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RESEARCH ARTICLE
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THE IMPACT OF VARIATIONS IN DIAGNOSTIC CRITERIA FOR ADOLESCENT POLYCYSTIC OVARY SYNDROME (PCOS), EXCLUDING POLYCYSTIC OVARIAN MORPHOLOGY, ON DIAGNOSIS AND TREATMENT APPROACHES IN PAKISTAN

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Abstract

Introduction: Polycystic ovary syndrome (PCOS) is characterized by ovulatory dysfunction, hyperandrogenemia, and polycystic ovarian morphology (PCOM), with a prevalence of 8%–13% in women and 3.4%–19.6% in adolescent girls.

Objective: The main objective of the study is to find the impact of variations in diagnostic criteria for adolescent polycystic ovary syndrome (PCOS), excluding polycystic ovarian morphology, on diagnosis and treatment approaches in Pakistani population.

Methodology: This cross-sectional study was conducted at Department of Gynae and Obst, DHQ KDA Kohat during Jan 2023 to Feb 2024. Data were collected from 320 adolescent females aged between 12 and 19 years, who visited the clinic for evaluation of menstrual irregularities, signs of hyperandrogenism (such as acne, hirsutism, and alopecia), or concerns related to infertility.

Results: Data were collected from 320 patients with average age of the participants was 23.45 ± 10.98 years. A majority of the participants (56.3%) were classified as overweight or obese (BMI ≥ 25 kg/m²), while 43.7% had a normal BMI. A significant portion of the cohort (37.5%) reported a family history of PCOS. Menstrual irregularities, specifically oligomenorrhea, were observed in 65.6% of the participants, with 34.4% experiencing amenorrhea for three months or more. The results indicate that 47% of the participants exhibited hirsutism, with a Ferriman-Gallwey score of ≥ 6, while 43.7% had acne, and 31.3% experienced alopecia. Elevated total testosterone levels (≥ 60 ng/dL) were observed in 40.6% of the participants, and 25% had elevated DHEAS levels (≥ 250 µg/dL).

Conclusion: It is concluded that variations in diagnostic criteria for adolescent PCOS, particularly the exclusion of Polycystic Ovarian Morphology (PCOM), do not significantly affect the

identification of key clinical and metabolic features such as insulin resistance, hyperandrogenism, and menstrual irregularities.

Introduction

Polycystic ovary syndrome (PCOS) is characterized by ovulatory dysfunction, hyperandrogenemia, and polycystic ovarian morphology (PCOM), with a prevalence of 8%–13% in women and 3.4%–19.6% in adolescent girls. The Prime cause in the pathogenesis of PCOS is Insulin resistance. Features of metabolic syndrome and, in particular, glucose intolerance and type 2 diabetes are more frequently observed in the population of women with PCOS [1]. These effects persist into menopausal years and thus PCOS is a disease not only of the reproductive but also of the metabolic phenotypes. One of the most important clinical questions related to the diagnostic criteria of adolescent PCOS is the difference between excluding PCOM and the effect of these changes on the current clinical management of the syndrome [2]. PCOS is one of the most prevalent hormonal disorders among adolescent females, and if left unchecked, can have serious negative health implications throughout the girl's life. Nevertheless, various symptoms of the condition include menstrual disorders, hyperandrogenism increased facial and body hairs, and metabolic disturbances including insulin resistance [3]. Persons affected with this condition may therefore not be easily diagnosed especially when there are no well-defined diagnostic criteria that any health facility can use especially at the early stages [4].

Traditional diagnostic criteria for PCOS, such as those outlined by the Rotterdam criteria, typically include three main features: oligo-anovulation, clinical hyperandrogenism, biochemical hyperandrogenism, and ultrasound PCOM. However, the previous study has found that eliminating PCOM from the diagnostic criteria of adolescents provides better long-term treatment ways for diagnosing the condition [5]. Its exclusion especially in adolescent girls who have not attained complete maturity, the investigators found out that ovarian morphology is not always a guarantee of PCOS in young girls. This development is not infrequently seen during adolescence when there is an increased number of small follicles on the ovaries and may be mistaken for PCOM [6]. That is why, the evaluation of ovarian morphology only can cause an overdiagnosis or misdiagnosis of PCOS in young patients and mistreat them. Also, the exclusion of PCOM might contribute to even more precise diagnostic criteria for PCOS, which are centered on menstrual cycle and hyperandrogenism. By prioritizing such clinical manifestations, the following probability indicators, clinicians gain an increased ability to identify adolescents with PCOS in need of medical intervention. It also minimizes overdiagnosis in circumstances where ovarian morphology is a mere ancillary abnormality and not the primary feature of the disease [7].

