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EXAMINING THE PREVALENCE OF POLYCYSTIC OVARIAN SYNDROME AND ITS RELATIONSHIPS TO BIOCHEMICAL AND CLINICAL INDICATORS IN RURAL ADOLESCENT FEMALES

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ABSTRACT:

BACKGROUND: Polycystic ovarian syndrome (PCOS) has been defined by the National Institute of Health and Rotterdam criteria as a hormonal disorder characterized by the presence of at least one polycystic ovary (accompanied by ovulatory dysfunction and excessive secretion of androgens. According to its suggestions, PCOS in adolescents should include all the three elements of Rotterdam criteria in which oligomenorrhea should be present after two years of menarche or primary amenorrhea at the age of 16 years; polycystic ovaries on ultrasound along with ovarian size of more than 10 cm3 and hyperandrogenemia should be present. Polycystic ovary syndrome (PCOS) is a common disorder occurring- in 6- 10% of women of reproductive age, it is characterized by chronic anovulation with either oligomenorrhoea or amenorrhea and hyperandrogenism and is the most common cause of anovulatory infertility and hirsutism.

AIM: Examining the prevalence of polycystic ovarian syndrome and its relationships to biochemical and clinical indicators in rural adolescent females

MATERIAL AND METHOD: The present study is a descriptive, observational cross-sectional study. After obtaining permission from our Institutional Ethics Committee this study was conducted Department of Obstetrics and Gynecology. Adolescents age group 10-19 years attending adolescent OPD were included in my study. Informed written consent was obtained prior to conducting the study. In case an individual is lesser than 18 years, consent was obtained from the parent/guardian, self-administered questionnaire was used to collect the preliminary data. To assess Hypothalmo- pituitary-ovarian function Serum LH, and FSH levels were measured. To diagnose disorders of glucose metabolism fasting BSL and Fasting insulin levels were obtained after an 8-12 hrs fast.

RESULTS: A total of 500 adolescent girls satisfying the inclusion/exclusion criteria were invited to participate in the study to achieve a sample size of 350. Amongst them, 300 adolescent girls volunteered, got enrolled, and underwent clinical examinations, biochemical blood tests, and ultrasound examinations. The mean Fasting BSL, insulin level, and HOMA-IR, in PCOS adolescent girls, were found to differ significantly as compared to Non-PCOS. These mean values were significantly higher in PCOS cases than in Non-PCOS subjects. T3, T4, and TSH showed no significant difference in PCOS adolescents and Non-PCOS girls. There was no association observed between TFT and PCOS.

CONCLUSION: Based on observations in this study, it is clear that PCOS is a common disorder among young adolescents in rural areas. And its prevalence increasing in rural areas also. Menstrual problems are the commonest reason for gynecological OPD consultation among adolescent girls. Childhood obesity, a sedentary lifestyle, lack of exercise, and the popularity of junk food in adolescence are responsible for the increasing PCOS incidence in adolescent girls and is a challenge for gynecologists treating them.

KEYWORDS: Polycystic ovarian syndrome, National Institute of Health, Functional ovarian hyperandrogenism, polycystic ovarian Morphology, sex hormone binding globulin.

INTRODUCTION:

Polycystic ovarian syndrome (PCOS) is the most frequent endocrinological disorder affecting 5-10% [1] of women of reproductive age. Its prevalence ranges from 2.2% to 26% in adult women from 18-45 years.[1] In a recent study, the prevalence of a confirmed diagnosis of PCOS in adolescents aged 10 to 19 years was 5-10%, which increased to 10-15%[1,2] when undiagnosed cases with documented symptoms qualifying for PCOS according to NIH (National Institute of Health) criteria were included. Its wide continuum of clinical manifestations such as oligomenorrhea, cosmetic deformities such as hirsutism, alopecia, obesity, and the impending fear of infertility with the anxiety of future metabolic complications has a remarkable impact on the psychology, of young women. Further, it is associated with a wide spectrum of morbidity, including cardiovascular abnormalities, type 2 diabetes mellitus, dyslipidaemias, risk of malignancies, and infertility.[2]

The cause of PCOS is unknown.[3] Considerable evidence suggests that it arises as a complex trait with contributions from both heritable and nonheritable intrauterine and extrauterine factors, among which insulin resistance and obesity are the most common. [3, 4] Functional ovarian hyperandrogenism (FOH) is usually the major source of the androgen excess and can account for the major features of the syndrome, i.e., hirsutism, anovulation, and polycystic ovarian Morphology (PCOM). This ovarian dysfunction is unique: it appears to be intrinsic and is characterized by abnormal ovarian steroidogenesis and folliculogenesis that are manifested clinically by androgen excess and anovulation. The diagnostic criteria for PCOS in adolescence are controversial, primarily because the diagnostic pathological features used in adult women, e.g. acne, irregular menses, and PCOM, may be normal pubertal physiological events.[5,6]

