Research article

Clinicopathological features of polycystic ovarian syndrome in adolescence

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Abstract

Objectives: To evaluate the clinicopathological features of adolescence diagnosed with polycystic ovarian syndrome.

Methods: This is a descriptive study conducted at the Gynecology Clinics of University Obstetric Unit, Teaching Hospital-Jaffna to evaluate the clinicopathological features of adolescence diagnosed with polycystic ovarian syndrome (PCOS) over a period of 3 years. A total of 56 adolescent girls were diagnosed with PCOS during this period with the currently accepted diagnostic criteria recommended by the Pediatric Endocrine Society and all of them were included in the study.

Clinicopathological features at the time of diagnosis of PCOS obtained from medical records were analyzed and descriptive statistics were calculated.

Discussion: Emphasizing the importance of early detection of PCOS in women especially during the adolescent periods, its diagnosis should be based on the presence of clinical and/or biochemical hyperandrogenism and irregular menses for at least 1 year as recommended.

Our results suggest that the commonest feature of clinical hyperandrogenism being moderate hirsuitism (89.3%) and the commonest type of abnormal uterine bleeding being oligomenorrhea (54%). An obvious rising trend in the number of diagnosed patients with age was also observed.

Though the prevalence anovulatory pattern of bleeding among adolescence diagnosed with PCOS consistent with larger studies in Caucasian population, commonest manifestation of clinical hyperandrogenism was moderate hirsutism which was significantly higher compared to other studies.

This could be explained by its variation across ethnicities especially with a higher prevalence of hirsuitism among South Asian population.

In the absence of any published data on clinicopathological features of adolescence diagnosed with PCOS in Sri Lanka, our series highlights its pattern at the time of diagnosis.

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Introduction

Polycystic ovary syndrome (PCOS) affects 6-15% of women of reproductive age and accounts for almost 75% of hyperandrogenism in adults[1].

Though the cause of PCOS is unknown, considerable evidence suggests that it is a complex trait arising from heritable influences, nonheritable intra- and extrauterine environmental factors, variations in insulin resistance, alterations in steroidogenesis/steroid metabolism, and alternative adaptations to energy excess[2,3].

Its complex interactions generally mimic an autosomal dominant trait with variable penetrance and metabolic syndrome prevalence is high in parents, siblings and correlates in identical twins[4,5].

Adult women present with classic features that includes chronic anovulation associated with relative infertility, polycystic ovarian morphology, and hirsutism[6].

Diagnostic criteria for adult women have been developed by three international conferences namely National Institutes of Health (NIH) conference criteria (1990), the Rotterdam consensus criteria (2003) and the Androgen Excess-PCOS Society consensus criteria (2006)[7,8].

Though they are somewhat different many criterions overlap. While the first signs of PCOS can be perceptible even during childhood, the unique features of the syndrome in adolescence are not very clear[9].

Hyperandrogenemia, anovulatory cycles, oligo-menorrhea, insulin resistance and hyperinsulinemia are intrinsic reproductive and metabolic manifestations in adolescents and applying the same diagnostic criteria of adult PCOS to this group is controversial and questions still exist regarding the features of PCOS in adolescence[10].

Despite these difficulties, an early diagnosis of PCOS is of great importance since its presence is related to a greater risk of future infertility, type II diabetes mellitus, metabolic syndrome / abnormalities and cardiovascular disease[11,12].

With long-term complications due to adolescent PCOS, the temptation to make this diagnosis and consider medical therapy during adolescence should be tempered against the real benefits of such therapy, and the possible risks of the drugs employed to treat this condition[13].

With growing experience and evidence there are clear indications to treat adolescence PCOS with lifestyle intervention, local therapies/cosmetic, additive pharmaceuticals and consider future reproductive aspects and the psychological impact of PCOS also constitutes a major concern in adolescent PCOS[14].

The presence of Polycystic Ovarian Morphology (PCOM) in an adolescent who does not have hyper-androgenism/oligo-anovulation does not indicate a diagnosis of PCOS. Anyway, the measurement of ovarian volume, follicle number and size, and uterine dimensions may be useful in the evaluation of amenorrhea, but is not needed for PCOS diagnosis in adolescents[15].

