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Clinical and Hormonal Profile in Non Obese Women of Polycystic Ovarian Syndrome

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a complex syndrome showing the clinical features of an endocrine/ metabolic disorder, including hyperinsulinemia and hyperandrogenism. Two phenotypes are present, either lean or obese, with different biochemical, hormonal, and metabolic profiles. The objective of present study was to analyze the clinical presentation and its correlation with hormonal profile in non obese women with polycystic ovary syndrome (PCOS).

Material and Methods: This prospective study was carried out on 70 non obese PCOS women (BMI < 25 kg/m^2), diagnosed on the basis of Rotterdam's criteria, in department of Obstetrics and Gynaecology, Gajra Raja Medical College, Gwalior (M.P.). The data of the anthropometric measurements, clinical manifestations of hyperandrogenism, serum levels of luteinizing hormone (LH), follicle stimulating hormone (FSH) and total testosterone were collected and ultrasonography was done. **Results:** Maximum number of cases (34.28%) were in age group 26-30 years. Menstrual irregularity was the most common complaint in 80% women. 54.28% women were hirsute. Serum LH and serum total testosterone were raised in 68.56% and 65.71% women, respectively. Mean serum testosterone was 2.5 ± 0.4. The most common phenotype was phenotype A (55.71%).PCOS women with hirsutism had raised LH:FSH ratio in 41.02% group A, in 58.33% group B and in 50 % group Cwomen, as compared to only 20% women in group D had raised LH:FSH ratio.

Conclusion: The patients with PCOS, irrespective of their weight, demonstrate clinical manifestations such as irregular cycles, acne, hirsutism; hormonal abnormalities such as higher LH, LH/FSH, and testosterone levels.

Keywords: Polycystic ovarian syndrome (PCOS), hyperandrogenism, Rotterdam's criteria.

Introduction

Polycystic ovarian syndrome is the most common endocrine disorder of reproductive aged women and affects approximately 4 to 12 percent. Although symptoms of androgen excess may vary between ethnicity, PCOS appears to equally affect all races and nationalities.[1]

Despite the high prevalence of PCOS, the diagnosis and differential diagnosis remains confusing due to lack of well defined diagnostic criteria. In 2003 in Rotterdam, Netherlands, a consensus meeting between the European Society of Human Reproduction and Embryology and the American Society for Reproductive medicine (ESHRE / ASRM) redefined PCOS. Affected individuals must have two out of the following three criteria: 1. oligo- and / or anovulation (O), 2. hyperandrogenism (clinical and / or biochemical) (H) and (3) polycystic ovaries on

sonographic examination (P). However, because other etiologies, such as congenital adrenal hyperplasia, androgen-secreting tumors, and hyperprolactinemia, may also lead to oligo-ovulation and / or androgen excess, these must be excluded. Thus PCOS is at present a diagnosis of exclusion. [1].

The underlying cause of PCOS is unknown. However, a genetic basis that is both multifactorial and polygenic is suspected, as there is a well- documented aggregation of the syndrome within families. [2].

Although PCOS is commonly associated with excessive body weight and obesity, a lean phenotype also exists. Studies have demonstrated differences in insulin resistance, visceral adiposity, hormone profile, serum lipid profiles and psychological / neurological parameters between the obese and lean phenotype. [3].

PCOS is associated with various endocrine abnormalities such as increased serum LH levels, increased ratio of LH:FSH, increased serum testosterone. Hormonal profiling may help in decision making as regards to treatment modalities and can also be used for differential diagnosis. In addition, changes in hormonal profile may assist the assessment of efficacy of therapy. In the light of this background, the current study was conducted to analyze the clinical presentation and its correlation with hormonal profile in non obese women with polycystic ovary syndrome.

Material and Methods

This prospective study was carried out at Department of Obstetrics and Gynaecology, Kamla Raja Hospital, Gwalior (M.P.), during a period of 1 year from July 2016 to June 2017. The study included 70 lean (non obese) (BMI < 25 kg/m^2) polycystic ovary syndrome women, in the age group of 18 – 35 years. The exclusion criteria was hyperandrogenism due to any other endocrine disorders. Patients receiving hormonal / non-hormonal treatment for PCOS were also excluded from the study.