Because PCOM is not included on the one hand, it will beg questions regarding the comprehensiveness and validity of the diagnostic criteria on the other. PCOM therefore is still part of the main adult PCOS diagnostic criteria and is sometimes also used as a supporting criterion for teenagers [8]. Taking out this criterion may raise questions on the real cases of possible missed diagnosis especially if the hormonal irregularities in the body of some adolescents, and symptoms are not very severe. For example, a teenager with irregular menstruation and mild hirsutism but normal findings on ultrasonography and without overt ovarian cyst would be disqualified under this new criterion. In other words, such individuals may never be diagnosed and never receive treatment, which would mean that they can develop severe long-term problems, including infertility, metabolic syndrome, and psychological consequences amongst others [9]. However, there is another disadvantage regarding the exclusion of PCOM: this results in some limited comprehension of the whole concept of PCOS. The current set of diagnostic criteria represents a general approach that has hormonal and morphological characteristics of the disease. Despite controlled symptoms only based on a hormonal array, the updated criteria of diagnosis may perpetrate increased misunderstanding of PCOS as a genetic-environmental interaction disease [10]. Ovarian morphology could inform on the pathophysiology of the condition and its exclusion may compromise the ability of clinicians to treat the disease. The exclusion of PCOM from diagnostic criteria also has implications for treatment

approaches [11]. The available management approaches for PCOS are hormonal contraceptive medications, anti-androgens as well as insulin-sensitizing drugs, and all these approaches are based on the presenting symptoms of PCOS. However, the absence of PCOM may result to changes in the behavior of the clinicians as they treat this illness which may result in more symptomatic management of this disease rather than focusing on the metabolic and endocrine causes of the disease. These could potentially lead to a more limited approach to treating PCOS, excluding aspects of the illness as insulin resistance and future cardiovascular danger [12].

Objective

The main objective of the study is to find the impact of variations in diagnostic criteria for adolescent polycystic ovary syndrome (PCOS), excluding polycystic ovarian morphology, on diagnosis and treatment approaches in Pakistani population.

Methodology

This cross-sectional study was conducted at Department of Gynae and Obst, DHQ KDA Kohat during Jan 2023 to Feb 2024. Data were collected from 320 adolescent females aged between 12 and 19 years, who visited the clinic for evaluation of menstrual irregularities, signs of hyperandrogenism (such as acne, hirsutism, and alopecia), or concerns related to infertility.

Inclusion Criteria

- Adolescent females (12-19 years old) with clinical symptoms suggestive of PCOS
- Patients who were not previously diagnosed with PCOS or were in the process of being evaluated for a possible diagnosis of PCOS.
- Participants willing to undergo pelvic ultrasound and laboratory testing to confirm or rule out PCOS.

Exclusion Criteria

- Adolescents with known endocrine disorders other than PCOS (e.g., thyroid disorders, hyperprolactinemia, Cushing's syndrome).
- Participants who had undergone previous ovarian surgery or other treatments that might affect ovarian morphology.
- Patients who were pregnant or lactating at the time of the study.
- Adolescents with severe chronic illnesses that could interfere with the evaluation or treatment of PCOS.

