

Clinical Profile Polycystic Ovarian Syndrome - 100 Cases

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ABSTRACT

Introduction: Polycystic ovary syndrome (PCOS) is most common endocrine disorders of reproductive age affecting 5% to 10% of women worldwide. It is a heterogeneous, multifactorial, complex genetic disorder. The objective of this study was to determine pattern of presentation PCOS in patients presenting at our hospital.

Material and Methods: A cross sectional observation study of 100 PCOS patients was carried out between Gynecology outpatient. The clinical, biochemical and hormonal profile of these patients were analyzed and correlation was done between clinical features and biochemical and hormonal profile.

Results: Out of 100 patients, 87 presented with the complaint of oligomenorrhea, 48 with hirsutism, 10 with acne, 7 members presented with amenorrhea, 13 with menorrhagia. Obesity observed in 56, infertility is the presenting complaint in 54 patients and acanthosis nigricans observed in 14 patients. Mean BMI found to be 34.4 ± 6.6 kg/m². Diabetes mellitus observed in 9 patients, Hypertension in 4 patients, hypothyroidism in 3 patients, hyperprolactinemia in 3 patients. Ultrasound suggestive of PCOS is seen in 96 patients and total testosterone is increased in 27 patients.

Conclusion: Abnormal ovarian morphology was significantly less common in the majority of control women selected on the basis of normal reproductive and metabolic parameters in PCOD patients.

Keywords: Body Mass Index, Hirsutism, Obese, Polycystic Ovary Syndrome, Ovarian Volume, Testosterone.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is common endocrine disorders of reproductive age affecting 5% to 10% of women worldwide.¹ It is a heterogeneous, multifactorial, complex genetic disorder. PCOS was first described by Stein and Leventhal in 1935. For diagnosis two out of three criteria should be fulfilled, they are:

- Oligo-ovulation or anovulation;
- Clinical and/or biochemical signs of hyperandrogenism (with the exclusion of other causes of androgen excess like cushing's syndrome, congenital adrenal hyperplasia, thyroid abnormalities, androgen-secreting tumours and hyperprolactinemia);
- Polycystic ovaries (PCO) detected on ultrasound.

The PCO definition was revised in 2003. Then Balen and co-workers suggested that 12 or more follicles in one ovary, each follicle measuring 2-9 mm in diameter and/or volume of the ovary >10ml.⁴ PCOS is frequently associated with obesity and insulin resistance. Obesity has long been recognized as one of the features of PCOS, and 40-80% of women with PCOS are overweight or obese.

Prevalence of PCOS is estimated as highly as ranging from 2.2% to 26%.¹ The aim of the present study was to investigate the clinical, biochemical and ultrasonographic characteristics

of the women with polycystic ovarian syndrome, taken in to study as per Rotterdam criteria and correlation in between these characteristics. The objective of this study was to determine pattern of presentation PCOS in patients presenting at our hospital.

MATERIAL AND METHODS

100 women in reproductive age group attending gynecology outpatient department with any 2 out of 3 Rotterdam criteria were taken for study. According to joint consensus meeting between the European society for human reproductive embryology (ESHRE) and American society for reproductive medicine (ASRM) PCOS can be diagnosed by the presence of 2 out of 3 criteria.

1. Oligo and / or an ovulation.
2. Hyperandrogenism (clinical/biochemical)
3. Polycystic ovarian morphology on ultra sonogram-presence of 12 or more follicles in each ovary (with one ovary being sufficient for diagnosis) measuring 2-9mm in diameter or increase ovarian volume >10ml.

Exclusion Criteria

- Congenital adrenal hyperplasia
- Cushing's syndrome
- Androgen secreting tumors

Informed consent and ethical committee clearance was obtained from each patient. Women presenting with irregular cycles / amenorrhea and /or features of hirsutism are taken .In patients presenting with amenorrhea, pregnancy and other causes of amenorrhea are excluded. All patients are subjected to ultrasonography for polycystic ovarian morphology and ovarian volume.

Amenorrhea was defined as absence of cycles in the past 6 months and oligomenorrhea as menses >35 days. Infertility was assessed only in married patients and was defined as failure of spontaneous pregnancy after one year of marriage in the absence of male infertility and other factors of infertility.

For every patient detailed menstrual history regarding age of menarche, menstrual cycle is noted. Each patient questioned about H/O diabetes / hypertension / epilepsy / drug intake / childhood obesity.

Personal history—dietary habits, life style are given importance. Family history—similar complaint in mother/ siblings, and also the family H/O diabetes and hypertension are taken.

All were healthy with a spontaneous onset of puberty and a

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normal sexual development. None of them received medication known to affect carbohydrate metabolism and plasma sex steroids for at least 3 months before the study.

Weight was measured using a conventional Seca scale with a precision of 100 g, and height was measured with a Harpenden stadiometer.