To overcome these uncertainties the Pediatric Endocrine Society invited an expert group of representatives from the Androgen Excess-PCOS Society and stakeholder international pediatric and adolescent specialty societies with the goal of defining which criteria have sufficient evidence to be used for the diagnosis of PCOS in adolescents. Consensus has recently been reached by international pediatric subspecialty societies that otherwise unexplained persistent hyperandrogenic anovulation using age- and stage-appropriate standards are appropriate diagnostic criteria for polycystic ovary syndrome (PCOS) in adolescents[16].

The World Health Organization (WHO) defines adolescents as those people between 10 and 19 years of age and it is currently accepted that the diagnosis of PCOS in adolescents should be based on the presence of clinical and/or biochemical hyperandrogenism and irregular menses for at least 1 year. Polycystic ovarian morphology (PCOM) on ultrasound is not a diagnostic criterion in adolescents[17].

Though prevalence of leading clinical manifestations and laboratory findings of PCOS in adolescence have been studied, information on prevalence of the clinico-pathological features as per above recommendation to make a diagnosis is lacking in these studies[18].

In the absence of any published data on clinico-pathological features of adolescence diagnosed with PCOS, our study was designed to investigate the features based on the recommendations and criteria of international pediatric and adolescent specialty societies amongst adolescences diagnosed with PCOS.

Our study was conducted among 56 adolescence girls who were diagnosed with PCOS over a period of three years in a single center at University Unit Gynaecology Clinic, Teaching Hospital Jaffna.

Methods

The study was conducted at the University Gynaecology Clinics, Teaching Hospital. All procedures performed were in accordance with good clinical practice.The information was obtained from the case records of adolescence diagnosed with PCOS during a period of 3 years, from 2017.

A total of 56 adolescent girls were diagnosed with PCOS during this period with the currently accepted diagnostic criteria and all of them were included in the study.

Though ultrasound is not a criterion to make a diagnosis of PCOS in adolescents, all the subjects underwent a trans abdominal ultrasound scan to exclude unexpected pelvic pathology and to visualize the ovaries.

The detailed diagnostic criteria are summarized in Box 1 and the definitions of types of abnormal uterine bleeding in adolescents are summarized in Box 2[17,18].

Box 1. Diagnostic criteria for PCOS in adolescents

Otherwise unexplained combination of:

1. Abnormal uterine bleeding pattern

    a. Abnormal for age or gynecologic age

    b. Persistent symptoms for at least 1year

AND

2. Evidence of hyperandrogenism

    a. Persistent testosterone elevation above adult norms in a reliable reference laboratory is the best evidence.

    b. Moderate-severe hirsutism is clinical evidence of hyperandrogenism.

    c. Moderate-severe inflammatory acne vulgaris is an indication to test for hyperandrogenemia.

Based on Witchel S, Oberfield S, Rosenfield R, Codner E, Bonny A, Ibanez L, et al. The Diagnosis of Polycystic Ovarian Syndrome during Adolescence Horm Res Pediatr. 2015; 83 (6): 376-389.

Box 2. Definitions of types of abnormal uterine bleeding in adolescents

Descriptor	Definition
Primary amenorrhea	Lack of menarche by 15 y of age or by 3 years after the onset of breast development
Secondary amenorrhea	Over 90 days without a menstrual period after initially menstruating
Oligomenorrhea (infrequent AUB)	Postmenarcheal year 1: average cycle length>90 d (<4 periods/y) Postmenarcheal year 2: average cycle length>60 d (<6 periods/y) Postmenarcheal years 3-5: average cycle length >45 d (<8 periods/y) Postmenarcheal years ≥6: cycle length>38-40 d (≤9 periods/y)
Excessive anovulatory AUB[†]	Menstrual bleeding that occurs more frequently than every 21 d (19 d in yr 1) or is excessive (lasts>7 d or soaks >1 pad or tampon every 1-2 h)

Based on Rosenfield RL. Clinical review: Adolescent anovulation: Maturational mechanisms and implications. J Clin Endocrinol Metab. 2013; 98: 3572-3583.

