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Assessing the Prevalence and Diagnosis of Polycystic Ovary Syndrome (PCOS) in Adolescents: A Systematic Review

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Abstract

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder, affecting an estimated 5% to 18% of women of reproductive age and 3% to 11% of adolescents. The diagnostic criteria for PCOS in adults are not entirely suitable for adolescents, as certain features may represent normal physiological changes during puberty. Ongoing research aims to refine these diagnostic criteria for teenagers. PCOS is linked to hormonal and metabolic disturbances and increases the risk of associated conditions, including obesity, metabolic syndrome, hypertension, type 2 diabetes, and non-alcoholic fatty liver disease (NAFLD). This review was conducted following PRISMA guidelines, employing a systematic search of three major databases: PubMed, Google Scholar, and Embase. Given the high prevalence of PCOS and its potential health complications, it is crucial to identify at-risk adolescent girls early, ensure accurate diagnosis, initiate timely treatment, and promote lifestyle modifications. Current research increasingly focuses on adolescent patients with PCOS. This review aims to explore recent findings on the prevalence, pathophysiology, and diagnostic approaches for PCOS in adolescents.

Keywords: Polycystic ovary syndrome, Prevalence, Diagnosis, Adolescent.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder, affecting an estimated 5% to 18% of women of reproductive age, with variations depending on diagnostic criteria and ethnicity [1,2]. Polycystic ovary syndrome (PCOS) is increasingly diagnosed in adolescence, affecting an estimated 3% to 11% of teenagers [3]. In adult patients, polycystic ovary syndrome (PCOS) is diagnosed based on the Rotterdam criteria, requiring at least two of the following: oligoovulation or anovulation, clinical and/or biochemical hyperandrogenism, and polycystic ovaries identified on ultrasonography [4]. However, these criteria are not suitable for diagnosing adolescent girls, as some of these features may be normal physiological changes during puberty [5]. In response, Ibanez *et al.*, [6] proposed PCOS diagnostic guidelines tailored to adolescents, emphasizing irregular menstrual cycles and clinical or biochemical hyperandrogenism as key criteria. Similarly, Pena *et al.*, suggested diagnostic criteria for adolescents, including clinical and/or biochemical hyperandrogenism and irregular menstrual cycles, with the assessment of cycle irregularity based on the time since menarche [7]. Polycystic ovary syndrome (PCOS) is linked to hormonal and metabolic disturbances, increasing the risk of conditions such as obesity, metabolic syndrome, hypertension, type 2 diabetes, and non-alcoholic fatty liver disease (NAFLD) [8-10]. Given the high prevalence of PCOS and its associated health challenges, it is crucial to identify at-risk adolescent girls, ensure accurate diagnosis, initiate appropriate treatment, and promote lifestyle modifications early. Research on PCOS increasingly focuses on teenage patients, with ongoing studies on its prevalence and refinement of diagnostic criteria for this

age group. This systematic review summarized scientific findings on the prevalence and diagnosis of PCOS in adolescents.

Objectives

The main objective of this review was to summarize scientific findings on the prevalence and diagnosis of PCOS in adolescents.

METHODOLOGY & MATERIALS

Study Design: This review was conducted using PRISMA guidelines. The review consisted of 5 steps: (1) problem identification; (2) literature searching; (3) data review and evaluation; (4) data synthesis and analysis; and (5) data presentation.

Search Method: The review aimed to systematically assess on the prevalence and diagnosis of PCOS in adolescents. To achieve this, a comprehensive search was conducted in three major electronic databases: PubMed, Google Scholar, and Embase.

Several studies were initially retrieved by scanning titles and abstracts, and those that met the strict inclusion criteria were selected for review. Only studies published in English were considered, and those who refused to be included were excluded.

