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Clinical and biochemical profile in adolescent and adult polycystic ovary syndrome patients

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Abstract
This study was conducted on 100 adolescent (11-19 years) and 100 adult (20-35 years) PCOS patients attending gynaecology outdoor at PGIMS Rohtak to compare clinical and biochemical profile in two groups.
On comparing, it was found that most of the clinical parameters (heavy menstrual bleeding- 9% vs 2%, weight gain- 38% vs 24%, hirsutism- 58% vs 47%, BMI- 36% vs 17%) and biochemical parameters (increased LH/FSH ratio- 51% vs 41%, serum testosterone- 44% vs 33%) were deranged more in adults as compared to adolescents whereas parameters like oligomenorrhoea (87% vs 88%), acne (44% vs 46%), acanthosis nigricans (9% vs 8%), triglycerides (19% vs 18%) were comparable in both the groups. It was incidentally noticed that age of menarche is decreasing in Indian population (13.46±1.24 vs 13.83±1.05 - adolescents vs adults). Hence, early detection and treatment is needed for the better outcome.

Keywords: PCOS, adolescents, adults, menarche

Introduction
Polycystic ovary syndrome (PCOS) also referred as hyperandrogenic an-ovulation (HA), or Stein Leventhal syndrome, first described by Stein and Leventhal in 1935, is one of the most common endocrine disorder of reproductive age group affecting 3%-26% of females worldwide whereas in India it is 3.7-22.5% in adults and 9.13%-36% in adolescents [1, 2]. Different sets of diagnostic criteria for PCOS have been developed one amongst which is the Rotterdam criteria according to which PCOS is diagnosed if any two out of the following three abnormalities are present: 1) chronic anovulation; 2) clinical and/or biochemical hyperandrogenism and 3) polycystic ovaries on pelvic ultrasound: a) one or both ovaries demonstrate 12 or more follicles measuring 2-9 mm in diameter or b) the ovarian volume exceeds 10 cubic $cm^{3,5}$ with the exclusion of other causes of hyperandrogenism, such as thyroid dysfunctions, hyper-prolactinemia, congenital adrenal hyperplasia, androgen secreting tumours and Cushing syndrome [3].
PCOS is heterogenous, multifactorial, complex genetic disorder, the exact aetiology of which is still unknown. But recent evidence suggest that the principal underlying disorder is one of the insulin resistance, with the resultant hyperinsulinaemia stimulating excess ovarian androgen production, [4] abnormalities in hypothalamic-pituitary-ovarian axis (HPO axis), inhibition of production of sex Hormone binding protein globulin (SHBG) and insulin-like growth factor-I binding protein (ILGF-I BP) from liver finally leading on to androgen excess [5].
All these alterations finally lead on to the clinical, reproductive, psychological and metabolic manifestations usually beginning in adolescence which include- weight gain, hyperandrogenism, acne, acanthosis nigricans, oligo and/or an-ovulation, menstrual irregularities, heavy menstruated bleeding, infertility, reduced efficacy of infertility treatment, recurrent abortions, high chances of impaired glucose tolerance, gestational diabetes, [6] anxiety, depression, poor self-esteem, reduced quality of life, and in long term leading to the development of type II diabetes mellitus, cardiovascular abnormalities and high risk for endometrial cancer [7].
Present study was planned keeping in view to assess the clinical and biochemical profile in adolescent and adult PCOS patients.

Material and methods
This prospective comparative study was conducted in the Department of Obstetrics and Gynaecology at Pt. B.D.Sharma PGIMS Rohtak on 200 women diagnosed with PCOS in 11-35

years of age. PCOS was diagnosed according to Rotterdam criteria and following two groups were made:

Group I -Comprised of 100 adolescent PCOS patients in age group of 11-19 years.

Group II -Comprised of 100 adult PCOS patients in age group of 20-35 years.

Patients having hyperprolactinemia, hyperthyroidism, hypothyroidism, acromegaly, functional hypothalamic amenorrhea, patients who have received any medication known to affect carbohydrate metabolism for at least three months before the study, females on oral contraceptive pills, pregnancy, lactation, any active liver or renal disease, history of diabetes were excluded from the study.

