

ORIGINAL ARTICLE

Diagonostic parameters of polycystic ovarian syndrome in outpatient setting

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is one of the most common endocrinopathy in reproductive age women. PCOS has complex etiopathology, diverse clinical presentation and diagnostic criteria.

Objective: Objective of this study was to find out the determinant clinical feature and investigations for improving diagnostic accuracy and assessment of PCOS, thereby evolving opportunity for proper treatment.

Methods: This prospective cross sectional observational study was conducted in Islami Bank hospital, Khulna, from January 2017 to February 2020. Women seeking gynecological consultation in outdoor with at least one complaint of oligomenorrhoea, hirsutism, weight gain or infertility were enrolled for study. Subjects were selected on the basis of inclusion and exclusion criteria. A structured proforma, based on relevant history, laboratory work up, risk factors and co morbidities were prepared before-hand. Diagnosis of PCOS was based on Rotterdam criteria, 2003. The clinical manifestations of PCOS, frequency of different sub phenotypes and associated morbidities were measured as outcome.

Results: Total study population was 202. Age of subjects were in between 13-37 years. Thirty seven (18%) were adolescent, one hundred forty (65.7%) patients were overweight and obese. Majority of cases were married. Complaint of infertility was present in 125 (61.9%) cases. Oligomenorrhoea, hirsutism, poly cystic ovary was present in 145 (71.8%), 137 (67%), and 130 (64.4%) patients respectively. LH/FSH ratio >2 in 45 (22.3%) cases, Serum free testosterone >0.79 ngm/ml were associated with hirsutism. PCOS with clinical sub phenotypes A, B, C, and D were 38(18.9%), 72 (35.6%), 27 (13.4%) and 65 (32.2%) cases respectively. Case morbidities were Hypertension 75 (37.1%), Diabetes mellitus 18 (8.9%) and Metabolic syndrome 44 (20.1%). Link with Hypothyroidism Hyperprolactinemia were identified in 47 (19%) cases.

Conclusion: Oligo-anovulatory woman with hyperandrogenism with or without poly cystic ovary were diagnosed as a largest group of PCOS-A and B sub phenotypes. Infertility, hypothyroidism, hypertension, diabetes mellitus, metabolic syndrome and endometrial hyperplasia were common.

Key words : Oligomenorrhoea, Hirsutism., Infertility, Metabolic Syndrome

Introduction

Worldwide prevalence of PCOS vary from 4% to 21% depending on diagnostic criteria and population assessed.¹ It is a polygenic syndromic disorder of ovulatory dysfunction having heterogenous presentation.² The pathology is chronic anovulation, polycystic ovary, over

production of ovarian androgens. Risk factors are obesity, insulin resistance, diet and life style and family history of PCOS.³ Stein and Leventhal in 1935, described it among 7 cases who had classical triad of bilateral enlarged ovaries, hirsutism, and oligo/amenorrhoea, some of them were overbuilt,

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hirsute, acneic and infertile.⁴ It was also curable, as following wedge resection of enlarged ovary they were able to conceive.⁵

Different category of characteristic criteria recommended by different society, workshop, consensus and meeting are used to define PCOS. Among them Rotterdam consensus in 2003 is well known for more than a decade.^{6,7} The fundamental addition in Rotterdam criteria for adult PCOS included imaging criteria of polycystic ovary beyond National Institutes of Health (NIH) criteria 1990. Diagnosis of PCOS require at least any two of the three features namely, clinical and or biochemical hyperandrogenism, oligo/anovulation, and polycystic ovary with exclusion of other disorder of androgen excess and anovulation that can mimic PCOS like manifestations.⁸ The Poly cystic ovary morphology (PCOM/PCO) are imaging hall mark of PCOS. In PCO ovaries are usually enlarged in volume, hyperechogenic stroma with increased number of developing follicles (³12 in Rotterdam criteria) and typically 2-9 mm in diameter. The Transvaginal, ultrasound (TVS) is currently the gold standard for diagnosing PCO appears as "string of pearls" and significant only with functional abnormalities.^{9,10} Treatment and long term life style modification, have positive impacts in PCOS. Unfortunately, awareness of the disease is lacking, and many physicians do not perform necessary investigation to diagnose PCOS. PCOS is the most common cause of anovulation, WHO type II. A fair percentage of PCOS could remain undiagnosed, until fertility issues arise in adulthood.¹¹

