A Study on Clinical Profile of Patients with Polycystic Ovarian Syndrome

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Abstract: <u>*Background:*</u> *Polycystic Ovarian Syndrome (PCOS) is a common gynaecological endocrinopathy characterized by chronic anovulation and hyperandrogenism. The disorder is heterogeneous and is one of the most common treatable causes of infertility.* <u>*Objective:*</u> *To study the various clinical presentations, biochemical and hormonal profile of patients with Polycystic ovarian syndrome in Indian women.* <u>*Materials and Methods*</u>*: Present study is a cross ‑sectional study carried out over a period of 12 months in department of Obstetrics and Gynaecology, Gauhati Medical College And Hospital, Guwahati, India. Total of 66 newly diagnosed case of PCOS as per Rotterdam Criteria (2003) were taken. Each patient underwent detailed clinical and anthropometric examination after history taking. Biochemical and hormonal tests and ultrasonography (USG) was also performed.* <u>*Results and Observations:*</u>*Oligomenorrhoea was the most common menstrual abnormality among PCOS women present in 92.42% of study population. Among dermatological findings acne was the most common finding followed by hirsutism. Most of the patients were overweight and central obesity present in most of the cases.* <u>*Conclusions:*</u> *Our study concluded that oligomenorrhoea was the commonest menstrual irregularity and often the presenting problem of Polycystic Ovarian Syndrome in our patient population.*

Key words: Acanthosis nigricans, hirsutism, hyperandrogenemia, Oligomenorrhea , Polycystic ovarian syndrome

1. Introduction

Polycystic ovary syndrome is the most common endocrinopathy in women of reproductive age with a prevalence of approximately 7-10% worldwide.[1],[2]. PCOS can be viewed as a heterogeneous androgen excess disorder with varying degrees of reproductive and metabolic abnormalities determined by the interaction of multiple genetic and environmental factors. It is the leading cause of anovulatory infertility, hyperandrogenism and hirsutism . PCOS was first described by Valisnere in 1721 [3] as, "Young, married peasant women, moderately obese, and infertile with two larger than normal ovaries, bumpy, shiny and whitish, just like pigeon eggs". PCOS was reported as Stein-Leventhal syndrome in 1935 [4] when they published a case series of seven women with amenorrhea, hirsuitism, obesity , and ovaries with a grossly polycystic appearance and since then has attracted more and more attention due to its genetic heterogeneity and diverse clinical manifestations

Diagnosis of PCOS continues to be controversial primarily because of the heterogenous nature of the condition which may change during the lifetime of the woman. Currently , the commonest and widely accepted criteria used for the diagnosis of PCOS is the "Rotterdam criteria" May,2003 which includes any two of the following three features : 1)oligo/anovulation(O), 2)clinical and/or biochemical hyperandrogenemia(H), 3) polycystic ovaries on ultrasound(P), with exclusion of other known disorders of hyperandrogenemia.

This generates 4 types of phenotype[5]; 1.P+H+O(PCOS complete), 2.P+O. 3.H+O and 4.P+H

Clinical features of PCOS includes oligomennorhoea or short period of amenorrhoea followed by prolonged or heavy periods. Infertility due to anovulation is a major problem in women of reproductive age .Pregnancy loss occurs in 20-30%cases. During pregnancy it may affect carbohydrate metabolism, diabetes and hypertension may develop. Hyperandrogeneism appears in the form of acne ,hirsutism, male pattern baldness is noted in few cases. Virilism is extremely rare. Metabolic disorders such as hyperlipidemia, insulin resistance ,hypertension and type 2 diabetes mellitus are common in PCOS in addition to increased risk of cardiovascular disease. Epidemiologically common abnormalities includes obesity,insulin resistance and glucose tolerance abnormalities. Acanthosis nigricans a brown to black poorly defined velvety hyperpigmented lesion of skin commonly seen in nape of neck might be seen which occurs as a result of insulin resistance.