BMI: Obesity and overweight were defined according to WHO criteria as a body mass index (BMI) ≥ 30 kg/m² and ≥ 25 kg/m² respectively.

Waist circumference was measured to the nearest 0.5 cm, using a flexible measuring tape at the narrowest circumference between the lower costal margin and the iliac crest in the standing position. The hip circumference measurement was obtained at the maximum perimeter at the level of the femoral trochanters. Waist to hip ratio was calculated as the ratio of these two circumferences.

Clinical examination — importance given to search for hirsutism/Acanthosis Nigricans/acne. Hirsutism is graded as per Ferriman-Gallway scoring system. Clinical hyperandrogenism was diagnosed if the FG score was 8 or greater or the patient had moderate to severe acne, defined by the presence of inflammatory lesions and their extension.

Biochemical hyperandrogenism was defined if T or FT/C or androstenedione were above the 95% confidence interval for the 97.5 percentile in C women.

The clinical studies were conducted during the early follicular phase (day 3–6 after menses) after a spontaneous or progestin-induced menstrual flow in the oligomenorrhoeic patients. At 8 a.m., after fasting overnight for 10–12 h, blood samples were obtained. Patients underwent also an oral glucose tolerance test (OGTT): blood samples were collected before and 30, 60, 90 and 120 min after ingestion of 75 g glucose in 150 ml water. Glucose levels were assayed in all samples. The serum total testosterone levels and lipid profile are measured in all patients. The same day, a trans vaginal pelvic ultrasound was performed on each patient using a 6.5 MHz endo vaginal probe. The ultrasound examinations were performed by one of the well-trained observers. were not aware of the patient's endocrine profiles.

The following parameters were evaluated echo graphically:

1. Presence, number and disposition of follicles in each ovary,
2. Ovarian volume, estimated according to the formula: $0.523(A \times B \times C)$, where A, B and C are the three ovarian diameters.
3. Endometrial thickness

A normal glycemic response, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) to OGTT was defined according to the criteria of the American Diabetes association (Wahl et al., 1998).

3. Polycystic ovarian morphology on ultra sound, defined as the presence of 12 or more follicles in each ovary (with one ovary being sufficient for diagnosis) measuring 2-9 mm in diameter and/ or increased ovarian volume > 10 ml (With the exclusion of other etiologies).

Polycystic ovarian syndrome is very common in obese women with body mass index greater than 30 kg/m². Insulin resistance is very common in PCOS which results in hyperinsulinemia. The sequelae of PCOS reach beyond reproductive health, these women are at increased risk of cardiovascular disease and Type

2 Diabetes mellitus. They may develop endometrial hyperplasia, thereby at increased risk of endometrial carcinoma.

Diagnosis of PCOS involves radiological and biochemical studies. Radiological studies include pelvic ultrasound and biochemical tests include estimation of serum concentrations of LH, FSH, and Testosterone etc. In the past 21 years progress in characterizing the relationship between insulin and PCOS has been substantial, pointing the way to new and novel therapy of PCOS. Insulin reduction whether by weight reduction or by insulin sensitizing agents like metformin appear to be of paramount importance in reducing circulating total or free testosterone in women with PCOS.

STATISTICAL ANALYSIS

Microsoft office 2007 was used for the interpretation. Total and percentages was done for results interpretation.

RESULTS

100 patients who fulfilled the Rotterdam criteria are selected for the study, each patient was analyzed methodically as per case sheet proforma.

Out of 100 patients 91 belong to below 30 years, 9 cases are seen above 30 years. 56% of patients are having BMI > 30 (OBESE) whereas 29% patients were under over weight group.

In 94% presented with oligomenorrhea and 52% are having hyper androgenism whereas 96% are having USG suggestive of PCO (table-1).

Out of 100 cases, 87% are having oligomenorrhea, 7% presented with amenorrhea, regular cycles observed in 6% and 13% presented with menorrhagia.

Out of 52 patients, only hirsutism is observed in 42 patients, only acne is observed in 4 patients and both hirsutism and acne observed in 6 patients. Out of 100 cases, only 27 had elevated levels total testosterone remaining all are having total testosterone within normal limits. in 52 hirsutism patients, only 27 had elevated total testosterone level (table-2).

In 91 patients, both increased ovarian volume and polycystic ovarian morphology observed in 65 patients only increased ovarian volume in 11 patients and only polycystic ovarian morphology in 15 patients.

Normal ovarian volume observed in 15 patients and increased ovarian volume in 76 patients. Normal ovarian volume observed in 4 patients of hirsutism and increased ovarian volume in 44 patients of hirsutism (table-3).

Acanthosis nigricans (AN) was described in 16% and 6% of these patients were overweight, 94% were obese and 32% were very obese (BMI ≥ 40 kg/m²). The mean BMI of those with AN was 38 ± 6.4 kg/m², while those without AN had BMI of 30.4 ± 6.8 kg/m² (table-4).

