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Original Research Article

Clinical, ultrasonographical and hormonal correlation in women with polycystic ovarian syndrome

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ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder in women of fertile age. The prevalence, time of onset and severity of clinical presentation vary among different ethnic and racial groups. Though there is significant reproductive, endocrine and metabolic morbidity of PCOS, very little is known about its different modes of presentation in Indian population. It is a cross sectional observational study. The objective To study the correlation between the clinical, ultrasonographical and hormonal features in women diagnosed as PCOS based on the revised diagnostic criteria, 2003.

Methods: A cross-sectional study of 74 PCOS women who had oligo ovulatory cycles and polycystic ovarian morphology on ultrasound was done. Data about menstrual history and anthropometric measurements were collected. Clinical observations of acne and hirsutism were made. Transvaginal ultrasonography and biochemical analysis for free testosterone was done.

Results: In all, 74 PCOS women were studied and analyzed. The mean age was 24.88±4.03, mean BMI was 25.48 ±3.75 and mean free testosterone was 3.81±4.05. Among the PCOS women 39.8% were hirsute, 10.1% were obese, 2.3% had acne and 38% were hyperandrogenemic. Of the hyperandrogenemic women 61.2% were hirsute, 53.22% were obese and 36.54% had acne. The association between BMI and free testosterone level was statistically significant (p=0.0023). BMI was moderately correlated with hyperandrogenemia (r=0.446). The mean left ovarian volume was higher in obese than in non-obese women, which was statistically significant (p=0.003). The mean left ovarian volume was high in hyperandrogenemic women which was statistically significant (p=0.00034).

Conclusions: In the present study it was found that there is association between obesity and free testosterone level which was significant. There was statistically significant association between ovarian volume and obesity. Similarly, there was association between ovarian volume and hyperandrogenemia which was significant. Hirsutism and acne had no association with hyperandrogenemia.

Keywords: Free testosterone, Hirsutism, Hyperandrogenesim, PCOS, Polycystic ovaries, Ultrasound

INTRODUCTION

'An enigma wrapped in riddle and surrounded by mystery,' a quote by Sir Winston Chirchill holds good for polycystic ovarian syndrome (PCOS). PCOS is a multifaceted heterogeneous disorder and the most common endocrine abnormality in women of reproductive age.[1] The prevalence of PCOS varies from 3% to 11% depending on the diagnostic criteria used and the population studied.[1-6]

PCOS is a syndrome of ovarian dysfunction. The cardinal features being hyperandrogenism and polycystic ovarian morphology (PCOM) along with chronic anovulation.[7]

The clinical manifestations may include menstrual irregularities, signs of androgen excess like hirsutism, acne and obesity. It is also associated with increased risk of type 2 diabetes, dyslipidemia, cardiovascular disease and endometrial carcinoma. So, it is believed by some that PCOS is the ovarian expression of metabolic syndrome.[8-11] A precise and uniform definition of the syndrome was lacking. It presents with varied spectrum of symptoms and signs, several attempts have been made to define the diagnostic criteria in the past.[12-15] Although PCOS occurs universally, the prevalence, the time of onset, severity and type of clinical presentation differ between ethnic and racial groups.[16-18] There had been an on-going debate between gynecologists in Europe and North America about how best to define PCOS. In an attempt to resolve the problem, a revised diagnostic criterion was derived in the conference held at Rotterdam, Netherlands in 2003. According to this consensus, the workshop group agreed that two of the following three criteria were required in order to diagnose the condition, after exclusion of other causes of androgen excess. Those three criteria were oligo and/or anovulation, clinical and/or biochemical signs of hyperandrogensim and PCOM on ultrasound scan, with exclusion of related disorders.[19]

Notwithstanding the significant reproductive, endocrine and metabolic morbidity of PCOS, little is known of its different modes of presentation in Indian population. Present study is conducted to know the correlation of clinical, ultrasonographical and hormonal features of woman diagnosed as PCOS, based on the revised Rotterdam criteria, 2003, in this part of our country. The aim was to study the correlation between clinical, ultrasonographical and hormonal features in women diagnosed as PCOS based on the revised diagnostic Rotterdam criteria, 2003

METHODS

Cross sectional observational study was carried out in the department of Obstetrics and Gynecology at Vydehi institute of medical science and research centre, Bengaluru, Karnataka, from October 2014 to September 2016. Total number of women enrolled for the study were 84. Ethical committee clearance was taken.

Inclusion criteria

- All the women attending gynecology out-patient department and presenting with oligo-ovulatory cycles and having evidence of polycystic ovaries (PCO) on trans-vaginal sonography (TVS).

Exclusion criteria

- Women with clinical evidence of thyroid disorder, those clinically suspected to have Cushing's syndrome, androgen secreting neoplasms, congenital adrenal hyperplasia and women with hyperprolactinemia.

Informed consent was taken and all women were subjected to detailed questionnaire which included detailed menstrual history, reproductive history and family history. Clinical examination was performed, anthropometric measurements taken, transvaginal sonography and hormonal analysis were done.