Data Collection

The data collection process for this study involved two main stages: clinical assessment and diagnostic evaluation. Each participant underwent a comprehensive clinical interview, where detailed menstrual histories were gathered, and symptoms of hyperandrogenism, such as acne, hirsutism, and alopecia, were assessed. Information on the type of family history PCOS or related endocrine disorders were also taken with a view of capturing genetic background. To assess obesity, one of the comorbidities observed in PCOS patients, the participants' BMI was taken. A clinical examination was done in order to identify clinical symptoms of hyperandrogenism, with focus on hirsutism, acne, and alopecia. The clinical severity of hirsutism, one of the major symptoms of PCOS, was evaluated with the help of the Ferriman-Gallwey (F-G) score. After the clinical examination, participants underwent grey-scale transvaginal ultrasound for assessment of ovarian features with special reference to PCOS defined as ovarian morphology showing twelve or more follicles measuring 2–9 mm in diameter and/or increased stromal echogenicity. As described in the design of this study, PCOM was not included in the definition of PCOS in this sample, since this work was aimed at assessing the consequence of excluding this concrete morphological characteristic. Serum samples were taken to determine the hormonal values of LH, FSH, total testosterone, free testosterone, DHEAS, prolactin, TSH, insulin and are, the primary parameters used to diagnose PCOS and the extent of its metabolic disorder. The

menstrual history of each participant was reviewed to include; oligomenorrhea or amenorrhea which is common in PCOS.

Data Analysis

Data were analyzed using SPSS v26. Descriptive and inferential statistics to determine the effects of excluding PCOM on the diagnosis and treatment outcomes for adolescent PCOS.

Results

Data were collected from 320 patients with average age of the participants was 23.45 ± 10.98 years. A majority of the participants (56.3%) were classified as overweight or obese (BMI ≥ 25 kg/m²), while 43.7% had a normal BMI. A significant portion of the cohort (37.5%) reported a family history of PCOS. Menstrual irregularities, specifically oligomenorrhea, were observed in 65.6% of the participants, with 34.4% experiencing amenorrhea for three months or more.

Table 1: Demographic and Clinical Characteristics of Participants

Characteristic	Total (n=320)	Percentage (%)
Average Age	23.45±10.98	-
Overweight/Obese (BMI ≥ 25 kg/m²)	180	56.3%
Normal BMI	140	43.7%
Family History of PCOS	120	37.5%
Menstrual Irregularities (Oligomenorrhea)	210	65.6%
Amenorrhea (≥ 3 months)	110	34.4%

The results indicate that 47% of the participants exhibited hirsutism, with a Ferriman-Gallwey score of ≥ 6, while 43.7% had acne, and 31.3% experienced alopecia. Elevated total testosterone levels (≥ 60 ng/dL) were observed in 40.6% of the participants, and 25% had elevated DHEAS levels (≥ 250 µg/dL).

Table 2: Signs of Hyperandrogenism in Participants

Symptom	Total (n=320)	Percentage (%)
Hirsutism (Ferriman-Gallwey Score ≥ 6)	150	47%
Acne	140	43.7%
Alopecia	100	31.3%
Elevated Total Testosterone (≥ 60 ng/dL)	130	40.6%
Elevated DHEAS (≥ 250 µg/dL)	80	25%

The hormone test results revealed that 43.7% of participants had an abnormal Luteinizing Hormone (LH) to Follicle-Stimulating Hormone (FSH) ratio greater than 2:1, a common indicator of PCOS. Additionally, 40.6% showed low levels of FSH, and 40.6% had elevated total testosterone (≥ 60 ng/dL). Elevated Dehydroepiandrosterone Sulfate (DHEAS) levels (≥ 250 µg/dL) were observed in 25% of participants, and 46.9% had elevated fasting insulin levels (≥ 20 µU/mL), suggesting a significant prevalence of metabolic disturbances and androgen excess in this cohort.

Table 3: Hormonal Assays in Participants

Hormone Test	Abnormal Results	Percentage (%)
Luteinizing Hormone (LH)	140 (LH:FSH ratio > 2:1)	43.7%
Follicle-Stimulating Hormone (FSH)	130 (Low levels)	40.6%
Total Testosterone (≥ 60 ng/dL)	130	40.6%
Dehydroepiandrosterone Sulfate (DHEAS) (≥ 250 µg/dL)	80	25%
Fasting Insulin (≥ 20 µU/mL)	150	46.9%

The diagnostic criteria results show that 75% of the participants were diagnosed with PCOS based on the presence of menstrual irregularities and clinical hyperandrogenism. Among these, 65.6% exhibited irregular menstrual cycles, including oligomenorrhea or amenorrhea, while 59.4% showed signs of clinical hyperandrogenism, such as hirsutism, acne, and alopecia. Additionally, 40.6% of the participants had biochemical hyperandrogenism, indicated by elevated testosterone or DHEAS levels.

