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A CROSS SECTIONAL STUDY OF POLY CYSTIC OVARIAN SYNDROME (PCOS) AMONGST ADOLESCENT GIRLS IN LUCKNOW.

Obstetrics and Gynaecology

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ABSTRACT

Background: Polycystic ovary disease is a common endocrine condition which is rapidly gaining epidemic proportions. **Objectives:** Current study was undertaken to screen adolescents and young unmarried girls aged 15-24 years for PCOS. **Material and Methods:** A cross-sectional hospital-based study was undertaken in Lucknow to assess the prevalence of polycystic ovarian syndrome (PCOS) among 389 adolescents and young girls aged 15-24 years. Among them, 300 completed all clinical, ultrasonography (USG), and biochemical investigations. **Results:** The prevalence of PCOS among them was 22.5% by Rotterdam and 10.7% by Androgen Excess Society criteria. Nonobese comprised 71.8% of PCOS diagnosed by Rotterdam criteria. Mild PCOS (oligomenorrhea and polycystic ovaries on USG) was the most common phenotype (52.6%). History of oligomenorrhea had a positive predictive value of 93.3% and negative predictive value of 86.7% to detect a possible case of PCOS. Hyperinsulinemia (serum insulin >15 µIU/mL) was present among 19.2% of diagnosed PCOS cases. **Conclusion:** The study demonstrates that PCOS is an emerging disorder during adolescence and screening could provide opportunity to target the group for promoting healthy lifestyles and early interventions to prevent future morbidities.

KEYWORDS

Adolescents, Polycystic Ovarian Syndrome.

Background:
Polycystic ovarian syndrome (PCOS) is one of the most common reproductive endocrinological disorders with a broad spectrum of clinical manifestations affecting about 6-8% of women of reproductive years. [1] The diverse manifestations of PCOS start at an early age when a girl is maturing into a young woman. During this pubertal transition, several features may be in evolution and thus many findings may be transitory which stabilize later during adolescence. However, it is important to make an early diagnosis in order to prevent early and late sequel of the syndrome. PCOS a diagnosis of exclusion has been a topic of debate and many consensus definitions have evolved over time. The National Institute for Health (NIH) Criteria 1990 was revised in 2003 and Rotterdam criteria [2] has been adopted world over. However, recently in 2006, Androgen Excess Society (AES) has come up with a consensus statement, defining PCOS as a hyperandrogenic state and emphasises the presence of either clinical and/ or biochemical features of hyperandrogenism along with other features of PCOS for diagnosis.[3] Globally, prevalence estimates of PCOS are highly variable, ranging from 2.2% to as high as 26%.[4-8]

The varying prevalence of PCOS in general is mainly due to using different diagnostic criteria, the heterogeneous presentation of symptoms, logistic difficulty to carry out blood or ultrasound tests, and the varied age groups and ethnic populations that have been studied. This has resulted in prevalence studies being based on convenience samples such as university employees.[4-8] or blood donors.[7] without any representativeness of these subgroups.

AIM AND OBJECTIVES:
This study was undertaken in Lucknow, India to screen adolescents and young unmarried girls aged 15-24 years for PCOS.

MATERIAL AND METHODS:
It was a hospital based cross-sectional study, which was done using a simple random sampling method and was conducted in Lucknow from July 2019 to December 2019. A sample size of 450 was calculated assuming a prevalence of 10% and precision of 2% at 95% confidence level was taken. Considering a nonresponse rate of 10% the total sample to be enrolled was estimated to be about 500 cases. Girls aged 15-24 years, who had attained menarche more than 2 years before the study, who were unmarried and were willing to participate in the study were enrolled.

Operational definitions:
Adolescents Age group 10-19 years (for our study 15-19 years).
Young girls Age group 20-24 years.

Amenorrhoea In a girl who has been menstruating, the absence of periods for a length of time equivalent to a total of at least 3 of the previous cycle intervals or 6 months of amenorrhea.

Oligomenorrhea Indirect marker for anovulation in absence of any hormonal evidence, but considering infrequent menstrual cycles at intervals of more than 35 days.

Body mass index [9,10] Normal: BMI = 18-22.9 kg/m2 , Underweight: BMI < 17.9 kg/m2 , Overweight: BMI > 23 kg/m2 , Obese: BMI > 25 kg/m2 for girls above 18 years. Age matched cut offs for body mass index (BMI) for girls below 18 years.[9] Clinical hyperandrogenism Hirsutism was assessed by Ferriman-Gallwey.[11] score of ≥8 over 9 body parts.