Due to the complexity of this PCOS disease, we thought its needed time to conduct a community-based, cross-sectional observational study in adolescent females to estimate the strength of the association of PCOS with clinical and its impact on her reproductive life in rural areas.[7]

As with the variability in clinical symptoms, there is a lack of uniformity regarding biochemical testing for this disorder. For the initial evaluation of hyperandrogenemia, measurement of total and/or free testosterone is recommended. Elevated free testosterone is recognized as the single most sensitive indicator for hyperandrogenemia, as the free fraction is the bioactive portion of serum testosterone. Most circulating testosterone is bound to sex hormone binding globulin (SHBG), obesity and androgen excess lower the level of SHBG, thus increasing free testosterone fraction. Clinical evidence of virilization should prompt a workup for disorders mimicking PCOS. It's also important to Obtain baseline thyroid and prolactin levels in any adolescent with chronic anovulation to exclude hyperprolactinemia and thyroid disorders. Most patients with PCOS have a higher luteinizing hormone/follicle stimulating hormone (LH/FSH) ratio[7,8,9] However, the test does not have robust diagnostic utility due to the variability of serum LH levels commonly seen during the different stages of the menstrual cycle.

Because of the heterogeneous nature of the disorder, recognizing adolescents with PCOS may be challenging. However, early recognition and management are important to prevent some of the long-term reproductive and metabolic complications associated with this syndrome. Clinical and USG Criteria are the gold standard for diagnosis of P.C.O.S. Doing an assessment of PCOS by using Free testosterone/LH/FSH and HOMAIR index is an additional novelty in my study. In a rural area it will help to improve the outcome of my study. It will be helpful to improve in implementation of timely treatment to prevent future sequels of complications in our rural adolescent

population. PCOS may be a major health concern in the future.

MATERIAL AND METHODS

The present study is a descriptive, observational cross-sectional study. After obtaining permission from our Institutional Ethics Committee this study was conducted Department of Obstetrics and Gynecology. Adolescents age group 10-19 years attending adolescent OPD were included in my study. Informed written consent was obtained prior to conducting the study. In case an individual is lesser than 18 years, consent was obtained from the parent/guardian, self-administered questionnaire was used to collect the preliminary data. To assess Hypothalmo-pituitary- ovarian function Serum LH, and FSH levels were measured. To diagnose disorders of glucose metabolism fasting BSL and Fasting insulin levels were obtained after an 8-12 hrs fast.

INCLUSION CRITERIA:

- ✓ adolescent girls age groups -19yrs
- ✓ Adolescent girls who have attained menarche.

Adolescents girls who have come to seek treatment from obstetrics and gynecology and adolescent OPD of the hospital for

- ✓ Menstrual complaints (irregular menses/oligomenorrhea/anovulation) Signs or symptoms of hyperandrogenaemia (clinical and biochemically) or
- ✓ Abdominal USG showing at least 12 follicles (2-9 mm in diameter) arranged peripherally around a dense core of ovarian stroma or scattered throughout an increased amount of stroma in at least 1 ovary or ovarian volume >10cc and diagnosed as PCOS according to Rotterdam 2003 criteria (This is modified in collaboration of international guidelines of AE-PCOS Society in 2006 and ESHRE 2018)

EXCLUSION CRITERIA:

- ✓ Adolescent girls having any major systemic illness, congenital adrenal hyperplasia, hyperprolactinemia, acromegaly, functional hypothalamic amenorrhea, and patients receiving drugs for any other systemic illness (except hypothyroidism)

The questionnaire was intended to obtain information regarding the age of the subject, age at menarche, socio-economic status, menstrual pattern, Menstrual complaints like irregular cycle and oligomenorrhea, menstrual loss, dysmenorrhea, past and present surgical and medical problems, family h/o diabetes/thyroid disorder/menstrual irregularities were asked, dietary habit, h/o migration after attaining menarche and habit of daily physical exercise were asked. Study subjects with or without suspected PCOS were then investigated for an abdominal-pelvic ultrasound scan, hormonal profile, and other blood tests.

- ✓ To assess Hypothalmo- pituitary- ovarian function Sr. L.H., and F.S.H. levels were measured.
- ✓ To diagnose disorders of glucose metabolism fasting BSL and Fasting insulin levels were obtained after an 8-12 hrs. fast.