Table 4: Diagnostic Classification of PCOS in Participants (Excluding PCOM)

Diagnostic Criterion	Total (n=320)	Percentage (%)
PCOS Diagnosed (Based on Menstrual Irregularities and Hyperandrogenism)	240	75%
Irregular Menstrual Cycles (Oligomenorrhea or Amenorrhea)	210	65.6%
Clinical Hyperandrogenism (Hirsutism, Acne, Alopecia)	190	59.4%
Biochemical Hyperandrogenism (Elevated Testosterone or DHEAS)	130	40.6%

The outcome measures show that 79.2% of participants experienced an improvement in menstrual regularity, with 50% reporting normalized menstrual cycles. In terms of clinical features, 62.5% of participants showed improvement in hirsutism, with a reduction of ≥ 2 points on the Ferriman-Gallwey (F-G) score. Biochemically, 60% of participants demonstrated a reduction in both testosterone and DHEAS levels. Additionally, 55% of participants showed improvement in insulin sensitivity.

Table 5: Folleow-up and Treatment Efficacy (6 Months)

Outcome Measure	Total (n=240)	Percentage (%)
Improvement in Menstrual Regularity	190	79.2%
Normalized Menstrual Cycles	120	50%
Improvement in Hirsutism (Reduction in F-G Score ≥ 2 points)	150	62.5%
Reduction in Testosterone Levels	60%	-
Reduction in DHEAS Levels	60%	-
Improvement in Insulin Sensitivity	55%	-

Irregular menstrual cycles were observed in 83.3% of overweight/obese participants, compared to 42.9% in those with normal BMI, with a p-value of < 0.001. Clinical hyperandrogenism (hirsutism, acne, alopecia) was more prevalent in overweight/obese individuals (77.8%) compared to those with normal BMI (35.7%), with a p-value of < 0.001. Elevated testosterone levels were found in 61.1% of overweight/obese participants, versus 14.3% of those with normal BMI ($p < 0.001$), and elevated DHEAS levels were more common in overweight/obese participants (38.9%) compared to those with normal BMI (7.1%) with a p-value of < 0.001. Finally, insulin resistance, indicated by fasting insulin levels ≥ 20 μU/mL, was found in 66.7% of overweight/obese participants and 21.4% of those with normal BMI, again with a highly significant p-value of < 0.001.

Table 6: Correlation Between BMI and Diagnostic Features of PCOS

Diagnostic Feature	Overweight/Obese (n=180)	Normal BMI (n=140)	Total (n=320)	Percentage (%)	p-value
Irregular Menstrual Cycles (Oligomenorrhea/Amenorrhea)	150 (83.3%)	60 (42.9%)	210	65.6%	< **0.001**
Clinical Hyperandrogenism (Hirsutism, Acne, Alopecia)	140 (77.8%)	50 (35.7%)	190	59.4%	< **0.001**
Elevated Testosterone Levels	110 (61.1%)	20 (14.3%)	130	40.6%	< **0.001**
Elevated DHEAS Levels	70 (38.9%)	10 (7.1%)	80	25%	< **0.001**
Insulin Resistance (Fasting Insulin ≥ 20 µU/mL)	120 (66.7%)	30 (21.4%)	150	46.9%	< **0.001**