DISCUSSION

The most common clinical features of PCOS include menstrual irregularities, hirsutism and obesity. Oligomenorrhea was present in 85% of our cases as compared to 86% in patients of Najem et al.² In a study carried out by Balen et al³ oligomenorrhea was found in 47% of the cases. The reason for this lower frequency of oligomenorrhea in patients of Balen et al was the presence of other menstrual irregularities like amenorrhea in greater proportion in their patients. Amenorrhea was present in 19.2% the patients of Balen et al³ as compared to 7% in our patients

Variable	No of patients
Age distribution in years	
>20 yrs	14
20-24yrs	41
25-29yrs	36
30-34yrs	5
>35yrs	4
Marital status	
Married	74
Single	26
Body Mass Index	
<20	2
20-24	20
25-29	23
>30	56
Glucose tolerance test	
NORMAL	84
Impaired glucose tolerance	11
Suggesting diabetes	5
Rotterdam criteria	
Chronic anovulation(irregular cycles)	94
Hyperandrogenism	52
USG suggestive of PCO	96
Criteria for PCOS	
Chronicanovulation+hyperandrogenism+USG of PCO	42
Chronic anovulation+USG of PCO	48
Chronicanovulation+hyperandrogenism	4
Hyperandrogenism+USG of PCO	6
Total	100
Menstrual cycle irregularities	
Oligomenorrhea	87
Amenorrhea	7
Menorrhagia	13
Regular cycles	6

Table-1: Demographic data.

and 7.5% in patients of Najem et al of libya. In a study carried out by Fauzia et al⁴ on Pakistani patients oligomenorrhea was found in 75% of their cases which is comparable to 85% in our cases.

Hirsutism was present in 66.2% patients of Balen et al³ which is quite high as compared to 52% in our cases. The higher incidence of hirsutism in the cases of Fauzia et al⁴ may be due to smaller number of patients (52) in this as compared to larger number of patients (100) included in our study. Although amenorrhea and oligomenorrhea are the most common findings, normal menses may be present in PCOS, Balen et al found normal menses in 29.7% of their cases where as in our study 8% had normal menses. Our study correlates better with the figures for normal menses in other two studies carried out by Goldzieher et al⁵ and Lobo et al⁶ which are also half of what was noted by Balen et al.³ The reason may be very strict criteria for selection of patients in the studies carried out by us as well as Goldzieher and Lobo et al.⁵ At least one ovary exceeded 10 cm³ in size (PCOV), and/or there was polycystic ovary morphology (PCOM, at least 10 peripheral follicular cysts 8 mm or less in diameter as well as increased central ovarian stroma) in 91% of women with PCOS. There also were no significant correlations total ovarian volume

Total testosterone	
Normal	73 (73%)
Increased	27 (27%)
Total	100 (%)
Hirsutism	
Normal	25 (48%)
Increased	27 (52%)
Total	52 (100%)
Ultrasonographic criteria	
Both increased ovarian volume and polycystic ovarian morphology	65 (71.5%)
Only increased ovarian volume	11 (12%)
Only polycystic ovarian morphology	15 (16.5%)
Total	91 (100%)

Table-2: Levels of testosterone and USG findings in study

Ovarian volume	No of patients	No of patients with Hirsutism	%
Normal ovarian volume	15	4	26.6
Increased ovarian volume	76	44	57.8

Table-3: ovarian volume

Body mass index	No of patients	No of patients with acanthosis nigricans	% of an in particular group of BMI	% of an in total
<25	21	Nil	Nil	NIL
25-29	23	1	4.34	7.15
30-34	46	7	15.2	50
>35	10	6	60	42.85
Total	100	14		100

Table-4: Acanthosis nigricans and BMI data.

and, any aspect of glucose metabolism, or levels of reproductive hormones.

Out of the 100 studied patients, 74% were married and 26% were single. Mean age at presentation was 25.8, and about 67% of the patients were 20-29 years old. Oligomenorrhea was noted in 87%, amenorrhea in 7% while 6% had normal menses. Hirsutism was observed in 42%, acne in 12%, infertility in 40%, and galactorrhea in 4%. Mean BMI was 34.3 ± 6.6 kg/m², about 57% of patients were obese and nearly 24% were overweight.

Acanthosis nigricans (AN) was described in 16% and 6% of these patients were overweight, 94% were obese and 32% were very obese (BMI ≥ 40 kg/m²). The mean BMI of those with AN was 38 ± 6.4 kg/m², while those without AN had BMI of 30.4 ± 6.8 kg/m².