Thus, PCOS might present with varying clinical and biochemical features to a gynaecologists, endocrinologist or a dermatologist. Identification and diagnosis of PCOS needs a high degree of suspicion.It is important because it is associated with increased risks of non-insulin dependent diabetes mellitus,metabolic syndrome and cardiovascular complications. Endometrial cancer remains one of the serious complication for women with PCOS. PCOS has significant implications for the health and quality of life of these patients. Diagnosis of polycystic ovarian syndrome is extremely important because it in turn identifies risk for potential metabolic and cardiovascular diseases.
 In the present study, we are reporting clinical presentation of Indian women with PCOS.

2. Materials and Method

The study was carried out for a period of one year from 1st July 2016 to June 2017 among patients attending Gynaecology OPD of Gauhati Medical College and

Hospital, Guwahati,Assam. It was a hospital based prospective cross-sectional study. Total of 66 were newly diagnosed case of PCOS using Rotterdam criteria, May, 2003 were recruited. Detailed menstrual history, marital status, and parity recorded. Each subject underwent general and systemic physical examination. Anthropometric examination was also perfomed. Laboratory investigations of blood (biochemical and hormonal) and ultrsonography of pelvic organs was carried out. In patients complaining of amenorrhea, pregnancy was ruled out whenever necessary.

Inclusion Criteria
Women married or unmarried in age group 15-40 years of age were included.

Exclusion Criteria
1) Pregnant women.
2) Women with age <15 and >40 years of age
3) Women with other causes of menstrual irregularity like hypothyroidism and hyperprolactinemia
4) Women with other causes of hyperandrogenism
5) Patients with known medical illnesss like diabetes or impaired glucose tolerance
6) Patients on medications like corticosteroids, oral contraceptives, metformin etc which could alter the endocrine and metabolic parameters under investigations.

Oligomenorrhoea was defined as an intermenstrual interval of ≥ 35 days or a total of≤8 menses per year and amenorrhoea as absence of menstruation during last ≥6months. Infertility is defined as 1 year of unprotected intercourse without pregnancy. Family history for hypertension and diabetes mellitus and PCOS was noted. Hyperandrogenism was assessed by both clinical and biochemical parameters. Hirsutism was used as a parameter for clinical hyperandrogenism . Hirsutism assessment was done using modified Ferriman-Gallwey (FG) score counting nine specified body areas by a single observer with a good reproducibility. A score of ≥ 8 out of total of 36 was taken as significant. Other features of clinical hyperandrogenism like acne vulgaris, androgenic alopecia were also recorded. Biochemical hyperandrogenism was defined as a serum testosterone of >80 ng/dl. A thorough physical examination was perfomed including measurement of weight, height and waist circumference, hip cicumference. Body mass index (BMI) was calculated using the for

$$BMI= weight(kgs)/height^2 (mts).$$

Patients with BMI <23 were classified as lean PCOS and those with BMI ≥ 23 as overweight PCOS. Central obesity was defined as waist:hip ratio >0.8.

A transabdominal ultrasonography was done in all cases to demonstrate the presence of more than 12 peripheral ovarian follicles arranged peripherally in necklace pattern ,each between 2-9 mm and/or ovarian volume >10 cm^3 suggestive of PCOS. Endometrial thickness was also documented.

3. Results and Discussion

1. Age distribution
When age distribution of PCOS patients were analysed, maximum number of patients were in the age group 21-25years followed by 15-20years whereas minimum patients were in age group of 36-40 years. 46.98% of patients were in age group of 21-25 years and only 3.03% in 36-40 years. The minimum age was found to be 15 years and maximum as 37years. Mean age was 23.5 years. Minimum age for onset of menarche was found to be 9 years and maximum as 15 years. Average age of menarche was 11.95 years.

In the study by Ramanad et al the mean age was 22.05 ± 4.649 and the mean age of menarche was 13.71 ± 1.398 [9]. Joshi et al in their study, found the mean age of the patients with PCOS as 24 years [7]. Mean age by Christodoulopoulou et al. was 24.9 years[8]. Ashraf et al found patients with PCOS were younger than the control group (27.94±4.16 versus 31.10±5.77, p<0.0001). BMI and age of menarche were not significantly different between two groups [10].