Discussion

The findings from this study shed light on the significant impact that variations in diagnostic criteria, particularly the exclusion of Polycystic Ovarian Morphology (PCOM), can have on the diagnosis and treatment of Adolescent Polycystic Ovary Syndrome (PCOS). The findings discussed here regard the association and difference between clinical, hormonal, and metabolic aspects of PCOS and its correlation with BMI and the efficiency of the treatment approach to those aspects. Overweight and obese participants had a statistically significant higher prevalence of irregular cycles, clinical hyperandrogenism, elevated serum levels of testosterone, and insulin resistance compared to normal-weight women [13]. These observations accord with prior research which indicated that obesity aggravates hormonal and metabolic impairments normally associated with PCOS. For instance, insulin resistance which is characteristic of PCOS, is well understood to be likely to occur in women with a higher BMI and this, is likely to accentuate facets of PCOS such as irregular menstruation and high levels of androgens [14]. This exclusion of some factors such as the PCOM may affect the ways that these metabolic features are perceived and addressed. Although the comparatively small study group may be a limitation of this study, it is noteworthy that PCOM status is not mutually exclusive with metabolic disturbances even among women without PCOS. A total of 90 pre- and post-pubertal females with PCOS in our cohort presented clinical features of hyperandrogenism and insulin resistance of weight and obesity, including 43 % of those without PCOM. This underlines the necessity to enhance the current diagnostic approaches that pinpoint more to the morphological parameters than clinical and metabolic ones [15].

The study also revealed that testosterone levels and clinical hyperandrogenism including hirsutism, acne, and alopecia were higher in patients with a higher BMI than in normal-weight patients [16]. This strengthens prior research evidence indicating that high androgen levels in PCOS are not solely due to hyperandrogenic ovaries but that obesity, which predisposes those with PCOS, can boost peripheral androgen conversion. While many of the girls in both groups had normal DHEAS levels, which slightly increased with the progression in weight status, similarly to other studies, the proportion of adolescents with actually elevated DHEAS levels was significantly greater in overweight/obese girls, indicating that obesity affected androgen status in PCOS R but also revealed a broad heterogeneity in DHEAS regulation [17]. These findings indicate the usefulness of clinical and biochemical markers including testosterone and DHEAS in diagnosing PCOS in adolescent girls when PCOM is unrealizable as a diagnostic criterion [18].

For treatment response, the findings informed the collective analysis indicated statistically significant improvement in menstrual cyclicity and insulin sensitivity in all diagnostic subgroups, with more favorable outcomes by individuals with insulin resistance and irregular menstrual cycles. This is in line with metformin and combined oral contraceptives in the Management Guideline; specifically for adolescents with metabolic complications. Metformin, one of the most common drugs used to enhance the impact of insulin, stood out when discussing the improvement of insulin sensitivity that is used

mostly for the long-term management of PCOS and other associated diseases including type 2 diabetes mellitus and cardiovascular diseases [19].

Not surprisingly, the changes in hirsutism and testosterone levels were more significant in patients with clinical hyperandrogenism since medicines like spironolactone and oral contraceptives are useful in PCOS due to their hyperandrogenic effect [20]. A considerable decrease in testosterone levels in this group also supports the importance of individual treatment approaches as a function of dominant clinical symptoms. Although the treatments' effectiveness was high, the investigation pointed out the fact that youth with severe signs needed a longer time to have their symptoms improved, such as hirsutism. This is consistent with the clinical knowledge that the management of hyperandrogenism can probably take a long and that it may take months of treatment [21]. However, the present study has several limitations, which must be stated for the sake of clarity and disclosure. First, several symptoms such as irregularities in menstruation and hirsutism were elicited through self-report questioning hence the possibility of reporting biases. Moreover, the study was cross-sectional, and thus could not track the impacts of treatments that might cumulatively mitigate PCOS symptoms or the changes in the Pathophysiology of PCOS symptoms over time. The subsequent future longitudinal trials with better follow-up and more prolonged period may depict more effective approach to the management and outcomes of adolescents with PCOS based on different diagnostic criteria.

Conclusion

It is concluded that variations in diagnostic criteria for adolescent PCOS, particularly the exclusion of Polycystic Ovarian Morphology (PCOM), do not significantly affect the identification of key clinical and metabolic features such as insulin resistance, hyperandrogenism, and menstrual irregularities. The study emphasizes the importance of a comprehensive diagnostic approach, incorporating both clinical signs and biochemical markers. Effective treatment, especially for menstrual irregularities and insulin resistance, was observed, highlighting the need for personalized management strategies.

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