Diagnosis of PCOS was based on Rotterdam's criteria 2003 (presence of two of first three criteria such as oligo- and/or anovulation, signs of clinical hyperandrogenism and/or biochemical signs of hyperandrogenism and polycystic ovaries on ultrasonography after exclusion of specific identifiable disorders).

Patients were evaluated on outpatient basis. Complete history was taken especially menstrual and obstetric. Obstetric history included fertility status of the patient. Clinical examination was done with focus on anthropometry; height in cm, weight in kg was measured and BMI was calculated by dividing the body weight in kg by the squared height in meters. Waist : hip ratio was calculated and a value of > 0.88 was taken significant. Hirsutism was graded on the basis of modified Ferriman Gallway score. A score $\geq$ 8 was taken significant.

The blood sample for hormonal assay was collected on 2nd or 3rd day of the follicular phase of either spontaneous or progesterone induced menstrual cycle. Blood sample was taken either in morning or after 10 -12 hrs fasting and analyzed for LH, FSH and total serum testosterone.

For FSH normal values were taken as 2.5-10.2 mIU / ml. For LH normal values were taken as 2.4 - 12.75 mIU / ml. LH : FSH ratio 2 : 1 was taken significant. For testosterone normal ranges for were taken as 0.8–2.4 nmol/L.

The Rotterdam consensus defined polycystic ovarian morphology as the presence of 12 or more follicles with a diameter of two to nine millimeters and/or increased ovarian volume (over 10 milliliters) in at least one ovary.

Phenotypes based on Rotterdam criteria were also evaluated. Subjects were divided into 4 subgroups based on the criteria outlined in the Rotterdam PCOS consensus workshop. [4]

Table No. 1. Phenotype groups.

Phenotypical groups	Oligoovulation/ Anovulation (O)	Clinical and/or biochemical hyperandrogenism (H)	Polycystic ovaries (P)
A (O+H+A)	+	+	+
B (O+H)	+	+	
C (H+P)		+	+
D(O+P)	+		+

Analysis was done with the excel computer software and results were reported as percentage.

Results

77 PCOS women, with BMI < 25 Kg/m2, diagnosed on the basis of Rotterdam's criteria were selected for study.

Table No 2: Distribution of cases as per age

Age (in years)	Number of cases	Percentage
<20	16	22.85
20 – 25	22	31.42
26- 30	24	34.28
>30	8	11.42
Total	70	100.0

Maximum number of cases were in age group 26-30 years (34.28 %). Only 11.42 % cases were >30 years. (Table 2)

Table No 3. Clinical parameters

Clinical feature	Number	Percentage
Menstrual disorders	56	80
Hirsutism	38	54.28
Acanthosis nigricans	5	7.14
Acne	14	20
Infertility	10	14.28
Sonographic features of PCOS	45	64.28

Menstrual irregularity was the most common complaint in 80% women. 54.28% women were hirsute. Infertility was the presenting complaint in 14.28% women. (Table 3)

Table No 4. Hormonal profile in lean PCOS patients

S.N.	Hormone	Number of cases	Percentage
1.	Serum LH (mIU /ml)		
	<12.75	22	31.42
	12.75-20	46	65.71
	>20	2	2.85
2	Serum testosterone (nmol)		
	<2	24	34.2
	>2	46	65.71

Serum LH was raised in 68.56% women and serum total testosterone was raised in 65.71% women. Mean serum testosterone was 2.3± 0.4 nmol/l. (Table 4)

Table No 5. Prevalence of 4 phenotypical groups in lean PCOS

Phenotypical group	Number of cases	Percentage
A	39	55.71
B	12	17.14
C	14	20
D	5	7.14
Total	70	100

The most common phenotype was phenotype A (55.71%). Phenotype A met all 3 current criteria for PCOS. (Table 5) . The obtained results were further analyzed in terms of these 4 groups.