Reproductive symptoms and effects like infertility, social health, mental health, sleep disorder, concern for body image, Hypertension, Diabetes mellitus, cardiovascular risks, endometrial cancer risks are issues for clinical assessment. Objective of this study was to determine clinical features and investigations of PCOS in a structured format. This will improve accuracy in diagnosis and priority for treatment at earliest possible time. Broader aim was to support PCOS diagnosing capability of health professionals to deliver proper care with wider age range of subjects.

Materials and Methods

This prospective cross sectional observational study was conducted in Islami Bank hospital Khulna, from January 2017 to February 2020. Women seeking gynecological consultation in outdoor with at least one complaint of oligomenorrhoea, hirsutism weight gain or

infertility were enrolled for study. 202 subject were included for study on the basis of inclusion and exclusion criteria. With consent, a structured proforma based on available literature on clinical diagnosis and laboratory workup for PCOS, was used as a tool for each subjects. Subjects were from both urban or rural inhabitance.

Main domain of focused history was whether any menstrual dysfunction, sign of hyperandrogenism, infertility, weight gain, acanthosis nigricans, obesity, disturbances in mood, sleep apnea, family history of PCOS, past pregnancy complication, and review of infertility workup. Hirsutism scored by modified Fairman Galley score (mF-G), and score of 6 used for moderately hirsute. Body mass index (BMI) was categorized by WHO scale for Asian.

Hormonal evaluation were estimation of serum TSH, Serm Prolactin, Glucose tolerance test by 2 h post 75gm glucose, lipid profile, serum free Testosterone (fT), Cycle D3 serum FSH, serum LH. serum 17(OH) progesterone in selected patients. Imaging for ovarian volume by transabdominal scan (TAS) of pelvic organ and by TVS (7.5MHz) at cycle day 3 (D3), Comments on endometrium were done by consultants of same hospital according to patients feasibility.

Rotterdam criteria in 2003 was used for clinical sub phenotyping of PCOS with any two of the following, oligo or anovulation (OA), clinical and/or biochemical signs of hyperandrogenism (HA) and polycystic ovaries (PCO). Phenotypes were grouped into A: OA+HA+PCO, B: OA+HA, C: HA+PCO, and D: OA+PCO. Exclusion criteria were Nonclassical congenital adrenal hyperplasia (NC CAH), adrenal tumor, Cushing syndrome, pathology in uterus and cervix, adolescent with post menarche less than 2 years, age beyond 13-37 years, pregnancy. ovarian surgery, user of oral contraceptives.

Hyperthyroidism. Hypoprolactinemia was mentioned separately. Main outcome measures were clinical characteristics and phenotypes of PCOS with imaging and laboratory parameters. Data were analyzed by IBM version 24 in frequency and mean.

Results

Total study population was 202. Age range were in between 13-37 years. The most common age group were in between 20-30 years, mean age 24.6 (\pm 5.3), thirty seven (18%) were adolescent. One hundred forty two (70.3%) were married, multipara in 39(19.4%) cases (Table I).

Table I
Demographic profile of study population

| Characteristics | N= 202 (%) |
|---------------------|------------|
| Age group | |
| 13-19 yrs | 37(18) |
| 20-30 yrs | 137(67.9) |
| 31-37 yrs | 28(14.8) |
| Ummarried | 60(29.7) |
| Married | 142(70.3) |
| Para ³ 1 | 39(19.4) |

Most of the subjects were overweight and obese, mean wt. 67.4 (\pm 13.4) kg, BMI 24->25kg/m² in 140 (65.7%) subjects. Oligomenorrhoea, hirsutism, poly cystic ovary was present in 145 (71.8%), 137 (67%), and 130 (64.4%) cases respectively. Infertility were in 125 (61.9%). Hypertension in 75 (37.1%), complication in past pregnancy in 35 (17.3%) cases (Table-II).