After taking the informed and written consent and explaining the nature of study to the participants a detailed history, general physical, systemic examination and investigations were carried out. Hirsutism was graded according to modified Ferriman-Gallwey score as: mild < 4, moderate 4-7 and severe ≥ 8. Waist circumference was measured at the mid point between the lower margin of the last palpable rib and the top of iliac crest and hip circumference was measured around the widest portion of the buttocks with a stretch resistant tape kept parallel to the floor. Waist-hip ratio was calculated according to WHO criteria as: a) normal built < 0.80, b) over weight 0.80 – 0.84, c) obese > 0.85. Haemoglobin, fasting blood sugar, thyroid stimulating hormone (TSH), serum testosterone, serum LH, serum FSH, lipid profile and ultrasound (on day two to day three of menses) for number, size and arrangement of follicles, size of the ovaries and endometrial thickness were done in all the patients.

Prevalence of different types of phenotypes of PCOS among the patients was also evaluated. According to the Rotterdam and AE-PCOS Society criteria four different types of phenotypes have been classified which are as follows:

Phenotype A (Frank PCOS)-patients having irregular menses (IM), polycystic ovaries on ultrasound (PCO) and hyperandrogegism (HA) (IM/PCO/HA)

Phenotype B (Non PCO PCOS)-patients having irregular menses and hyperandrogenism but normal ovaries on ultrasound (IM/HA)

Phenotype C (Ovulatory PCOS)-patients having hyperandrogenism and polycystic ovaries but normal menstrual cycles (HA/PCO)

Phenotype D (Mild or Normo-androgenic PCOS)-patients having irregular menses and polycystic ovaries on ultrasound but no hyperandrogenism (IM/PCO) [8].

Results

The present study was conducted as a prospective comparative study in the department of obstetrics and gynaecology at Pt. B.D.Sharma PGIMS Rohtak. The study consisted of 200 polycystic ovary syndrome patients (PCOS) in 11-35 years of age. Rotterdam criteria was used to diagnose PCOS. Two age groups of PCOS patients were taken 11-19 years (group I-Adolescents) and 20-35 years (group II-Adults) and clinical and biochemical parameters were compared in them.

Table 1: Distribution of PCOS patients as per history and menstrual irregularities

Parameters	Adolescents N (%)	Adults N (%)	P value
Oligomenorrhea	88 (88%)	87 (87%)	0.83
Heavy menstrual bleeding	2 (2%)	9 (9%)	0.03 (S)
Hypomenorrhea	9 (9%)	4 (4%)	0.12
Secondary Amenorrhea	2 (2%)	2 (2%)	0.6
H/o weight gain	24 (24%)	38 (38%)	0.001 (S)
Acne	46 (46%)	44 (44%)	0.59
Avanthosis nigricans	8 (8%)	9 (9%)	0.88

Heavy menstrual bleeding was found to be more common in adults as compared to adolescents which was related to other causes like two patients had copper T, two had uterine fibroids, one had uterine polyp and one had ovarian cyst.

Table 2: Distribution of PCOS patients as per clinical findings

Parameters	Adolescents (mean score ±SD)	Adults (mean score ±SD)	P value
Age of menarche	13.46±1.24	13.83±1.05	0.02 (S)
Hirsutism	8.28±6.04	9.18±6.28	0.02 (S)
BMI	21.72±2.97	23.81±3.96	0.001 (S)
WHR	0.77±0.04	0.806±0.05	0.001 (S)
WC	27.63±2.69	30.49±4.48	0.001 (S)

All the clinical parameters were significantly more common in adults as compared to adolescents. Also adolescents attained menarche earlier than adults.

Table 3: Distribution of PCOS patients as per biochemical parameters

Parameters	Adolescent cases N (%)	Adult cases N (%)	P value
FBS >100 mg/dl	5 (5%)	4 (4%)	0.18
TGA ≥150 mg/dl	18 (18%)	19 (19%)	0.907
HDL (<50 mg/dl)	48 (48%)	36 (36%)	0.02 (S)
LH/FSH (≥2)	41 (41%)	51 (51%)	0.01 (S)
Testosterone (≥60 ng/dl)	33 (33%)	44 (44%)	0.03(S)

No significant difference was noticed in the fasting blood sugar levels in the two groups but hormonal profile was deranged more in adults owing to the long-standing disease in them.