Moderate-severe hirsutism is considered clinical evidence of hyperandrogenism and it was diagnosed using the Ferriman-Gallwey hirsutism scoring. Figure 1[19].

Moderate-severe inflammatory acne vulgaris is an indication to test for hyperandrogenemia and the scoring system for acne is summarized in Box 3[20,21].
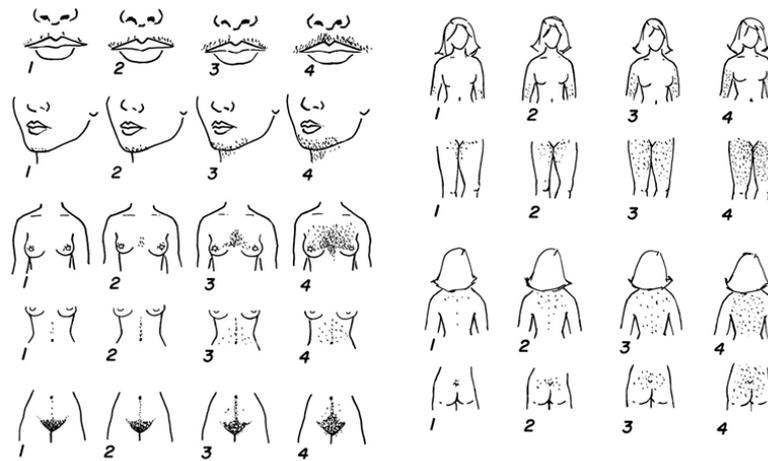
Figure 1. **Ferriman-Gallwey hirsutism scoring system.**

Based on Martin KA, Chang RJ, Ehrmann DA, Ibanez L, Lobo RA, Rosenfield RL, et al. Evaluation and treatment of hirsutism in premenopausal women: An Endocrine Society Clinical Practice Guideline. J Clin Endocrin Metab. 2008; 93: 1105-1120.

Each of the 9 body areas most sensitive to androgen is assigned a score from 0 (no hair) to 4 and these separate scores are summed to provide a hormonal hirsutism score.

Box 3. Acne scoring system for adolescents

Severity	Comedonal Lesions[b]	Inflammatory Lesions[c]
Mild	1-10	1-10
Moderate	11-25	11-25
Severe	25	25

Based on Lucky AW, Biro FM, Simbartl LA, Morrison JA, Sorg NW. Predictors of severity of acne vulgaris in young adolescent girls: Results of a five-year longitudinal study. J Pediatr. 1997; 130: 30-39.

a. Face, chest, shoulders, and back may be graded separately.
b. Open ("blackheads") or closed ("whiteheads") comedones (>1 mm diameter).
c. Pustules, papules (≤5 mm) and nodules (>5mm).

Clinicopathological features at the time of diagnosis of PCOS obtained from medical records were analyzed and descriptive statistics were calculated using SPSS Statistics Version 23.

Results

The age distribution of adolescence diagnosed with PCOS is reflected in Figure 2 and demographics are summarizedin Box 4.
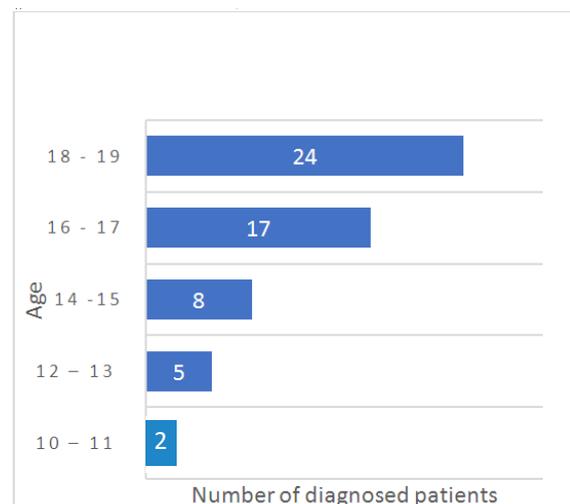
Figure 2. **Age distribution of adolescence diagnosed with PCOS.**

Box 4. Age of adolescence diagnosed with PCOS and their demographics

Varable			Values		
Age Range (y)	10 - 11	12 - 13	14 - 15	16 - 17	18 - 19
Number diagnosed with PCOS	3	5	6	10	20
Weight (kg)	46	45.4	49.2	52.3	57.8
Height (cm)	147	149.8	149	158	161
BMI (kg/m^2)	21.3	20.2	22.2	21	22.3

BMI (body mass index), Data are mean

The types of abnormal uterine bleeding in the 56 adolescence are summarized in Box 5 and Figure 3.