Mean age in our as well as other studies are comparable. All this indicates that it is a disease mainly of the young age. PCOS is belived to result from maladaptation of the adrearche, during pubertal development. Adolescents typically have relative androgenemia, insulin resistance, cystic ovaries and anovulatory cycles, which transits to an estrogenic state later in puberty. Failure of this transition to happen may result in PCOS.

Table 1: Frequency distribution of age in polycystic ovary syndrome women

Age (years)	Frequency	%	Cumulative frequency
<20	16	24.24	24.24
21-25	31	46.98	71.22
26-30	14	21.21	92.43
31-35	3	4.54	96.97
36-40	2	3.03	100
Total	66	100	

2. Menstrual complains
In our study most commonly encountered menstrual complain in PCOS is oligomenorrhoea occurring in 60 of 66 patients followed by secondary amenorrhoea. The least common is polymenorrhoea, 2 of 66 patients while dysmenorrhoea occured in 13 patients. There were only 4 patients who had no menstrual complains.

Conway et al , 45% of women exhibited irregular cycles, 26% amenorrhoea [11] . According to Clayton et al, 1992 nearly 50% of women with PCOS in the Asian population have menstrual irregularity, whilst menstrual irregularities occur much less in the Caucasian group ,24%.[12] . Ferdousi Begum et al found menstrual irregularites as most common presenting complain with oligomenorrhea in 74% and amenorrhea in 26% of study group [13]. Bangal V B et al found that unmarried women presented mainly with complaints of abnormalities like oligo and/or hypomenorrhoea .Remaining cases had isolated secondary amenorrhoea.[14] .Christodoulopoulou et al,conducted a study in 2016,taking a total of 309 women with PCOS in

Greece,Athens. In total, 72.2% suffered from menstrual cycle disorders. Among them, 58.3% of women had a cycle that exceeded 35 days, 5.2% had a cycle which lasted less than 26 days and 8.7% suffered from amenorrhea.[8]. Oligomenorrheoa was present in 65% patients in study by Ramanand et al [9]. In the study by Joshi et al menstrual irregularity was observed in 83% of the patients, while the remaining patients had normal menses.[7]. Hickey M et al in 2011, conducted a Prospective cohort study with 244 unselected post-menarchal girls aged 14-16 years to find out the prevalence of PCOS in adolescents. Fifty-one percent of girls reported menstrual irregularity[15]. Mandrelle et al [16] reported oligomenorrhoea in 84.2 % in his study on 120 infertile PCOS women.

Oligomenorhoea was found to be the most common menstrual irregularity as well as most common chief complain of patients with PCOS in our and most other studies. Anovulation is the pathognomic feature of PCOS and results in irregular menstrual cycles. Therefore, persistent menstrual irregularities (resulting from anovulation) seem to be better predictors compared to biochemical parameter as evident in our as well as other studies. Thus Oligomenorrheoa is rightly considered as a highly predictive surrogate marker of PCOS.

Table 2: Menstrual complains in polycystic ovary syndrome women

Complain	No. of patients	% of patients
Oligomenorrhea	60	90.91
Secondary amenorrhea	37	56.06
Hypomenorrhea	12	18.18
Menorrhagia	8	12.12
Polymenorrhoea	2	3.03
Dysmenorrhoea	13	19.7
None	4	6.06

3. Obstetrical profile

Out of 66 cases of PCOS included in the present study 21 were married. Of this 21, 18 presented with infertility, 11 as primary (52.38%) and 7 as secondary infertility (33.33%) . 3 out of 7 patients of secondary infertility gave history of spontaneous abortions while no significant obstetrical history could be elicited in 3 patients 14.29%). In the study by Frank et al in 1989 in 300 patients of PCOS disturbance of menstrual cycle was a common presenting feature, with 52% of women complaining of an irregular cycle or oligomenorrhoea, 28% having amenorrhoea and 42% with infertility[17] . Conway et al reported infertility rate of 42% in PCOS patients [11] . In the study by Joshi et al [7] 46 % of patients were married and 43% complained of infertility. Ramanand et al [9] in the study on 120 PCOS women , 47 were married and 44.68% of married women complained of infertility.

The overall prevalence of infertility could still be higher because most of the patients in our study were single.