Table 4: Distribution of PCOS patients according to phenotypes

Phenotypes	Adolescents	Adults	P value
Phenotype A(IM/PCO/HA)	68 (68%)	72 (72%)	0.98
Phenotype B (IM/HA)	20 (20%)	12 (12%)	0.7
Phenotype C (HA/PCO)	12 (12%)	13 (13%)	0.63
Phenotype D (IM/PCO).	1 (1%)	3 (3%)	0.54

Phenotype A was the most common and D was the least common phenotype in both the age groups.

Discussion

In this study we aimed to evaluate and compare the clinical and biochemical profile of adolescent and adult PCOS patients. No significant difference was noticed in the prevalence of oligomenorrhea which was found to be the most common complaint in both the age groups (88% adolescents and 87% adults, p value-0.83) and similar results were found by Kavita *et al.* [9] (84.2%) in India and Ziba Zahiri *et al.* [10] (85.1%) in Iran in 15-35 year old PCOS patients. But heavy menstrual bleeding was found to be significantly higher in adult PCOS patients as compared to adolescents (9% vs 2%, *p* value-0.03) and was found to be attributed to additional factors which were present in them like intrauterine copper device, fibroid, polyp and ovarian cyst. Rest no significant difference was noticed in other menstrual problems in the two groups. Quite a large number of adolescent and adult patients (24% and 38%) complained of weight gain and similarly Swetha Balaji *et al.* [11] observed weight gain in 19%. Although most of the authors did not compare the association of acne in adolescents (46%) and adults (44%) and a wide variation was found by different authors 20% by Spandana *et al.* [12] and 74% by McManus *et al.* [13]. And, similarly Acanthosis nigricans was found to be associated with 8% adolescents and 9% adults but much more strong association was observed by different authors like 15.7% by FI Najem *et al.* [14] and 44.16% by Sunita Ramanand *et al.* [15] in an overlap of age group which could be due to different geographical areas studied.

The mean age of menarche was significantly lower in adolescent (13.46±1.24) PCOS as compared to adults (13.83±1.05, p value 0.02) and almost similar findings were observed by Beena Joshi *et al.* [16] (13.22±1.3) and Minh Tam *et al.* [17] (14.24±1.35) in their studies in adolescents and adults respectively which may be due to the changing lifestyle. Mean modified FG score was found to be higher in adult PCOS patients (9.18±6.28) as compared to adolescents (8.28±6.04) and similarly severe hirsutism was found to be significantly more prevalent in adult PCOS patients as compared to adolescents (58% vs 47%, p value-0.02). Although no study compared the two age groups but Bronstein *et al.* [18] observed hirsutism in 71% and Sunita *et al.* [15] in 44.16% of the post pubertal females. Obesity by all the parameters was found to be more common in adults as compared to adolescents (BMI-23.81±3.96 vs 21.72±2.97; WC-30.49±4.48 vs 27.63±2.69; WHR-0.806±0.05 vs 0.77±0.04). However no studies compared the obesity in adolescents and adults but almost similar values were observed by Spanadan *et al.* [12] in BMI and WHR but quite a large number of patients were found to be obese in terms of WC by Gomathi *et al.*[19] in their study on PCOS patients of 18-35 years of age.

No significant difference was found in the number of patients having deranged fasting blood sugar and triglyceride levels in adolescent and adult PCOS patients (5% vs 4%, *p* value-0.18 and 18% vs 19%, p value-0.907 respectively). Although no study compared the low levels of high density lipoprotein (HDL) (42%) in adolescent (48%) and adults (36%) but almost similar number of PCOS patients (46.3%) were found to have low HDL by Indu *et al.* [20] in their study on PCOS patients of age 15-35 years. Hormonal profile (LH/FSH ratio) was found to be deranged more in adults as compared to adolescents (51% vs 41%, p value-0.01). No study compared the two age groups and wide variation was reported by Spandana *et al.* [12] (35%) and FI Najem *et al.* [14] (16%) in their study. Similarly, testosterone was found to be high in more number of adults (44%) as compared to adolescents (33%) and almost same was observed by Spandna *et al.* [12] (44%) in an overlap of age groups.

Phenotype A was found to be the most common in both the age groups (72% adults vs 68% adolescents) and phenotype D was least common (3% vs 1%) which was similar to the findings of Sharami *et al.* [21] (most common - type A) in their study, however they found phenotype C as the least common.

Conclusion

Adult PCOS patients had more deranged clinical and biochemical parameters as compared to adolescents pointing to the fact that early and timely treatment of PCOS may slow down the progress of the disease. Further studies are needed to corroborate the findings.

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