Polycystic ovaries 12 or more follicles measuring 2-9 mm in diameter with or without ovarian volume >10 mL[12]

Biochemical hyperandrogenism Free Androgen Index level of two standard deviations above the mean level among normal controls.

Apart from personal information, details of menstrual cycles (current and over last 2 years), any previous illness, treatment sought, were noted. Height in meters, weight in kgs, and blood pressure (mm Hg) were measured using standard methods. Signs of hyperandrogenism, galactorrhea, and thyroid disorders were noted. All the girls were then subjected to abdominal sonography performed twice a week by a single trained gynaecologist and sonologist using HD6 Ultrasound Colour Doppler system. A fasting blood sample was collected between 3rd and 7th days of menstrual cycle, including for those who had cycle length of 6-8 weeks and stored at -800 C for biochemical and hormonal parameters.

Total testosterone, insulin and SHBG levels were estimated by radioimmunoassay method using commercial kits. Enzyme-linked immunosorbent assay was used to measure follicle-stimulating hormone, luteinizing hormone, serum prolactin (PRL) 17-hydroxy progesterone (17-OHP), thyroxine (T4), and thyroid-stimulating hormone using commercially available kits. Glucose oxidase-peroxidase method was used to estimate blood glucose. Lipid profile was estimated by using enzymatic colorimetric technique.

Data were analysed in the Statistical Package for the Social Sciences software (version 19.0, IBM SPSS Statistics). Frequencies and percentages were used for categorical data. Mean, median, and standard deviations were calculated for continuous variables. Pearson's Chi-square test was used to assess differences in the groups for categorical data. All hypothesis tests were two sided and $P < 0.05$ were considered statistically significant. Distributions were compared using "unpaired Student's t test."

RESULTS:
A total of 500 girls in the area full filling the inclusion criteria were

invited to participate in the study to achieve a sample size of 450. Among them, only 380 girls volunteered, got enrolled and underwent clinical examination. However, only 343 of them completed ultrasound examination (88.3%) and 300 of them completed all the biochemical and hormonal tests (77%). The nonparticipation rate for enrolment was 13.5% unlike the assumed 10%. Further drop out at stage two for sonography examination was 11.7% and 12.7% during the last stage, that is, for blood investigations. Participants were considered as dropouts when they failed to come for required visits even after five rounds of home-based health educative sessions with validated written information brochures. Reasons for dropout, as informed by participants, included refusal by parents, marriage and/or shift of residence, absence of clinical complaints (in about 80% of drop outs), unwillingness for investigations, and inconvenience to come fasting between 3rd and 7th days of the cycle for blood investigations due to work/educational schedule.

The mean age of the participants was 18.15 (±2.4) years. Majority of the participants (73.2%) were adolescents (15-19 years) from lower socioeconomic strata. The mean age at menarche was 13.22 (±1.3) years. We divided the enrolled girls into three groups as shown in Table 1. Group A comprised of girls who completed all desired investigations (n = 300), Group B were girls who completed only clinical and ultrasonography examinations (n = 44), and Group C who underwent only clinical examination (n = 45). As seen in the Table 1, all three groups had similar mean ages. All groups had mean BMI within normal range. History of irregular cycles was more among girls in Group A and feature of hirsutism was more in Group C. Groups A and C had almost same number of girls with PCO picture on USG.

Table 1: Difference in three groups of enrolled girls

	Completed all examinations (Group A) n=300	Completed clinical and USG examination (Group B) n=44	Completed only clinical examination (Group C) n=45
Age (mean±SD)	18.2±2.3	18.2±2.3	18.1±2.3
BMI (mean±SD)	19.5±3.8	18.5±4.0	19.4±4.0
Irregular cycles	74(24.7)	08(17.2%)	10(22)
Hirsutism	41(13.7)	05(11.5%)	08(16.5%)
PCO on USG	114(38.2)	17(39.1)	NA
PCOS	True PCOS 22.5%- Rotterdam 10.5% by AES criteria	Probable PCOS 19.5%	Probable PCOS 3.3%

Table 2: Difference between metabolic and endocrine profile of PCOS vs Non PCOS girls.