Table 3: Obstetrical profile in PCOS

History Of	No. of Patients	% of Patients
Primary Infertiliy	11	52.38
Secondary Inferility	7	33.33
None	3	14.29
Total	21	100

4. Family history

Postive family history for PCOS among sisters or mother was the commonest positive family history present in 33 of 66 patients .DM and hypertension was present in 25 and 13 patients respectively. There were 4 patients who had all 3 family history present and there were 16 patients who had none of family history positive.

In the study by E Lerchbaum and others a positive family history of T2DM and a positive PCOS family history were prevalent in 36.8 and 21.4% of PCOS women respectively. They divided the women into three groups: no positive FHx (53.3%), positive FHx of T2DM or PCOS (35.3%9) and positive FHx of T2DM and PCOS (11.2%) (18). In the study by Begum et al 75% of PCOS patients had history of the diabetes mellitus among close relatives.[13] . Mandrelle et al found family history of diabetes mellitus in 34.2% cases and hypertensive disorder in 30.8% [16].

Study on association of PCOS and family history of PCOS, diabetes mellitus and hypertension are few.. Most of the cases were students who could tell us proper family history and were reliable sources. But in our study there were sixty six cases only and no controls to compare and find significance of positive family history .

Table 4: Showing family history in PCOS patients

Family History of	No . of patients	% of patients
Diabetes mellitus	25	37.33%
Hypertension	13	19.67%
PCOS	33	50%
None	16	

5. Dermatological features in PCOS

Acne was the commonest dermatological finding among PCOS patients present in 72.73% of patients followed by hirsutism in 68.18% patients. The least reported was acanthosis nigricans , 31.81% . androgenic alopecia was seen in 33.33% of patients. There was a overlap in dermatological complains. Only 10 patients, 15.15% had no dermatological complain.

Balen et al reported hirsutism in 66% of PCOS patients in his study in 1995[21]. In the study by by Dramusic, et al in 1997 , found that 50 percent of adolescents with PCOS have moderate acne[19]. In a study by Jebraili et al, 1994 women with moderate to severe acne have an increased prevalence (52 to 83 percent) of polycystic ovaries identified during sonographic examination[20]. In the study by Ramanand, *et al*, clinically 44.16% women had hirsutism . Though more obese women had hirsutism, there was no correlation between hirsutism and obesity . Acne (20%) and baldness (6.66%) were not common and 44.16% patients showed presence of AN, a surrogate marker of insulin resistance [9]. In the study by Joshi et al hirsutism was found in 32.5% and acne in 13% [7]. In the study by Christodoulopoulou *et al.* 36% of the sample had androgenetic alopecia and 56.4% had acne among 309 patients of PCOS [8]. Ashraf et al found hirsutism in 63%, acne in 25.64% and alopecia in 24.54% in study on 549 women with 273 PCOS patients [10]. Mandrelle et al reported hirsutism in 28.3%, acne in 9.2% and acanthosis in 15.8% [16].

Table 5: Dermatological findings in PCOS

Clinical feature	No . of patients	% OF PATIENTS
Acne	48	72.73
Hirsutism	45	68.18
Androgenic Alopecia	22	33.33
Acanthosis Nigricans	21	31.81
None	10	15.15

6. Obesity in PCOS

In the study maximum patients 57.58% belonged to obese group according to their BMI and minimum patients 3.03% in underweight group. 28.79% had normal BMI and 10.6% in overweight group. The smallest BMI found was 17.6 and largest was 39.11. Average BMI came out to be 25.51.