Table No 6: Hormonal status and clinical parameters in lean PCOS

S.N.	Hormonal parameter	A(n=39)		B(n=12)		C(n=14)		D(n=5)	
		No.	%	No.	%	No.	%	No.	%
1.	LH:FSH Ratio								
	1-1.5	10	25.64	2	16.66	3	21.42	1	20
	1.5-2	13	33.33	3	25.00	4	28.57	3	60
	>2	16	41.02	7	58.33	7	50	1	20
2.	Serum testosterone (nmol)								
	<2	15	38.46	4	33.33	6	42.85	3	60
	≥2	24	61.53	8	66.66	8	57.14	2	40

PCOS women with hirsutism had raised LH:FSH ratio in 41.02% group A, in 58.33 % group B, in 50% group C women, as compared to only 20% women in group D had raised LH:FSH ratio.Ttestosterone was raised in 61.53% group A, 66.66% group B, 57.14% group C women as compared to 40% women in group D. (Table 6)

Discussion

A majority (80%) of women with PCOS have an above average or high body mass index (BMI), insulin resistance (IR), and the typical PCOS symptoms (e.g., ovarian cysts, male pattern baldness, acne, and hirsutism). Many of these women are not diagnosed until fertility issues arise in adulthood. Some women with PCOS having a normal, if not low BMI may or may not have IR and exhibit symptoms that are typical to female pubertal maturation during adolescence (e.g., acne, irregular menstrual cycle, and potentially depression) and the pathophysiology of the disorder in these women may differ from that in obese women.

Age has a significant effect on the syndrome as regards both hormonal and metabolic profiles. In present study, maximum number of cases were in age group 26-30 years (34.28%). Only 11.42 % cases were >30 years. The clinical suspicion for PCOS in the lean group may have been lower, leading to an older age at diagnosis. Given the reproductive and metabolic risks linked to PCOS, it is important to identify these women early in order to prevent morbidity and even mortality linked to these risks throughout life.

Saxena P et al reported average age of 28.4 ± 4.2 years in the lean PCOS group. [5] In a study by Nitasha et al, mean age of non obese PCOS women was 24.2 ± 9.8. [6]

The most common presenting complaint was menstrual irregularity in 80% women. In study by Akshaya S et al, 90.9 % lean PCOS women reported with menstrual irregularity. In her study the presentation of menstrual irregularity was comparable in obese and lean group.[7] In study by Saxena P et al, 92.8 % lean PCOS women had menstrual irregularity.[5]

Hyperandrogenism is the second common defining characteristic features of PCOS. The increased androgen levels are principally ovarian in origin, clinically commonly manifested by hirsutism, and acne. In present study, hirsutism was the next most common presenting symptom present in 54.28% women. In studies by Akshaya S et al, 81.8 % and in study by Saxena P et al, 80.9%, lean PCOS women had hirsutism. [5,7] In study by Gupta et al, varying degrees of hirsutism were seen in 34% of nonobese women. [6]

Majumdar et al, reported a significantly higher prevalence of both menstrual irregularities (79.2% vs. 44%) and clinical hyperandrgenism (74.2% vs. 50.6%) in the obese versus lean PCOS women .[8]

In present study acne was the present in 20% women, while in studies by Akshaya S et al, and Saxena P et al acne was present in about 9.1% lean PCOS women. [4, 6] In contrast, in study by Sakina S et al, 65% of lean PCOS cases had acne.[9]

In PCOS, high androgen causes insulin resistance and acanthosis nigricans is a marker for its severity. In present study, acanthosis nigricans was present in 7.14% women.

In study by Akshaya S et al, it was present in 9.1 % , comparable with our study.[7] In a study by Sakina S et al, 10% of lean PCOS cases had acanthosisnigricans. [9]

In present study alopecia was not found in any patient. In study by Gupta et al also, male pattern baldness was not reported in both obese and non obese PCOS women. [6] In contrast, in study by Sakina S et al, 55% of lean PCOS cases presented with aloepecia. [9]

In study by Saxena P et al, presence of hirsutism, hirsutism score, irregular menstrual cycles, endometrial thickness of >4 mm, and acanthosis nigricans were comparable in obese and non obese PCOS . [5]

In our study, 64.28% lean PCOS women had polycystic ovaries on sonogram. Silfen et al, who studied 33 adolescents (11 nonobese and 22 obese) with PCOS reported that polycystic ovaries on ultrasound were more likely in the nonobese group than the obese group. [10]