Data Collection:

We systematically gathered information by extracting specific data from various studies, following several structured steps to ensure accuracy. First, a comprehensive computerized database search was conducted using targeted search terms relevant to the review's focus on PCOS in adolescents. The initial search yielded data, including author names, titles, keywords, and abstracts. These were reviewed against predefined exclusion criteria. When abstracts lacked sufficient detail, full-text journal articles were retrieved for further examination. The assessment of each study focused on critical elements such as the study design, number of participants, outcomes measured, study duration, and overall quality. After thoroughly evaluating the articles, we abstracted relevant data to compile a detailed overview.

The search resulted in 140 articles which were identified in the initial databases (Figure 1). After duplicates were removed, 95 articles remained. Of these, 55 were excluded based on titles and abstracts screened; 17 full articles were excluded for not meeting inclusion criteria. Finally, 23 publications met the criteria and were included in this review.

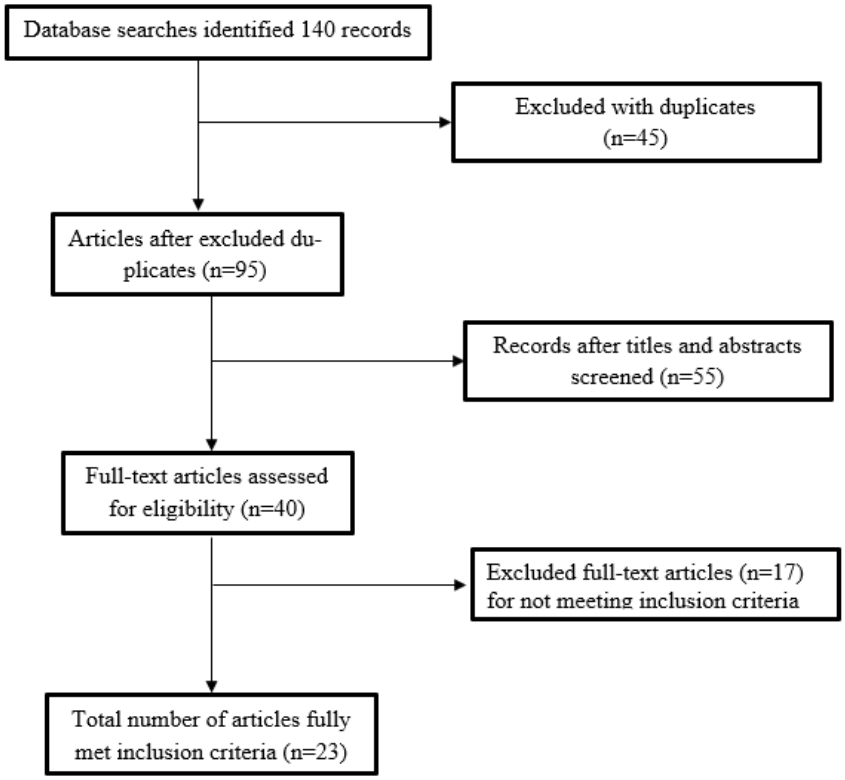

Figure 1: Flow chart of systematic review of literature selection process for the present research

Prevalence and pathophysiology

Polycystic ovary syndrome (PCOS) is a common condition affecting women of childbearing age, with its prevalence influenced by factors such as age, ethnicity, and diagnostic criteria. Increasing evidence suggests that PCOS often begins during adolescence. A population study in Korean women reported an age-adjusted PCOS incidence of 2.8%, with rates rising in the