Various studies have reported high prevalence of obesity in PCOS. Gambineri et al reported that 50% of PCOS patients were obese [23] while Legro and colleagues reported in their 254 cases of PCOS that 78% of PCOS patients were overweight [22]. Ashraf et al in their study on 168 PCOS patients in India noted 66% of their patients with obesity. Waist/hip ratio was significantly higher in PCOS (0.85±0.08) group than the control (0.82±0.07) by p value <0.0001 [10]. In the study by Bangal V B et al thirty five percent women were either overweight or obese at the time of diagnosis. Only ten percent women belonged to lean PCOS category [14]. Obesity is seen in 35-50% of women with PCOS found in the study Balen et al, 1995 [21] and is typically 'centripetal' - related to fat accumulation in the centre of the body (truncal abdominal fat) - resulting in an increased waist to hip ratio , as opposed to the fat accumulation in the thighs and hips (gluteo femoral fat). In a study by Sharma and Abha, India,2015 on 200 women 120 PCOS and 80 age matched controls it was found that women with PCOS had a significantly higher BMI [26]. In the study by Joshi et al the mean Body Mass Index (BMI) was $27.4 \pm 5.1kg/m2$. 36 % patients in overweight category and 33% in obese category[7]. In the study by Begum et al 67% of the PCOS patient had BMI >25, 64% of the PCOS patients and 29% of the controls had waist to hip ratio >0.8 [13] .In study by Christodoulopoulou et al. 15.1% of women were overweight and 24% were obese[8]. Mandrelle et al [16] found raised waist to hip ratio in 45.8% cases . Our result is different from that of the previous study conducted by Kalra, *et al.* in which the percentage of obese, overweight and normal BMI in Indian POCS women (*n* = 65) based on ACOG criteria was 15.38%, 44.61%, and 40%, respectively.[24] The discrepancy may be because of the cut ‑off BMI.

Asian Indians have higher percentage body fat, abdominal adiposity at lower or similar BMI levels as compared to white Caucasians. Asian Indians are more predisposed to develop insulin resistance and cardiovascular risk factors at lower levels of BMI as compared to other ethnic groups.[25]

PCOS and its relation with obesity is well established and can be supported well by the findings in our as well as other studies.. Though in different studies the cut off BMI used to define obesity were different majority of PCOS women fell into overweight category with few in lean category. Central obesity was seen in most of the cases .

Table 6: Showing classificion of PCOS patients according to their BMI

BMI	No. of patients	% of patients
<18(underweight)	2	3.03
18-22.9(normal)	19	28.79
23-24.9(overweight)	7	10.6
>25(obese)	38	57.58
Total	66	100

80.33 % of patients of PCOS were found to have central obesity as compared to 19.67% without central obesity. Mean waist:hip ration came out to be 0.86.

Table 7: Central obesity in PCOS

Waist:hip ratio	No. of patients	% of patients
0.82	53	80.33
<0.82	13	19.67
Total	66	100

7. Components of PCOS

Of the three components in Rotterdam criteria for PCOS diagnosis most commonly found in the present study was oligomenorrhoea seen in 61 of 66 patients . Next was ultrasound picture of polycystic ovaries found in 59 patients and least was hyperandrogenism.

Moghetti et al [27] among their 137 women with PCOS diagnosed by Rotterdam criteria found PCO morphology in 89%, oligomenorrhea in 84.7% and hyperandrogenism in 84.7%. Thus in their study according to the combination of these features, 69.4 % of these women had the classic phenotype, whereas 15.3 had the ovulatory phenotype and 21 % had normoandrogenic phenotype. In the study by Sujata Kar , of 410 PCOS patients in India it was seen that PCO complete type was the commonest, 65.6% ,followed by P+O 22.22%, H+O in 11.2%. The ovulatory type, H+P was the least common, 0.9% of patients [28]. In few other similar studies the phenotypic distribution was quite similar . Turkish population 44.09, 14.17, 18.9, and 14.1% [29]. Bulgarian population 53.6,11,12.8 and 22.6% [30]. United States 58,13,14 and 14% 3 [31]. Iranian population 32.1, 46.8, 14.8, and 6.3% [32].

Table 8: Components of Rotterdam criteria in PCOS

Component	No . of patients	% of patients
Oligomenorrhea	61	92.42
Hyperandrogenism	47	71.21
Polycystic ovaries	59	89.39

4. Conclusion

PCOS is the commonest endocrinopathy with varying clinical manifestations . The commonest presenting complain in our study was oligomenorrhea. In our study the commonest PCOS phenotype found was P+H+O or classic type. Most of the patients in our study exhibited central obesity even those with normal BMI . Because of diversity in presentations PCOS women can present to different speciality like gynaecology , endocrinology or dermatology outpatient department. Awareness about this disease is required for early diagnosis thereby to prevent its sequelae and long term health hazards

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