PCOS is associated with various endocrine abnormalities such as increased serum LH levels, increased ratio of LH:FSH, increased serum testosterone. In present study, serum LH was raised in 68.56% women and serum total testosterone was raised in 65.71% women. Mean serum testosterone was 2.5 ± 0.4. In study by Gupta N et al, mean serum testosterone levels were significantly higher in non obese PCOS subjects (32% vs. 20%) when compared obese PCOS.[6] Saxena P et al reported higher levels of serum LH, LH/FSH ratio and testosterone in both lean and obese PCOS. [5]

In study br Ramanand et al, comparison between normal weight and overweight/obese PCOS women showed that, the LH, LH:FSH ratio and testosterone levels were higher in normal weight PCOS women and difference between LH:FSH ratio is highly significant.[11]

Depending on the pathogenesis and the interactions among different hormones, the clinical presentation and biochemical profile varies in an individual PCOS woman. All features of this syndrome may not be present in an individual patient. The Rotterdam and AE-PCOS Society criteria recognize at least 3 unique clinical phenotypes: (1) Frank PCOS (oligomenorrhea, hyperandrogenism, and PCO), (2) Ovulatory PCOS (hyperandrogenism, PCO, and regular menstrual cycles), and (3) Non-PCO PCOS (oligomenorrhea, hyperandrogenism, and normal ovaries). The Rotterdam criteria also recognize a fourth phenotype, Mild or Normoandrogenic PCOS, which is defined by oligomenorrhea, PCO, and normal androgens. Whether these 4 phenotypes represent a spectrum of the same condition is currently an area of debate.[4]

In present study, most common phenotype was phenotype A (55.71%). Phenotype A met all 3 current criteria for PCOS. The prevalence of phenotype A noted by Dewailly D et al., was 60.6%, slightly higher than our study. In present study minimum prevalence was of phenotype D (7.14%), while in study Dewailly D et al., reported minimum prevalence of phenotype B.[12]

The presented division into four phenotypical groups and the observed correlations contribute to the greater understanding of the core of the polycystic ovary syndrome and to the better recognition of its pathogenesis.

PCOS women with hirsutism had raised LH:FSH ratio in 41.02% group A, in 58.33 % group B, in 50% group C women as compared to only 20% women in group D had raised LH:FSH ratio

Similarly testosterone was raised in 61.53% group A, 66.66% group B, 57.14% group C women as compared to 40% women in group D. It supports the idea that LH produced increased androgen by thecal stimulation, which in turn, caused hirsutism. The highest serum levels of testosterone were observed in women who presented with clinical evidence of hyperandrogenism (groups A, B, and C). The highest average levels of LH were detected in the group B caused hirsutism.

In lean PCOS women in group D, LH:FSH ratio was raised in 20% women and testosterone levels were raised

in 40% women, although levels were lower than reported in other groups. The above data implied that USG proved subjects of PCOS also showed biochemical diagnostic parameters like raised LH:FSH ratio and hyperandrogenemia. Pelvic ultrasonography may be very helpful in the evaluation as well, but polycystic ovaries are not specific for PCOS. The number of follicles and ovary volume are both important in the ultrasound evaluation. So, identification of polycystic ovaries by ultrasound alone does not confirm the diagnosis of PCOS.

In study by Welt CK et al, testosterone and free testosterone levels were highest in women with IM/HA, intermediate in women with HA/PCOM, and lowest in women with IM/PCOM and controls. They reported that Subjects with PCOS defined by HA are the most severely affected, with the highest androgen levels.[13] Diamanti-Kandarakis E et al, reported similar findings. [14]

Conclusion

In present study, the older age at diagnosis in non obese PCOS women group suggests that a higher index of suspicion may be necessary for earlier diagnosis of PCOS in non obese PCOS women with clinical evidence of hyperandrogenism.

Patients with PCOS, irrespective of their weight, demonstrate clinical manifestations such as irregular cycles, acne, hirsutism; hormonal abnormalities such as higher LH, LH/FSH, and testosterone levels.

Because of the small number of women in the investigated group and too short a period on the trial, this study needs to be the subject of further research.

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