late teenage years, peaking at age 20, and declining by age 30 [11]. A study among South Indian girls found a 6.8% prevalence of polycystic ovary syndrome (PCOS). Particularly 78.4% of those diagnosed were unaware of their condition, while only 6.8% had received prior treatment. The most common sources of PCOS knowledge were teachers (37%), followed by doctors (31.5%), the Internet (11%), and friends (7.5%). Awareness was significantly higher among young women (84.9%) compared to adolescent girls (4.5%). The primary reason for low awareness was attributed to a lack of information and publicity (63%), highlighting the need for targeted health education and awareness programs for teenagers [12]. A study conducted on patients aged 15–45 at Latifa Hospital, Dubai, UAE, revealed a rise in the annual point prevalence of PCOS from 1.19% in 2020 to 2.72% in 2022. This indicates that the risk of being diagnosed with PCOS in the study population increased 2.28 times in 2022 compared to 2020 [13]. A cross-sectional study conducted in India observed a rise in irregular menstrual cycles among young girls during the second wave of COVID-19. Within the study population, 11% of the girls were diagnosed with polycystic ovary syndrome (PCOS). The study identified insomnia, stress, and depression as significant risk factors contributing to menstrual irregularities. Additionally, it highlighted the crucial role of enhancing the lifestyles of young girls, emphasizing that such improvements have a substantial impact on their reproductive health [14]. A study on Iranian adolescents highlighted that the prevalence of polycystic ovary syndrome (PCOS) varies based on the diagnostic criteria used. The prevalence was reported as 4.2% using the Rotterdam criteria, 3.6% based on the National Institutes of Health (NIH) and Androgen Excess–PCOS Society (AES) criteria, 0.7% with the European Society of Human Reproduction and Embryology (ESHRE)/American Society for Reproductive Medicine (ASRM) (2012) criteria, and according to the Endocrine Society Clinical Practice (2013) [15]. A study among tenth-grade schoolgirls in the Guangzhou area estimated the prevalence of polycystic ovary syndrome (PCOS) at 3.86%. The frequency of PCOS was higher in girls with obesity compared to those of normal weight. Additionally, the incidence of PCOS showed a slight increase with age and gynecological age, though this difference was not statistically significant [16].

The research highlights the importance of prioritizing certain patient groups during the diagnostic process due to their heightened risk of developing polycystic ovary syndrome (PCOS). A cross-sectional study of US children revealed that patients with hidradenitis suppurativa (HS) are three times more likely to develop PCOS. As a result, pediatric patients with HS and hyperandrogenism should be carefully monitored for the presence of PCOS [17]. Daughters of mothers with PCOS often exhibit higher androgen levels during puberty, serving as a critical diagnostic clue for pediatric care providers. These girls should be closely monitored as they transition into adulthood, as they may develop characteristics indicative of PCOS [18]. A meta-analysis by Caiyi Long *et al.,* [19] revealed that women under 25 with type 2 diabetes have a PCOS prevalence of approximately 18%, higher than those without diabetes. Additionally, studies have explored the connection between PCOS and Pilonidal Disease (PD) in adolescents. Findings indicate that adolescent women with PD may exhibit PCOS features, necessitating further diagnostic evaluations if both conditions are suspected. The prevalence of PCOS among PD patients was 26.1% based on the original Rotterdam criteria and 28.7% using the modified criteria, with confidence intervals of 22.0–31.0 and 24.3–33.9, respectively [20].

Despite the high prevalence of PCOS among women of reproductive age, the exact cause of the disease remains unclear. Research is ongoing to better understand its pathophysiology, though it is recognized as having a multifactorial origin. A Mendelian randomization (MR) study highlighted obesity in children and adolescents as a key factor in the development of PCOS in adulthood. Overweight or obese adolescents are more likely to develop PCOS compared to overweight adults. For each standard deviation increase in body mass index (BMI) (4.8 kg/m^2), the likelihood of PCOS increased by 2.76, with childhood weight having an independent effect on PCOS risk, even when accounting for adult body size [21]. Another study examined the impact of childhood abuse on women's reproductive health, particularly focusing on symptoms of polycystic ovary syndrome (PCOS). The findings indicated that emotional abuse, across all forms of maltreatment, was consistently associated with PCOS. This suggests that emotional abuse may have a unique impact on the development of this endocrinopathy, though the underlying reasons remain unclear and require further investigation [22]. The causes of PCOS are also being explored in genetic factors. Variants of the miR-146a (rs2910164) and ADIPOQ (rs182052) alleles have been linked to birthweight in small-for-gestational-age (SGA) individuals, suggesting that these genetic factors may increase the risk of health problems such as PCOS and obesity [23]. The protein encoded by the YAP1 gene plays a crucial role in regulating cell and organism metabolism and contributes to the development of metabolic diseases. In a study by Lidak L *et al.*, [24] the frequency of single nucleotide variants (SNVs) in the YAP1 gene was compared among adolescents with PCOS, those at risk of developing PCOS, and healthy adolescents. The study found no significant associations between PCOS in adolescents and the five tested SNVs in the YAP1 gene [24].