Table II
Distribution of common history and clinical assessment of PCOS.

| Clinical characteristics | Frequency (%) | |
|-------------------------------------|---------------|-----------|
| Complaint | Evaluated | |
| Oligomenorrhoea | 101(50.5) | 145(71.8) |
| Amenorrhoea | 12(5.9) | 35(17.9) |
| Prolonged mense | 22(11.0) | 22(11.0) |
| Hirsutism, F-W score ³ 6 | 22(10.9) | 137 (67) |
| Acne | 04(2.0) | 15(7.4) |
| Baldness | 01(0.4) | 04(2.0) |
| Virilization | 00(00) | 00(00) |
| PCO | 30(14.9) | 130(64.4) |
| Acanthosis nigricans | 00(00) | 60(30.0) |
| Sleep and mood | 04(2.0) | 20(9.9) |
| Wt gain (BMI ³ 24kg) | 50(24.7) | 140(65.7) |
| HTN | 20(9.9) | 175(37.1) |
| Infertility | 70(34.6) | 125(61.9) |
| Drug history | 25(12.4) | 45(22.3) |
| Past pregnancy complication | 13(6.4) | 35(17.3) |
| Family history of PCOS | 00(00) | 22(10.9) |

In hormonal profile LH/FSH ratio ³2 found in 45(22.3%) subjects, mean free Testosterone (fT) level was 1.17(\pm 0.63), 17(OH) Progesterone level was normal in evaluated 10 cases. On imaging

ovarian enlargement was observed in 119 (58.9%), PCO in 130 (64.4%). No abnormality was detected in TAS and TVS in 60 (29.7%) and 12 (5.9%) cases respectively (Table-III).

Table III

Results of Imaging and Laboratory investigations.

| Investigations | N =202(%) | Interpretation |
|---------------------------|-----------|--------------------|
| TAS | 60(29.7) | Normal study |
| TVS at cycle D3 | 130(64.4) | PCO |
| TVS | 12(6.0) | Normal study |
| FSH(IU/L), mean \pm SD | 99(49.0) | 6.2+3.4 |
| LH(IU/L), mean \pm SD | 99(49.0) | 15.2+10.5 |
| LH/FSH >2mean \pm SD | 45(22.3) | 2.5+1.8 |
| ft (ng/ml), mean \pm SD | 50(24.8) | 1.2+0.6 |
| S.TSH> 5miu/l | 29(11.9) | Hypothyroidism |
| Prolactin>25ng/ml | 18(7.4) | Hyperprolactinemia |
| S.17(OH) P< 80 ng/dl | 10(4.9) | Normal |
| 2h post glucose | 73(36.1) | PreDM and DM |
| Triglyceride mg/dl mean | 87(43.0) | 230+20 |

Thickened endometriurn was observed in 33 (16.3%) cases. Abnormal Glucose test result were in 73(36.1%) including Diabetes mellitus, frequency of metabolic syndrome in 44(20.1%). Hypothyroidism-Hyperprolactemia were diagnosed in 47(23.3%) cases.

Table IV

PCOS Phenotypes based on Rotterdam criteria.

| Phenotype | OA | HA | PCO | Frequency(%) |
|-----------|----|----|-----|---------------|
| A | + | + | + | 38(18.8) |
| B | + | + | - | 72(35.6) |
| C | - | + | + | 27(13.4) |
| D | + | - | + | 65(32.2) |

OA-oligo anovulation, HA -hyperandrogenism, PCO -polycystic ovary.

In frequency of PCOS sub group, Phenotype B was common in 72 (35.6%) cases and Phenotype A was in 38 (18.8%) cases. Ovulatory PCOS phenotype C and mild PCOS phenotype D were in 27 (13.4%) and 65 (32.2%) cases (Table IV).

