Scientific Research Publishing

Open Journal of Obstetrics and Gynecology, 2025, 15(12), 1998-2019
https://www.scirp.org/journal/ojog
ISSN Online: 2160-8806
ISSN Print: 2160-8792

Challenges in the Diagnosis and Treatment of Polycystic Ovary Syndrome (PCOS) in Adolescents: A Narrative Review

Sandrine Modia Putshu[1*], Jean-Didier Bosenge-Nguma[2], Antoine Modia O'yandjo[2], Arsène Mputu Lobo[1], Justin Mboloko Esimo[1]

[1]Faculty of Medicine, Department of Obstetrics and Gynecology, University of Kinshasa, Kinshasa, Democratic Republic of Congo
[2]Faculty of Medicine and Pharmacy, Department of Obstetrics and Gynecology, University of Kisangani, Kisangani, Democratic Republic of Congo
Email: sandrinemodia@yahoo.fr

How to cite this paper: Putshu, S.M., Bosenge-Nguma, J.-D., O'yandjo, A.M., Lobo, A.M. and Esimo, J.M. (2025) Challenges in the Diagnosis and Treatment of Polycystic Ovary Syndrome (PCOS) in Adolescents: A Narrative Review. *Open Journal of Obstetrics and Gynecology*, **15**, 1998-2019.
https://doi.org/10.4236/ojog.2025.1512168

Received: November 6, 2025
Accepted: December 9, 2025
Published: December 12, 2025

Copyright © 2025 by author(s) and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/
Open Access

Abstract

Polycystic ovary syndrome (PCOS) is the most prevalent endocrine disorder in women of childbearing age, typified by hyperandrogenism and oligo- or anovulation. The diagnostic criteria for PCOS are well established for adult women. In adolescents, the clinical manifestations of PCOS are generally regarded as normal, attributable to the physiological changes associated with puberty. Patients diagnosed with PCOS are often concomitantly affected by other medical conditions, including obesity, insulin resistance, hypertension, metabolic syndrome, and an elevated risk of developing diabetes. Given the profound implications of metabolic impairment in PCOS, it is imperative to make an accurate diagnosis and manage these aspects. However, there is currently no international consensus on the diagnosis and management of PCOS in adolescents. A comprehensive review of the extant literature on the subject is imperative to inform the development of the recommendations. This objective constitutes the underlying rationale for the present literature review.

Keywords

Polycystic Ovary Syndrome, Adolescent, Anovulation, Hyperandrogenic

1. Introduction

Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder in women of reproductive age, with initial symptoms manifesting as early as adolescence. The prevalence of PCOS in the United States has been reported to range from 10% to 15%, depending on the diagnostic criteria employed [1] [2]. This range indicates

that PCOS is a significant public health concern in the United States. PCOS is the most commonly reported cause of dysovulation, infertility, and hyperandrogenism (HA). It has been identified as the primary etiological agent of hyperandrogenism in adolescents, affecting 6 to 18% of this demographic on a global scale [3]-[5]. The disease manifests signs and symptoms that are subject to variation, and it frequently gives rise to complications. Consequently, it is probable that a healthcare professional from a variety of disciplines will encounter it. These professionals may include, but are not limited to, gynecologists, endocrinologists, cardiologists, dermatologists, psychiatrists, and general practitioners [6].

From puberty to adulthood, the natural progression of the disease leads to metabolic, endocrine, reproductive, obstetric, tumor, and psychiatric complications [3] [7] [8]. These complications are likely to have more severe consequences in sub-Saharan Africa due to women's lack of awareness of this disease and limited access to appropriate resources for the treatment and monitoring of PCOS [2]. However, PCOS remains under-recognized by the general public. A significant proportion of women experience symptoms for extended periods without identifying the underlying cause. On average, it takes seven years of medical uncertainty before a diagnosis is made [9]. It has been established that PCOS can manifest during puberty, thereby offering a timely opportunity for diagnosis and intervention to influence the prognosis of the condition [10] [11].

The diagnosis of PCOS remains challenging in adolescents compared to adult women. The manifestations of this condition can be erroneously interpreted as a hallmark of typical pubertal development, potentially resulting in overdiagnosis or underdiagnosis. This phenomenon is particularly disconcerting, as these young girls seldom seek medical consultation for menstrual disorders or indications of hyperandrogenism, such as acne, which are often perceived as "normal" during puberty [12]-[14]. Additionally, a paucity of consensus exists regarding the definition of PCOS in adolescents, a circumstance that complicates the diagnostic process. According to the current body of knowledge, PCOS is considered incurable [9] [15]. However, there are treatment options for adolescents with PCOS or those at risk of developing it, which can help improve their quality of life and prevent long-term consequences on reproduction, cardiac metabolism, and mental health [16]. However, the efficacy of these interventions is contingent upon the accuracy of the diagnosis and the expeditious initiation of treatment. However, it is imperative to acknowledge that excessive diagnosis can also exert deleterious effects, adversely impacting the quality of life of young girls and engendering unjustified anxiety, particularly with regard to their future fertility.

In countries with limited resources, research on PCOS in adolescents remains less developed than that conducted in adults [16]. In the Democratic Republic of Congo, research by Mboloko *et al*. [17], Mbuyamba *et al*. [18], and Amisi *et al*. [19] has explored various aspects of PCOS in adult women. The present study has focused on the development of diagnostic criteria, the establishment of clinical profiles, and the identification of treatment options for this demographic. How-

ever, it is important to acknowledge that these studies did not specifically address PCOS in adolescents, resulting in a notable lacuna in the local scientific literature.