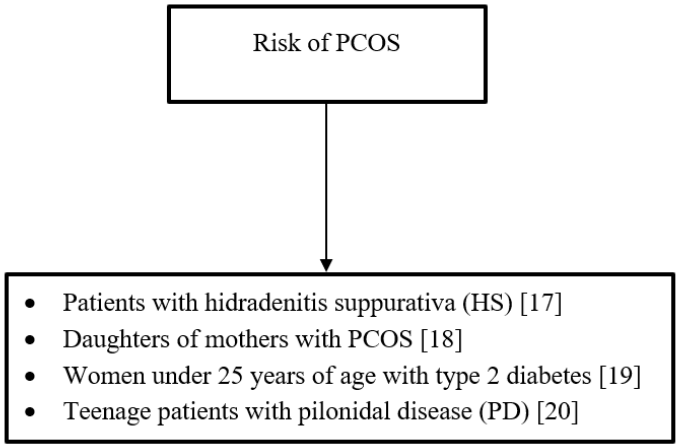

Figure 2: Adolescent at increased risk of polycystic ovary syndrome (PCOS)

Diagnosis of PCOS

The diagnosis of PCOS in adolescent girls remains a controversial and extensively studied subject. There is significant uncertainty about which characteristics can be deemed part of the normal maturation process and which indicate abnormalities. The diagnostic criteria for adults are not fully applicable to this unique group of adolescent patients. Research is ongoing to explore the differences in diagnostic approaches for adults and adolescents, establish appropriate cut-off points for diagnostic parameters, and identify new markers that could aid in diagnosis.