Parameters (mean±SD)	Non PCOS	PCOS	P value
BMI	18.5±2.7	21.1±4.8	0.000
Waist Circumference(cm)	72.5.5±7.6	78±12.2	0.000
Serum testosterone(ng/ml)	0.34±0.1	0.45±0.2	0.000
Free androgen index	2.3±1.8	4.1±3.2	0.000
FSH(mIU/ml)	4.2±1.6	3.8±1.1	0.243
LH(mIU/ml)	6.1±2.7	8.8±3.3	0.000
FBS(g/dl)	71.1±6.7	7.2±6.2	0.694
2h post 75gm Glucose(g/dl)	89.2±8.3	90.8±10.2	0.224
Insulin(µIU/ml)	10.97±4.3	13.46±9.9	0.000
HDL(mg/d)	43.4±9.0	45.8±9.97	0.287
Triglyceride(mg/dl)	63.9±10.5	64.0±13.1	0.071

Table 3: Difference between clinical, biochemical and hormonal features of obese vs non obese PCOS

Parameters (mean±SD)	Non Obese	Obese/Overweight	P value
Irregular cycles	18.5±2.7	21.1±4.8	0.010
BMI	18.6±2.2	27.6±3.8	0.002
Hypertension	4(4.3%)	5(15.2%)	0.052
Hirsutism	23 (23.7%)	17 (44.7%)	0.020
PCO on USG	89(91.8%)	37(97.4%)	0.243
FAI	3.15±2.27	6.59±3.78	0.000
FSH	3.8±1.1	3.8±1.0	0.789
LH	9.1±6.6	8.1±5.4	0.299
Testosterone (ng/ml)	0.43±0.2	0.49±0.2	0.662
FBS(g/dl)	71.3±6.3	70.9±5.8	0.523
2 hr post 75gmglucose(g/dl)	89.6±9.1	94.5±13.2	0.027
Insulin(µIU/ml)	12.2±8.0	16.7±13.1	0.001
Triglyceride(mg/dl)	62.7±2.4	66.4±14.0	0.341
HDL(mg/dl)	44.0±9.3	48.8±10.5	0.167

DISCUSSION:

PCOS among adolescents is an emerging problem that needs careful assessment, timely intervention, and appropriate treatment. As Rotterdam criteria is much more broad-based and does not necessarily require evidence of hyperandrogenism, the prevalence by Rotterdam criteria (22.5%) was almost double compared to that using AES criteria (10.7%). If all the enrolled girls would have participated in the study, the prevalence could further reduce as most girls who did not come for further investigations were symptom free. This prevalence is relatively higher than that reported by most studies, mainly due to use of different diagnostic criteria, study settings, age groups of the sample studied and hence cannot be compared.[4-8]

Puberty is a period when there is physiological hyperandrogenism and hyperinsulinemia which mimics some features of PCOS from Tanner stages I to III with return to prepubertal stage by Tanner stage V.[13] Hence, we enrolled girls 2 years post menarche when H-P-O axis settles down to normal. Due to this transitory appearance of symptoms and signs of PCOS during adolescence, care must be taken to avoid premature labelling of a case as PCOS to avoid over treatment and psychological stress. Presence of oligomenorrhea among adolescent girls, 2 years post menarche, can be a good screening indicator to diagnose a probable case of PCOS as reported earlier.[14,15] A diagnosis is confirmed if all three signs/symptoms of PCOS are present.[16] which was observed in 27.4% of PCOS cases in the study.

Community-based screening among Asian population found prevalence of PCOS among 6.3% of reproductive age women aged 15-45 years in Srilanka [17] and 5.6% in China[18] using Rotterdam criteria unlike the higher prevalence observed in our study among younger population aged 15-24 year olds or probably due to smaller group of girls who got enrolled due to more symptoms.

All the investigations were carried out by a single laboratory technician in a single laboratory which enhanced accuracy and consistency in the reports. Even the ultrasound examinations were carried out by a single-trained gynaecologist on a single machine. A retention rate of 77.2% in the study highlights the need to create awareness among general population about this disorder and its sequele. One of the limitations of the study was a poor representation of various socioeconomic strata; hence, the findings cannot be extrapolated to higher socioeconomic group with more westernised lifestyle and intake of junk food.

CONCLUSION:

It was one of few hospital based studies diagnosing PCOS and their phenotypes among adolescent and young girls in India. This study demonstrates that PCOS is an emerging disorder during adolescence and screening could provide opportunity to target the group for promoting healthy lifestyles and early interventions to prevent future morbidities.

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Limitations:

As it is a single centre study with a relatively small study population, results cannot be generalized to the entire population.

Another limitations of the study was a poor representation of various socioeconomic strata; hence, the findings cannot be extrapolated to higher socioeconomic group with more westernised lifestyle and intake of junk food.

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