Ovulatory dysfunction was defined as menstrual cycles ≥35 days in length or menstrual cycles of <8 cycles/ year. Height and weight were measured. Body mass index (BMI) was defined as weight (kg)/ height (m).^{2} Obesity was defined as BMI of 30. Presence of stigmata of insulin resistance like, acanthosis nigricans were noted. Presence of stigmata of hyperandrogenism were noted. Hirsutism was defined as excessive facial and or body terminal hair showing a male pattern distribution. Ferrimann and Gallwey scoring system was used to assess hirsutism.[20-23] A score of ≥8 was taken as hirsute. Acne was defined as presence of comedones on the face, neck, chest, upper back or arms. TVS was performed using Philips HD7 XE with 5.0 MHz transvaginal probe by two gynecologists experienced in transvaginal ultrasonography. The criteria to define PCO by ultrasound were: presence of 12 or more follicles in each ovary measuring 2-9 mm in diameter and/ or increased ovarian volume (>10ml). The follicle distribution and stromal echogenicity were omitted. Only one ovary fitting this definition was sufficient to define PCO.

Hormonal assay of free testosterone (FT) was done. Taking into account the bioavailability of the androgens, FT was chosen to be measured for hormonal analysis as the most representative ovarian androgen with minimal menstrual variation.[24-26] FT was measured by ELISA using the BioSource free testosterone ELISA kit. Normal range is: not detectable to 4.1 pg/dl. In present study, hyperandrogenemia was considered if FT was ≥4.1 pg/dl. A total of 84 women were enrolled for the study, however, 10 women were excluded from the analysis. Among the 10 women who were excluded, 4 had hyperprolactinemia and 6 had evidence of hypothyroidism. The total number of women included in the study and analysed were 74.

Statistical analysis

The data was analysed using Chi-square, unpaired student 't' test and Karl Pearson's correlation coefficient test. The statistical analysis was done using Medcalc Software.

RESULTS

A total of 74 women were included in the study and were analysed. Table 1 shows the mean values of different characteristics of the PCOS women. The mean BMI was 25.48±3.75 which was in the range of overweight. The

mean free testosterone was within the normal range. Mean left ovarian volume was higher than the mean right ovarian volume.

Table 1. Mean value of different patient characteristics.

Characteristics	Mean±SD
Age (years)	24.88±4.03
Married life (years)	4.63±3.0
BMI (kg/m²)	26.58±3.85
Free testosterone (pg/dl)	3.91±4.06
Ultrasonography	
Right Ovary	
No. of follicles	10.71±3.16
Ovarian volume (ml)	12.89±5.57
Left Ovary	
No. of follicles	12.23±2.17
Ovarian volume	15.25±6.11

Maximum number of patients accounting to 40%, presented between the age group of 25-29 years. It was found that hirsutism was present in 39.8% of PCOS women and 38% presented with hyperandrogenemia. Fifty four percent presented with bilateral involvement and rest had unilateral involvement of ovary on ultrasound. When the unilateral ovary was involved, it was the left ovary which was involved more frequently accounting for 30%. Right ovary was involved only in 11%.

When we analyzed these women in terms of their different modes of clinical presentation, it was found that 15.4% of women did not present with any clinical signs of hyperandrogenism. The most common presentation was hirsutism (39.8%), next common was hirsutism with acne which accounted for 11 %, hirsutism with obesity 10.6%, only obese with PCOS were 10.1 %; hirsutism with obesity and acne 6.3%; obese women with acne included 4.5%; the least being only acne 2.3%.

Table 2: Relation of hormonal status with clinical and ultrasonographic features.

	Hyperandrogenemic cases	Non hyperandrogenemic cases	χ^2 test (p value)
Hirsutism			
Score			
≥8	19	28	0.002 (0.96)
<8	12	17	Not significant
Acne			
Present	10	13	0.44 (0.51)
Absent	18	34	Not significant
BMI (kg/m²)			
<25	6	22	12.17 (0.002)
25-30	8	16	Significant
>30	16	7	
Ultrasonographic involvement			
Unilateral	8	26	8.34 (0.003)
Bilateral	23	18	Significant

It was found that the 61.2% of hyperandrogenemic women were hirsute, 53.22% were obese and 36.54% had acne. As shown in Table 2, the association between hirsutism and hormonal status was not significant. The association between acne and hormonal level (free testosterone) was also not statistically significant. The association between BMI and hormonal level was significant. Obesity was significantly associated with hyperandrogenemia.

Bilateral involvement of ovary on ultrasonography, was more associated with hyperandrogenemic women, when compared to unilateral involvement and also when compared to non hyperandrogenemic women, which was statistically significant. 75% of hyperandrogenemic women presented with bilateral involvement of ovary. As shown in Table 3, the association between normal BMI and overweight with hirsutism was not statistically significant. But the association of obesity and hirsutism was found significant.

Table 3: BMI and hirsutism.

BMI	Hirsutism score ≥8	Hirsutism score <8	χ^2 test (p value)
<24.9	20	6	4.54 (0.09) not significant
25-29	12	14	not significant
≥30	15	8	significant

BMI was moderately associated with hormonal level using Karl Pearson's correlation coefficient. (Table 4).