Box 5. The types of abnormal uterine bleeding

Primary amenorrhea	06 (11%)
Secondary amenorrhea	12 (21%)
Oligomenorrhea	30 (54%)
Excessive anovulatory bleeding	08 (14%)
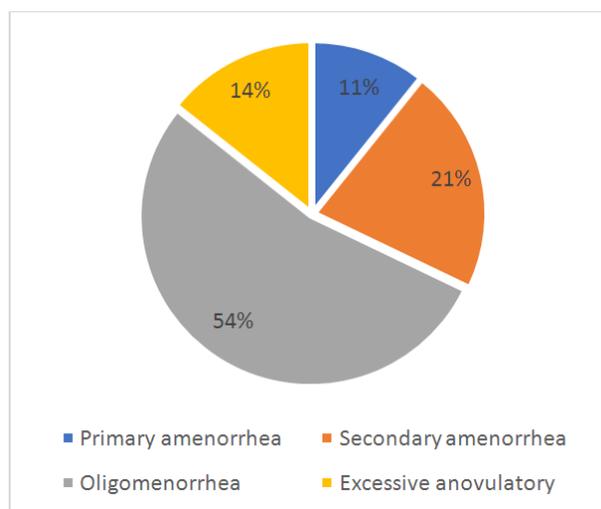
Figure 3. **The types of abnormal uterine bleeding.**

The commonest type of abnormal uterine bleeding-observed in this group was oligomenorrhea (54%, n=30) and the pattern of oligomenorrhea is summarized in Box 6 and Figure 4.

Box 6. Pattern of oligomenorrhea

Postmenarcheal year 1: average cycle length >90 d (<4 periods/y)	3
Postmenarcheal year 2: average cycle length >60 d (<6 periods/y)	5
Postmenarcheal years 3-5: average cycle length >45 d (<8 periods/y)	15
Postmenarcheal years ≥6: cycle length >38-40 d (≤9 periods/y)	7
Total	30
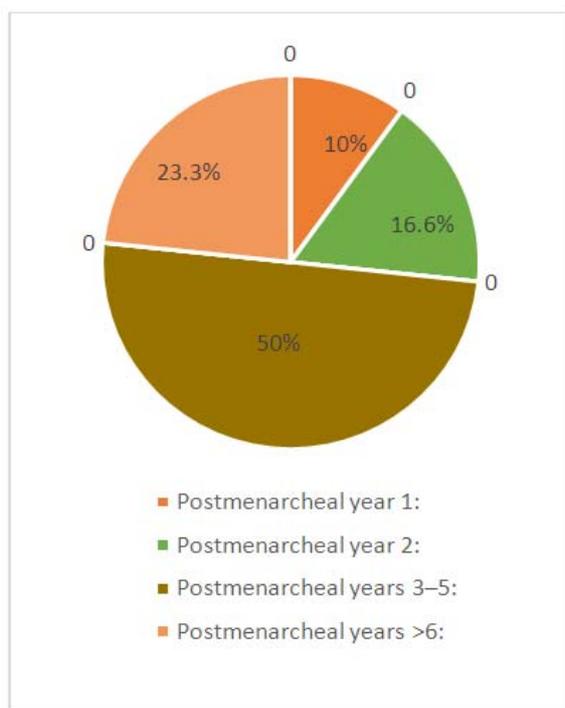
Figure 4. **The pattern of oligomenorrhea observed among the 30-adolescence diagnosed with PCOS in percentage.**

Of the 56-adolescence diagnosed with PCOS clinical evidence of hyperandrogenism in 50 was due to moderate hirsutism and 6 due to severe hirsutism. Though moderate-severe inflammatory acne vulgaris is not considered as clinical evidence of hyperandrogenism it is an indication to test for hyperandrogenemia. Five subjects underwent serum testosterone assays as they were diagnosed with moderate-severe inflammatory acne vulgaris. Two of them were diagnosed with hyperandrogenemia. Anyway, both were already included in the cohort of 56 as they were diagnosed with abnormal uterine bleeding and moderate hirsuitism. Box 7 summarizes the pattern of hyperandrogenism.