Discussion

Age of Study group was 13-37 years, comparable with a hospital based study in Oman which included 12 to 45 years group.¹² Obesity,

overweight and truncal obesity affect most of Phenotypes of PCOS that co relate with other study.¹³ Lean body mass could also had PCOS found in this study.¹⁴ Menstrual disorders, most commonly were oligomenorrhoea (71.8%), with infertility was common and were comparable with study by Ferdous et al in Bangladesh, where oligomenorrhoea, (75%) with sub-fertility.¹⁵ Women with oligo or amenorrhoea have about a 90% chance of being diagnosed with PCOS and up to 95% of affected adults have oligo-or amenorrhoea.¹⁶ In PCOS hirsutism is not rapid onset, develops gradually and intensifies with weight gain that differ from NC-CAH.¹⁷ Hirsutism scoring was moderate, like most South Asian study and were comparable.¹⁸ Acne was the second most common sign of Hyperandrogenism. Hair loss patterns are variable in women typically the vertex, crown or diffuse pattern, and with familial inheritance.¹⁹

For adolescent PCOS diagnosis is more constringent, even though common. So persistent oligomenorrhoea, at least 2-3 years of post-menarche with hyperandrogenism and exclusion of secondary cause is recommended, that were followed in our study.²⁰ TAS of ovary may be normal due to obesity. Future research-Transrectal scan and MRI of ovary may be better option for obese adolescent. Some study added serum AMH level to increase the diagnostic accuracy.²¹⁻²³ In IVF clinic 3D-TVS may be appropriate to minimize false positive diagnoses of PCO, but our study place provide level II infertility care.²⁴

Elevated Testosterone level, more suggestive for ovarian androgen, a cut off value of free Testosterone (fT) for hirsutism ≥ 0.79 ng/ml was observed in present study, but not statistically significant. Elevated testosterone may be associated with increased level of Serum LH.²⁵ Common cut offs for high LH: FSH ratio tested on CD3 was $\geq 2:1$ and observed in $<30\%$ women which are suggestive of PCOS but not diagnostic as like other study.²⁶

TVS was the main tool to diagnosing polycystic ovary, and also used to see response to ovulation induction and endometrial study on infertile population.²⁷ PCOS sub type A, was found relatively less in frequency in present study (18.8%), unmarried group might have affected frequency.²⁸ Current PCOS criteria expanded and diversified clinical sub group of PCOS spectrum, all symptoms may not present typically. There are variation of population and ethnicity in different

study.²⁹ The other three Phenotypes listed in Rotterdam criteria are in order of decreasing clinical severity and specificity to milder phenotypes, and diagnosis could be difficult. Like other study, classic PCOS (phenotype A and B) was largest group. PCOS -type B was most common PCOS in this study (35.6%). Non-hyperandrogenic PCOS phenotype:O+P was second most common and frequent, finding similar to study done in china.³⁰ Over all distribution of different phenotypes were comparable with study done in Mumbai except that of Phenotype D, which was found more in present study. Expertise in imaging and assessment of androgen level may influence clinical frequency. Phenotyping is important to find out new ways to treatment and health risks.³¹

Acanthosis nigricans are clinical surrogates for insulin resistance.³² Study results showed health risk of PCOS were abnormal OGTT, hypertension. Hypothyroidism as a common co-morbidities including metabolic syndrome that were similar to study at BIRDEM, showed that significant proportion of Bangladeshi women with PCOS had hypothyroidism with or without high prolactin and increased rate of metabolic syndrome.³³ PCOS is highly prevalent among middle and high income urban population in India as a lifestyle disorder.³⁴ Reproductive problems and Diabetes mellitus occur more earlier in Asian than Caucasians. Sleep apnea and snoring associated low mood were found in study (7.4%).³⁵ Strength of the study was clinical assessment was done by experienced gynecologists trained in reproductive medicine and homogenous ethnicity of study population, both from urban and rural inhabitant. This explored wide range of clinical characteristic in common of age group.

Limitation of study was selective laboratory evaluation due to self finance by the patient. Recent use of medications (metformin, Letrozole) may affect level of hormone assay. Moreover, snapshot study will not detect all parameters in acceptable range.

Conclusion

Oligomenorrhoea and infertility were common complaints of PCOS and phenotype A and B was diagnosed as a large phenotypes. Mild PCOS, Phenotype D was common. Hypothyroidism, Hyperprolactinemia and metabolic syndrome were common and should be screened. This findings could be helpful for further research on diagnosis, treatment and for creating awareness of PCOS.

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