All blood tests were done with fasting status between the 3rd and 5th day of the menstrual cycle including for those whose cycle length of 6-8 weeks and more, it stored at -80°C for biochemical and hormonal parameters. A waist-hip ratio of more than 0.85 was considered obesity. Finally, sample the size i.e. 300 was the minimum number of adolescent girls required to be studied in this research.

STATISTICAL ANALYSIS

SPSS 20 software (SPSS Inc. Chicago, and II, USA) was used for the statistical analysis. Continuous variables were expressed in mean ± standard deviation (SD) and categorical variables were expressed as proportions. Pearson's Chi-square χ^2) test was used to evaluate the differences in proportion between the groups. Student's t-tests were used to compare continuous variables. Binary logistic regression analysis was performed with PCOS as the dependent variable and other statistically significant variables ($p<0.1$) as independent to elicit the

strength of association. A p< 0.05 was considered statistically significant

RESULT: -

A total of 500 adolescent girls satisfying the inclusion/exclusion criteria were invited to participate in the study to achieve a sample size of 350. Amongst them, 300 adolescent girls volunteered, got enrolled, and underwent clinical examinations, biochemical blood tests, and ultrasound examinations.

Table No. 1: Difference in metabolic profiles between PCOS and Non-PCOS

Variable	PCOS as per Rotterdam	
	NON PCOS	PCOS
BSL	84.11 ±10.09	87.40± 5.72
Insulin	10.37± 12.11	13.43±08.02
HOMA IR	2.25± 3.06	2.24± 2.09

The mean Fasting BSL, insulin level, and HOMA-IR, in PCOS adolescent girls were found to differ significantly as compared to Non-PCOS. These mean values were significantly higher in PCOS cases than in Non-PCOS subjects.

Table 2: Association between TFT among PCOS and Non-PCOS populations.

Variable	PCOS as per Rotterdam	
	NON PCOS	PCOS
T3	107.57 ± 26.01	113.07 ± 29.61
T4	6.22 ± 5.13	6.22 ± 1.14
TSH	1.82 ± 1.63	2.28 ± 2.24

T3, T4, and TSH showed no significant difference in PCOS adolescents and Non-PCOS girls. There was no association observed between TFT and PCOS.

Table No. 3: Endocrine factors and Hyperandrogenism among PCOS and Non-PCOS population

Variable	PCOS as per Rotterdam	
	NON PCOS	PCOS
LH	6.70 ± 7.001	9.65 ± 7.42
FSH	7.55 ± 6.32	7.24 ± 2.75
LH: FSH Ratio	1.46 ± 2.52	1.64 ± 1.73
Free Testosterone	1.17 ± 1.24	2.46 ± 2.66
MFG	4.34 ± 1.12	6.53 ± 2.22

Similarly, LH, FSH, and LH/FSH Ratio also did not differ significantly in PCOS adolescents and Non-PCOS girls. There was no association observed in all measures of LH, FSH, and LH/FSH Ratio with PCOS. Free testosterone levels and MFG scores of PCOS adolescents differ significantly as compared to Non-PCOS. These values are significantly high in PCOS than in Non-PCOS.

DISCUSSION

The adolescent phase of life brings multiple physiological, anatomical, and psychological changes in girls. Due to familial, cultural, and social restrictions, most adolescent girls are not able to share and get the right advice for menstrual-related problems. PCOS is one of these conditions which is of serious concern. PCOS among adolescents is an emerging problem that needs early assessment by clinical

examination and investigations. It needs timely intervention and accurate treatment to prevent future series of complications.[10] Puberty is a period when there is physiological hyperandrogenism and hyperinsulinemia which mimics some features of PCOS from Tanner stages I to III with a return to the prepubertal stage by **Tanner stage V**.[11] Other studies done by **Frank S et al**[12] and **Nagarja bhuvanashree et al**[10] included girls in the age group of 10 to 19 years. They observed 64.7% were in the late adolescence age group. In a similar study done by **Sultan C et al** study group[13], they found PCOS was more common in late adolescence which accounts for about 76.2 % of cases. The reason behind it may be a late manifestation of clinical symptoms of PCOS after the onset of menarche, making parents alert to attend our clinic for further evaluation

The association of PCOS and its components with socioeconomic status (SES) might shed light on the role of the environment in the development of this condition.[14] Research has shown that individuals with lower SES are more at risk for engaging in adverse health behaviors, including smoking, lack of physical activity, and poor nutritional diet[15,16]; among women, obesity is associated with low SES. Studies have also shown that smoking and obesity can exacerbate insulin resistance, which is a condition highly correlated with any part of the pathogenesis of PCOS. Moreover, there is clear evidence of an association between low SES and cardiovascular disease (CVD),[17-18-19] as well as the metabolic syndrome and its various components. Considering that PCOS symptoms often begin in adolescence, we chose to examine the association between SES over the life course, from childhood to adulthood.