About 9% of the patients were diabetic according to fasting plasma glucose levels, and 17% of these were overweight and 83% were obese with mean BMI 38 ± 7.5 kg/m². About 8% of the patients had a family member diagnosed with PCOS and nearly 16% had a family member with a history of hirsutism, irregular menses, or infertility. Diabetes mellitus and hypertension in a first degree relative was reported by 16% and 8% of the patients, respectively. The mother was the affected family member in 82% of the diabetic relatives and in 88% of the hypertensive relatives. A family history of thyroid disease

was elicited in nearly 4% of patients.

There was no statistically significant difference in the clinical and biochemical features of PCO. The frequency of ultrasonographic features of polycystic ovaries (PCO) seen in our patients 96% is comparable with that reported by others (96.7%) who used trans-vaginal ultrasound in all their subjects. Trans abdominal ultrasound is less sensitive and more operator dependant than trans-vaginal ultrasound. The under utilization of Trans vaginal ultrasound is due to socio economic conditions and we preferred Trans abdominal USG in unmarried women. Only 4% are presented without USG picture of PCO The clinical and biochemical features of patients with normal USG did not differ from those with positive USG findings of polycystic ovary morphology.

Only 12% of our patients had acne as compared to 45% in Chinese women. Surprisingly, about 40% of the married patients were fertile without any medical intervention in contrast to only about 25% reported worldwide.⁷ Married PCOS patients are usually under gynecologist care because of their initial concern of infertility.

This study reports that obesity affects 57% of PCOS patients. Obesity is less common in PCOS women of Mediterranean descent, but more common in Hispanic, black, and white women with PCOS. Diabetes mellitus frequency was 9% in our patients, which is similar to the USA but less than what is noted in Asian women (17%) and more patients found to have impaired glucose tolerance. Hypertension was diagnosed in only 4% of our patients as compared to 12% in Tunisian patients.⁸ This is a large difference in the prevalence rate in two populations sharing a similar ethnic, and geographical background, however the Tunisian study was a prospective one which is more accurate than retrospective studies.

Obesity was clearly over-represented in both hypertensive and diabetic patients. Acanthosis nigricans (AN) was described in 14% of patients, which resembles that reported in China AND Libiya. The PCOS women with AN had significantly higher BMI, compared with those without AN, which is similar to observations from Thai and libiya study. AN is a marker of insulin resistance, as it is a result of insulin stimulation to the basal layers of the epidermis .

The finding of elevated total serum testosterone in 27% of our patients seems to be an underestimate to the actual rate of biochemical hyperandrogenism because we depend on total serum testosterone assays rather than free testosterone assays (due to availability issues), and different commercial kits have different cut off values .

Hirsutism and cycle disturbances are the major clinical features of PCOS patients None of the patients had signs or symptoms of severe virilism. The intensity of hirsutism in particular areas of the body varies in different patients and depends on the rate of androgen excess, or increased sensitivity of hair follicles to normal levels of androgens in the serum. The most frequently involved sites are face, peri umbilical and lower abdomen, areola, upper thighs, and chest.

Previous studies have shown very low intra- and inter observer variation for the measurement of ovarian volume by ultrasound^{9,10}, and this parameter has been used in a number of settings in women's health in addition to identifying polycystic ovaries.¹¹ The observer variation for the assessment of polycystic

ovaries is a more subjective measure¹² and may be higher.¹³ This suggests the need for evidence-based guidelines for the recognition of polycystic ovaries. Depending on the criteria- patients are divided into four groups.

- 1) All 3 criteria i.e chronic anovulation, clinical or biochemical hyperandrogenism and USG suggestive of PCO.-42%
- 2) Patients having only chronic anovulation and hyperandrogenism - 4%
- 3) Patients having only chronic anovulation and USG of PCO-48%
- 4) Patients having only hyperandrogenism and USG of PCO-6%

The patients who belong to first 2 groups fulfilled both the NIH and the ESHRE/ASRM ROTTERDAM criteria- 46. The patients who belong to 3rd and 4th groups will not come under PCOS according to NIH criteria as they fulfilled only 2 out of 3 criteria of Rotterdam and one criteria among the 2 is USG suggesting PCO- they will come under PCOS according to Rotterdam criteria only.

CONCLUSION

We conclude there is no association between either the morphology or size of the ovary and abnormal GTT or with total testosterone levels. These data suggest that the morphology and size of the ovaries are of little value in identifying distinctive metabolic or reproductive abnormalities in women with the endocrine syndrome of PCOS. Nonetheless, polycystic ovaries were highly and significantly prevalent, although not invariably present in women with PCOS. In fact, abnormal ovarian morphology was significantly less common in the majority of control women selected on the basis of normal reproductive and metabolic parameters.

These findings suggest that, in women with endocrine findings of PCOS, the size and morphology of the ovaries are of little help in identifying specific metabolic or reproductive abnormalities. Routine ovarian ultrasonography may not be necessary in women having hyper androgenic chronic anovulation.

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