A study was conducted to examine the differences between PCOS in adult and adolescent patients by comparing clinical, hormonal, biochemical, and ultrasound parameters. Interestingly, the findings revealed no statistically significant differences between the two groups. The menstrual cycles of adolescents and adults with PCOS showed no substantial variation. Laboratory analyses indicated that the mean serum LH/FSH (luteinizing hormone/follicle-stimulating hormone) ratio, free testosterone levels, and insulin ratios were significantly elevated in both adults and adolescents with PCOS compared to the control group [25]. Defining the diagnostic boundaries of PCOS in adolescents is crucial for accurate diagnosis. This issue was explored in an article published in the European Journal of Endocrinology. The study, conducted on a large and well-defined cohort of adolescents, found that the cut-off values for the modified Ferriman–Gallwey (mFG) score, free testosterone (free T), free androgen index (FAI), and menstrual cycle length were lower than previously accepted. The normative limits were as follows: mFG score – 1.0 (65th percentile), free T – 23.4 pmol/L (71st percentile), FAI – 3.6 (70th percentile), and menstrual cycle length – 29 days (59th percentile). These findings suggest a need to reassess the diagnostic criteria for the adolescent female population [26]. Anti-Müllerian hormone (AMH) is a well-researched parameter, and studies have consistently shown that AMH levels are significantly higher in adolescents with PCOS compared to controls [27-29]. Based on a meta-analysis, AMH cut-off values for diagnosing PCOS in adolescents have been established, varying between 6.1, 6.26, 7.03, 7.11, 7.2, and 7.25 ng/mL, with diagnostic accuracy showing 81% specificity and 66.3% sensitivity. The study concluded that an AMH level test with a cut-off point between 6 and 7 ng/mL can be effectively used as a diagnostic tool for PCOS in adolescents [27]. Another study investigated AMH levels in adolescent patients with irregular menstrual cycles and found that the highest concentrations of AMH were present in girls who had a combination of oligomenorrhea, hirsutism, and polycystic ovarian morphology (PCOM). The study revealed that AMH levels increased significantly as the clinical symptoms of PCOS, particularly oligomenorrhea, became more pronounced in adolescent girls [28]. A long-term longitudinal study published in *eClinicalMedicine* demonstrated that girls with high serum AMH concentrations (AMH > 30.0 pmol/L or 13.35 ng/mL) in mid-childhood (around 7.2 years old) showed significantly higher levels of LH, LH/FSH ratio, testosterone, a greater total number of follicles, and more frequent irregular cycles during adolescence. The study suggests that AMH levels in early life could potentially serve as a useful clinical tool for predicting future ovarian activity. However, further research is required to determine if AMH levels in childhood can be a predictor of PCOS in adulthood [30]. Recent studies have increasingly focused on examining androgen levels in PCOS patients. One study found that adolescent girls with PCOS had higher serum levels of 11-hydroxyandrostenedione (11-OHA4) and 11-hydroxytestosterone (11-OHT) compared to control groups without PCOS. Additionally, 11-oxyandrogens were found to correlate with the severity of hirsutism in untreated PCOS patients, though they did not correlate with markers of dysmetabolism. However, testosterone was a better predictor of PCOS status than 11-oxyandrogens. According to the ROC curve analysis, 11-oxyandrogens lack significant clinical utility in aiding the diagnosis of PCOS [31]. Another study on adolescent patients with oligomenorrhea revealed that

androstenedione (A4) levels were higher in adolescents with oligomenorrhea compared to those with regular menstrual cycles. Additionally, these levels were found to be elevated in the presence of hirsutism [28]. Current guidelines suggest that ultrasonography is not a primary diagnostic tool for PCOS in adolescents. However, its potential use in this group is still under investigation. Studies have shown that the presence of polycystic ovarian morphology (PCOM) significantly increases the likelihood of infrequent menstruation, with a tenfold higher probability in affected patients [28]. A comparative study of ultrasound parameters revealed significantly higher mean ovarian volume and mean follicle count, along with increased stromal echogenicity, in both adult and adolescent PCOS patients. Additionally, ovarian morphology in both groups showed a positive correlation with serum LH levels and free testosterone [25]. The endometrial stripe (EMS) thickness was examined in teenage patients, revealing that the EMS was thinner in the PCOS group compared to the control group. However, within the PCOS group, no significant differences in EMS thickness were observed when analyzing intermenstrual intervals, insulin resistance, or other biochemical factors [32].

PCOS patients can be categorized into groups based on their phenotype. Among adolescents, phenotype D (menstrual irregularities [MI] + polycystic ovarian morphology [PCOM] - hyperandrogenism clinical and/or biochemical [HA(C/B)]) was found to be the most common, affecting 49.43% of patients. This was followed by phenotype A (MI + HA + PCOM; 22.72%) and phenotype B (MI + HA - PCOM; 14.20%). The analysis revealed that hyperandrogenism in adolescents (phenotypes A and B) is linked to a more disrupted endocrine and metabolic profile compared to non-androgenic PCOS (phenotype D). This highlights the importance of early treatment, close monitoring, and lifestyle modifications for these patients to prevent the long-term consequences of PCOS [33]. A study by Kalra S *et al.,* [34] highlighted the importance of early diagnosis and appropriate referral for PCOS to enhance reproductive, metabolic, and overall health in adolescents and young adults. To support this goal, a simple screening questionnaire was developed. The tool is structured into three domains: Menstrual/Maternal, Metabolic, and 'Misfit Masculinity' (dermatological), each containing three potential symptoms. According to the study, an affirmative response in any two of the three domains should prompt PCOS screening and referral to specialist care. This questionnaire could be implemented in primary care settings to streamline the identification of patients who may require further diagnostic evaluation for PCOS [34].