Using Student 't' test, it was found that the mean ovarian volume was high in hyperandrogenemic women when compared to non hyperandrogenemic women, which was statistically significant only in left ovary (Table 5).

Table 4: Correlation between hormonal level and other parameters.

Parameters	Correlation coefficient	Association
Age	-0.03781	Negligible
Hirsutism	0.0149	Negligible
BMI	0.4456	Moderate
Ultrasound		
Right ovary		
No. Of follicles	0.235	Weak
Ovarian volume (ml)	0.2569	Weak
Lefy ovary		
No. Of follicles	0.3745	Weak
Ovarian volume (ml)	0.3396	Weak

Though mean right ovarian volume was also increased, it was not statistically significant. The mean ovarian volume was high in obese women when compared to non-obese women, which was again significant only in left ovary. In the right ovary, though the volume was high compared to non-obese, it was not statistically significant (Table 5).

Table 5. Ovarian volume, hormonal status and BMI.

	Ovarian volume (ml)	
	Right ovarian volume	**Left ovarian volume**
Hyperandrogenism	13.93±6.51	18.54±6.79
Non hyperandrogenism	13.00±3.97	13.75±4.70
p value	0.0783 not significant	0.00033 significant
Obese	12.69±5.72	18.75±5.89
Non-obese	12.72±5.77	13.72±5.60
p-value	0.463 not significant	0.003 significant

In the present study, it was found that 13% of the women had family history of oligo-ovulatory cycles and 22% of the women had history of diabetes mellitus in the family.

DISCUSSION

In the present study, the mean age among the PCOS women was 24.78 years which was in accordance with the study done in Greek Island of Lesbos.3 The mean BMI was 25.48 kg/m^2 which was also comparable with the above study and also with the Indian study done on Bengali women.[27]

The mean free testosterone was 3.81 pg/dl in present study which was in accordance with the study conducted in Greek Island of Lesbos.[3] The mean was higher in the study done in Finland.[28] In this study serum free testosterone was measured by equilibrium dialysis of undiluted serum and the RIA used was highly sensitive.

In present study 38% of women presented with hyperandrogenemia as measured by free testosterone levels. This was in accordance with the study done on Chinese women.[29] In the study conducted in Finland, only about half of the women with PCOS exhibited elevated free testosterone concentration.[28] In the Indian study done, 64% of women were hyperandrogenemic. In this study it was the total testosterone which was measured and not the free testosterone.[27]

In the present study, the occurance of hirsutism in PCOS women was 39.8% which was in accordance with the Indian study done on Bengali women.[27] In the study done in Finland, it was 59%. In the study done on Scandinavian women, the prevalence was higher (84%), which explained the ethnic variation in manifestation of hirsutism.[28,30]

In the present study, it was found that 61.2% hyperandrogenemic women were hirsute. In the Chinese study it was found to be 23.7%.[29] This means that not all hyperandrogenemic women present with hirsutism and also hirsutism did not correlate significantly with free testosterone level.[31] 10.6% of hirsute women were obese in the present study. In the Indian study, 40% of hirsute women were obese.[27] The correlation of biochemical hyperandrogenemia and acne was not significant in present study. This was in accordance with the study done on Thai women.[32]

The occurance of obesity was 10.1 % in present study. This was 28% in the Chinese study.[29] In the study conducted on Bengali women in India, the prevalence was 40%. Obesity was significantly associated with increased free testosterone level. This was also found in the study conducted in Finland, in which BMI had significant effect on serum levels of free testosterone.[28]

In present study, 44% of PCOS women had unilateral involvement of the ovary on ultrasound and 54% of them had bilateral involvement. In the unilateral involvement it was the left ovary which was involved more frequently accounting for 30%. Similar observations were also made in the Indian study.[27] It was also observed that in hyperandrogenemic women, usually bilateral ovaries were involved. Seventy six percent of hyperandrogenemic women had bilateral involvement of the ovaries.

The mean ovarian volume was increased in the hyperandrogenemic group as compared to the non-hyperandrogenemic group. The increase in the ovarian volume in the left ovary was statistically significant. This was in accordance with the study conducted in Rotterdam.[15] In the present study, it was also found that

mean ovarian volume had significant association with obesity. It was noticed that the polycystic ovarian morphology was more seen in the left ovary.

This was also found in one of the study done in UK.[33] and the possible explanation given was that the pre-pubertal girls have significantly larger right ovary compared to the left.[34] By contrast, there were no significant differences in ovarian volumes between the right and left ovaries in healthy women of the reproductive age group.[35] This, however, may be secondary to the process of monthly ovulation, which could diminish the discrepancy between ovaries. Chronic anovulation in PCOS could reveal this discrepancy and might account for difference in the morphology of both the ovaries.

CONCLUSION

The association between obesity and hyperandrogenemia was statistically significant. The increase in the mean ovarian volume was significantly associated with obesity and hyperandrogenemia more so, in the left ovary. In hyperandrogenemic women, usually the involvement of ovary was bilateral. Overall in PCOS women, bilateral ovaries were usually involved. In unilateral involvement, left ovary was involved more frequently.

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