According to a prospective study conducted by **Gainie MA et al 2004**[20] they found the prevalence of PCOS in adolescents was 22.5%. A similar study done by **Kamboj MK et al 2017**[21] shows a prevalence of PCOS at 23.8% by Rotterdam criteria and a similar prospective study done by **Nidhi et al 2011**[19] on 460 girls aged 15-18 years in a residential college in Andhra Pradesh, South India, the prevalence of PCOS was found to be 9.13% in adolescents by Rotterdam criteria. A study done by **Biradar et al 2015**[22] observed prevalence of PCOS by Rotterdam criteria was 11.98% similar to the present study. A study was done by **Lakshmi KS et al 2015**. showed that the prevalence of PCOS in a tertiary care hospital was 11.90%[23]. In the present study out of 401 enrolled adolescents, it was found that the prevalence of PCOS by Rotterdam criteria was 27.2% and it was 8.2% by AE-PCOS society criteria. Out of those Diagnosed with PCOS by Rotterdam criteria, 60% were obese PCOS and 14.8% were lean PCOS and the rest of them were either normal or overweight. Similar observations were seen in a study done by **Radha p et al2016 and Nitin Joseph et al2016**[24,25] The prevalence among late adolescents is slightly higher than in early adolescence. probably due to increasing in hyperandrogenism with age and hence early diagnosis and intervention could help us to reduce morbidities in older age groups women. As PCOS is considered a metabolic disorder, it has a link with all endocrine parameters. But in the present study, we found no significant relationship between Thyroid disorders with PCOS, we found only 2% of cases had Hypothyroidism rest of them had normal values, Study done by **Lakshmi KS et al2015**[23] observed that 1% of adolescents had hypothyroidism in PCOS, Similar Study done by **Swetha Balaji et al2015**[26] found hypothyroidism in 3% of the population. All these cases were seen in the late adolescence age group. Obesity and menstrual problems were observed in diagnosed Hypothyroidism cases.[27]

Although still there is no consensus about the best method for the detection of this disorder, the HOMA-IR has been considered to be a good diagnostic parameter.[28] In the present study, we calculated insulin resistance with the HOMA-IR method, which showed more elevated values in patients with diagnosed

PCOS than in Non-PCOS, which demonstrates the lower insulin sensitivity in these patients. With the present study, we conclude that there was a significant association between the patterns of menstrual irregularity, elevated HOMA-IR value, and PCOS. A study done by **Simi kumari et al2015** [29] shows a significant association between HOMA- IR index, menstrual irregularity, and PCOS similar to the present study. A high level of fasting insulin was observed in diagnosed cases of PCOS compared to Non-PCOS. In the present study, three cases of Diabetes were detected for the first time, and treatment was started after evaluation.

In the present study, we found that most hyperandrogenic adolescents had androgenic ovarian dysfunction and this was independent of serum LH elevation or PCOM in about half of the cases. This abnormality was termed functional ovarian hyperandrogenism (FOH). The evidence was consistent with ovarian hyperandrogenism being a functional abnormality that requires normal adult LH levels but not LH elevation. There was no significant change seen in LH/FSH ratio in this study. A study done by **Mishra et al 2009**[30] and **Simi Kumari et al2015** and[29] shows an increase in LH/FSH levels. A study done by **Vaidya R.et al 2017**[31] shows similarity with the present study on LH/FSH ratio in PCOS.

A major strength of this study was the wide range of the adolescent population of the age group 10 to 19 years. The reported younger onset of this syndrome in a rural area and the prevalence of associated risk factors such as glucose intolerance in the rural Indian population signify a need for intensified efforts in early detection. [32,33] The increased proportion reported not only among urban adolescents but also it was observed in this study done on rural girls which are of great concern.[34] The probable reason must be an increased sedentary lifestyle and lack of regular exercise and stress regarding education.[13] Further studies should be conducted to elucidate the predominant risk factors in urban adolescents and the possible protective factors among rural adolescents in order to offer preventive measures.[35,36]

CONCLUSION:

Based on observations in this study, it is clear that PCOS is a common disorder among young adolescents in rural areas. And its prevalence increasing in rural areas also. Menstrual problems are the commonest reason for gynecological OPD consultation among adolescent girls. Childhood obesity, a sedentary lifestyle, lack of exercise, and the popularity of junk food in adolescence are responsible for the increasing PCOS incidence in adolescent girls and is a challenge for gynecologists treating them. PCOS may be a major health concern in the future. Health education classes to create awareness regarding adolescent PCOS and other gynecological problems should be conducted regularly in schools and colleges in rural as well as urban areas.

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