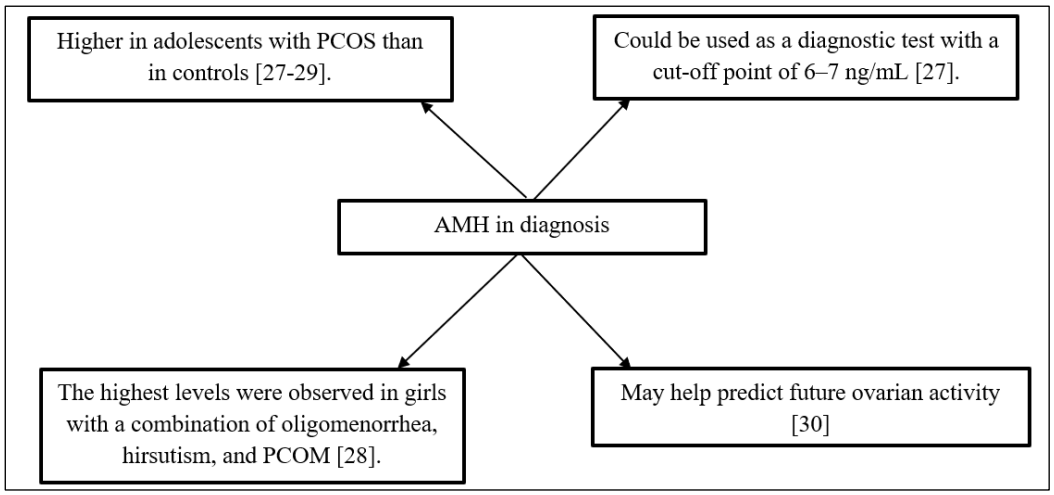

Figure 3: Anti-Mullerian hormone (AMH) in the diagnosis of adolescents; PCOS — polycystic ovary syndrome; PCOM — polycystic ovarian morphology

LIMITATIONS

There are several limitations to our current review. The studies included in this review utilized varying diagnostic criteria for PCOS, making it challenging to standardize findings and draw consistent conclusions, especially for adolescents. Most studies included in the review were cross-sectional, limiting the ability to assess long-term outcomes and the progression of PCOS from adolescence into adulthood. Additionally, this review included only studies published in English were included, potentially excluding relevant research conducted in other languages.

CONCLUSION

Polycystic ovary syndrome (PCOS) is an increasingly common condition among adolescent girls and young women globally, profoundly impacting mental health, reproductive health, and overall quality of life. The condition is associated with numerous complications that necessitate a multidisciplinary approach to care. Early diagnosis during adolescence is crucial to initiate treatment, mitigate the metabolic consequences of PCOS, and prevent long-term complications in adulthood.

The etiology of PCOS remains unclear but is recognized as complex and multifactorial, involving genetic, environmental, and lifestyle factors. Research indicates that the development of PCOS may begin even before birth, emphasizing the importance of identifying predisposing factors. However, further investigation is needed to fully understand the underlying causes of PCOS.

Significant debate continues regarding the appropriate diagnostic criteria for PCOS in adolescents. Establishing precise diagnostic thresholds and refining diagnostic parameters through research can enhance diagnostic accuracy. Detailed studies of large cohorts of adolescent PCOS patients and comprehensive data analysis are critical to addressing unresolved questions about the syndrome's prevalence and characteristics in this age group.

The prevalence and diagnosis of PCOS in adolescents present challenges for healthcare providers and researchers alike. Resolving these challenges requires a concerted effort to improve understanding, develop effective diagnostic tools, and implement strategies that enhance patient care and outcomes.

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