Box 7. Pattern of hyperandrogenism

Moderate hirsuitism (Clinical)	50 (89.3%)
Severe hirsutism (Clinical)	6 (10.7%)
Testosterone elevation (Both had moderate – severe acne and moderate hirsuitism).	2 (3.6%)

Though ultrasound is not a criterion to make a diagnosis of PCOS in adolescents, all the subjects underwent a trans abdominal ultrasound scan to exclude unexpected pelvic pathology and to visualize the ovaries. In 14 of the 56 adolescence (25%) who were diagnosed with PCOS, polycystic morphology of the ovaries was observed.

Discussion

Emphasizing the importance of early detection of PCOS in women especially during the adolescent period, its diagnosis should be based on the presence of clinical and/or biochemical hyperandrogenism and irregular menses for at least 1 year as recommended.

Abnormal uterine bleeding pattern being the first definitive criterion to make a diagnosis of PCOS in adolescence, the combination of oligomenorrhea (54%) and excessive anovulatory bleeding (14%) accounted for 68% in our study which could be categorized as anovulatory type of abnormal bleeding. This is comparable with symptomatology studies which quote 65% of anovulatory pattern of bleeding among adolescence diagnosed with PCOS[22].

The presence of clinical or biochemical hyperandrogenism being the second definitive criterion, our results suggest that the commonest feature of clinical hyperandrogenism being moderate hirsutism (89.3%). This is not comparable with studies which looked at the clinical manifestations of PCOS in adolescence, as hirsuitism has accounted for only 16.7% and acne being the leading symptom (30%) suggestive of hyperandrogenism[23].

Prevalence of hirsuitism by race suggest that it varies significantly across ethnicities and the lowest being observed among the Northern, fair-skinned Europeans and the highest among Mediterranean women[24].

An increased prevalence of hirsutism among South Asian adult women and a lower prevalence in Caucasian adult women with PCOS also has been reported and these findings could explain the observations in our Sri Lankan study population[25].

Though ultrasound is not a criterion to make a diagnosis of PCOS in adolescents a quarter (25%) of our study population had demonstrable polycystic ovarian morphology.

Polycystic ovarian morphology is an inconstant finding in healthy adolescents and up to 35% has been observed in this age group[26]. As does not appear to be associated with decreased ovulatory rate or metabolic abnormalities in healthy adolescents it reiterates that polycystic ovarian morphology should not influence the diagnosis of PCOS in adolescence.

Though the sample size of our study was modest we were able to analyze the clinicopathological features of polycystic ovarian syndrome in adolescence over a period of three years at a tertiary gynaecology hospital clinic. Further, the currently available literature on clinicopathological features of PCOS have been mainly on adults and lack similar studies on adolescence with the diagnostic criteria by international paediatric subspecialty societies.

In the absence of any published data on clinicopathological features of adolescence diagnosed with PCOS in Sri Lanka, our series highlights its pattern at the time of diagnosis.

We also emphasize to follow diagnostic criteria recommended by international paediatric subspecialty societies to diagnose PCOS among adolescence to improve early detection rate and at the same time avoid the possible risks of over diagnosis.

Similar studies with larger sample size in other centers in the country are recommended to understand the pattern clinicopathological features of adolescence diagnosed with PCOS in Sri Lankan population.

Author Declarations

Competing interests: The authors declare that they have no competing interests.

Financial disclosure: The study was self-financed.

Ethical consideration: The study was conducted at the University Gynaecology Clinics, Teaching Hospital, Jaffna, after obtaining ethical approval from Ethics Review Committee of the Teaching Hospital, Jaffna. All procedures performed were in accordance with good clinical practice.

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