/L)	Control	5.90	0.93	.00
	Cases	4.08	0.36	
Oestradiol (pmol/l)	Control	78.53	8.818	.00
	Cases	105.88	20.540	
Testosterone (nmol/L)	Control	6.25	2.68	.057
	Cases	6.44	2.90	
SHBG (nmol/L)	Control	16.31	14.26	
	Cases	16.84	15.19	0.965
Free testosterone index	Control	4.17	0.07	
	Cases	4.53	0.07	0.562

The data is presented as mean and standard deviation (SD). The result was analyzed by using an independent t-test. The p<0.05 is significant.

Out of two hundred and one women, fifty-three met the criteria for polycystic ovary syndrome, which accounts for 26% of all women with polycystic ovaries and 12.1% of all 434 women. Full these requirements, 233 were healthy women taken as control group and 201 women suffered from PCO and included in cases group. Only variables in cases women were correlated in pairing. According to the table III the LH with FSH were insignificant. But SHBG is negatively correlated with insulin (r2 = -0.013, p=0.039).

Table 3: Correlation of hormonal parameters and insulin.

Correlation	Person's Test	
	r2	P-value
LH x FSH	0.02	0.779
SBHG x Insulin	-0.013	0.039

The result was analyzed by using a Pearson's correlation. The p<0.05 is significant.

DISCUSSION

Other community-based studies have indicated prevalence rates between 17 and 22%, thus this is a significant increase with 26% of PCOS in cases.[12] In this study the women with polycystic ovaries compared on the basis of clinical observation with healthy women. While the correlation between polycystic ovaries and monthly irregularity was close to being statistically significant in cases in this cohort than among women with normal ovaries. Hospital based studies have shown a strong correlation between polycystic ovaries and menstrual irregularity. As compared to the rates of irregularity community-based studies by Yilei Hi et al, Jeena Nobles et al, and A Marina Sakiba and her team determined the frequency of irregularity recorded in the females with no PCO was substantially better in conditions.[13-15] As establishing regular menstrual cycles more than five years after menarche, the early age of the research cohort may account for the disparity. As previously mentioned in the study conducted by Anagnostis, Panagiotis et al.[16] In this study, just a 20th of the individuals had reached five or more years beyond menarche. It's also important to remember that different studies may employ different definitions of what constitutes a "irregular" cycle and different methods to gather this data. Yet, selection bias is most likely to account for the high incidence of irregular cycles. Women who are having menstruation issues may be more likely to participate for a study if a pelvic ultrasound is part of it.[17] Rothenberg, Stephanie S et al., suggested that serum testosterone concentration was the biochemical factor that significantly differentiated women with polycystic ovaries from those with normal ovaries who did not use hormonal contraception. Polycystic ovaries are often linked to increased levels of serum testosterone.[18] However, in this study there is no relation of testosterone found in PCO suffering women similarly found by Michelmore, K. F et al.[19] The free testosterone index showed no statistically significant difference between women with normal ovarian development and those with the polycystic ovarian disease. In the past, it has been hypothesized that lower levels of circulating SHBG in women with polycystic ovaries would lead to a higher bioavailability of testosterone. According to research (Diamanti-Kandarakis E), this study confirms the findings of numerous others showing no change in SHBG levels between women with polycystic and those with normal ovaries.[20] Serum concentrations of SHBG are inversely associated to body mass index by Narinx N et al., hence the lack of significant variations in BMI across the groups may account for the lack of significance in SHBG.[21, 22]

It has been well documented that both normal-weight and overweight women with polycystic ovarian syndrome have increased fasting blood insulin and impaired insulin sensitivity. Our study found statistically significant difference in fasting insulin and HOMA-IR between women with polycystic and those with normal ovaries. As obesity is known to be a crucial component in the development of insulin resistance in women, additional in-depth research is planned to account for the effects of fat mass and the use of hormonal contraception, described by Rashidi, Homeira.[23] Women with polycystic ovaries and PCOS, in contrast to the aforementioned results, exhibited lower fasting insulin concentrations and higher insulin sensitivity when the data were broken down by ovarian status.[24] Based on these results, it seems that hyperinsulinism and low insulin sensitivity are not usually features of polycystic ovarian syndrome in young women (PCOS). The small sample sizes in each category mean that we cannot draw any firm conclusions on whether or not PCOS is related with a more gradual or abrupt change in biochemical features, although we acknowledge that this may be due to chance. Diagnosing PCOS using the more stringent criteria, such as high blood testosterone or hirsutism, and anovulation or oligo-ovulation, is difficult we cannot say how many of the women in our trial ovulated since we did not monitor their blood progesterone levels during the luteal phase.[25] These findings showed that polycystic ovaries, as diagnosed by ultrasound, are relatively frequent in this 20–30 years old age range, but are not always accompanied by additional symptomatology. This raises again the issue of whether polycystic ovary appearance on ultrasonography is pathological or a "normal variety" of ovarian shape. In cases, the LH levels of those who had polycystic ovaries were considerably greater than those who had either PCOS or just oligoanovulation. It follows that PCO and oligoanovulation together point to the presence of PCOS.[26] As similar to our study, high levels of LH are linked to severe reproductive problems. An increase in LH during the middle of the follicular phase may have a negative effect on oocyte maturation, leading to the discharge of a "old" egg . Several problems plagued this research as LH and FSH levels fluctuate during the menstrual cycle, it was not able to account for the exact day of the cycle when the blood was sampled. As has been pointed out, none of these variables seems to significantly affect the therapeutic utility of circulating androgens demonstrated by Check, JH and Choe, JK.[27]

The study limitation with less no of diagnostic analysis including serum androgens such androstenedione and dehydroepiandrosterone sulphate were also not tested, despite their importance, since only total testosterone was assessed. As a result, the true incidence of PCOS may have been underestimated. Lastly, it is hard to know how many of these young women with polycystic ovaries may have symptoms in the future due to the constraints of a cross-sectional research design. There needs to be large-scale, prospective studies of women with polycystic ovaries throughout time to better understand the potential for long-term danger.

CONCLUSION

In conclusion, the majority of infertile women in Pakistan tertiary care hospitals have polycystic ovaries. Polycystic ovarian syndrome symptoms are not always present in women who have polycystic ovaries. But in this study, there were 26% women were suffering from PCOS. In polycystic ovaries the women are having hyperinsulinemia with significant resistance. However, LH and FSH is significantly increased and decreased in cases as compared to control but not significant corelated to each other. In this study, the level of testosterone is not affecting on PCO but in the patients who were high insulin revealed negatively corelated with SHBG hormone. Hence, the management of insulin can reduce the risk of PCO.

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