In the absence of an international consensus on the diagnosis and management of PCOS in adolescents, it is imperative to provide a comprehensive summary of the available recommendations in the literature. The objective of this literature review is to explore the implications of these findings. This comprehensive study will serve as a foundational framework for the diagnosis of PCOS in adolescents and will facilitate the development of subsequent studies aimed at determining the prevalence of PCOS in this demographic, as well as the regional characteristics of the condition. The present literature review commenced with an examination of the various diagnostic criteria and therapeutic approaches for PCOS in adult women, followed by a detailed discussion of the distinctive characteristics of adolescents.

2. Methods

A comprehensive literature search was conducted to identify articles that offered informative insights regarding diagnostic and therapeutic recommendations for PCOS in adults and adolescents. A series of studies were selected over the course of the summer months, from July to December of 2024, according to a rigorous set of criteria. The objective of this selection process was to establish a comprehensive summary of the subject. The studies utilized were derived from several recognized scientific databases, including Cochrane Library, PubMed, and UpToDate. The following keywords were utilized in the construction of the search equations: The following terms are to be defined: "polycystic ovary syndrome" (PCOS), "micro-polycystic ovary syndrome," "adolescent," and "adolescence."

These search terms enabled us to identify relevant publications concerning the diagnosis and management of PCOS in adults and adolescents. Furthermore, the bibliographic references of the various studies extracted from the search equations were reviewed manually to identify other publications that could enrich this review. This methodological approach guaranteed the comprehensiveness and relevance of the data that was subsequently analyzed. The present article was written in accordance with the recommendations of Saracci *et al*. [20] on writing narrative literature reviews, and the quality of the article was pre-evaluated using the SANRA scale [21].

3. Results

3.1. Diagnostic Overview of Polycystic Ovary Syndrome in Adults

The condition, known as PCOS, was first described in 1935 by Stein and Leventhal, who noted the presence of enlarged ovaries in obese, hirsute women with cycle disorders [22]. Since that time, PCOS has been found to be a complex condition with contingent etiopathogenesis and heterogeneous clinical signs. The diagnosis has evolved over time, and its development is subject to controversy [23]-[26]. These controversies are exemplified by the historical underrepresentation of

PCOS in adolescent girls in France, where it was considered rare or exceptional, in contrast to its predominance as the primary cause of peri-pubertal hyperandrogenism in Anglo-Saxon countries. This paradox underscores the existing uncertainties surrounding the boundaries of the syndrome.

In clinical practice, the diagnosis of PCOS in adult women is made using clinical and paraclinical criteria, as defined by the consensus of multiple learned societies. The three criteria that are generally taken into account are as follows: chronic oligo-anovulation (OA), clinical and/or biological hyperandrogenism (HA), and the presence of polycystic ovaries on ultrasound (PCOS) [26]. The following text is intended to provide a comprehensive overview of the subject matter.

Clinically, the condition known as oligo-anovulation is suspected in patients with irregular menstrual cycles. In the field of gynecology, menstrual cycles are classified as irregular if they occur less than 21 days or more than 35 days apart, or if there are fewer than eight cycles per year. This classification is particularly relevant for women who are more than three years past their gynecological age. Menstrual irregularities are regarded as physiological in the year following menarche. In the three-year period following menarche, cycle disorders are characterized by cycles that are either shorter than 21 days or longer than 45 days, or that occur with a frequency of fewer than four cycles per year.

Hyperandrogenism manifests clinically through acne and hirsutism. Alopecia is an uncommon manifestation of hyperandrogenism. Other clinical signs of hyperandrogenism include seborrhea, hyperhidrosis, and hidradenitis suppurativa [9]. In PCOS, acne is severe, often has an early onset, and affects at least two areas of the body. It manifests as microcysts, comedones, and papules or pustules. It is persistent, male-pattern (chin, neck, chest) with increased facial hair, and responds poorly to local treatments [27]. Hirsutism is abnormal hair growth due to its androgen-dependent location in women [28]. It is clinically defined by the modified Ferriman-Gallway score, which assesses hair growth in women in areas that are normally hairless (upper lip, face, chin, back, chest, linea alba, inguinal folds, inner and back of the thighs). However, the use of the Ferriman-Gallway score remains controversial for dark or olive skin tones [29].

The diagnosis of biological hyperandrogenism is confirmed by an increase in total and/or free testosterone [30]. In the context of PCOS, the absence of hyperandrogenism detection through blood tests has been documented in 20 to 60% of cases [31]. In instances where testosterone or free testosterone levels are not elevated, the consideration of additional testing for androstenedione and dehydroepiandrosterone sulfate (DHEAS) may be contemplated, taking into account the lower specificity of these assessments and the natural decline in DHEAS levels associated with aging [26]. The measurement of 17-hydroxyprogesterone (17-OHP) is primarily utilized to exclude alternative etiologies of hyperandrogenism [16].

The ultrasound criteria for PCOS have evolved in tandem with advancements in ultrasound machines and endovaginal probes. The confirmation of PCOS is

contingent upon the presence of at least 20 follicles per ovary in at least one ovary, utilizing an endovaginal probe operating at a frequency exceeding 8 MHz. In optimal conditions, the utilization of Sonography-based Automated Volume Count (SonoAVC) [32] is strongly advised. The number of follicles per ovarian cross-section (Follicle Number Per Cross-Section, FNPS) thus offers a practical and reliable alternative for refining the evaluation of ultrasound criteria in the diagnosis of PCOS [26].

This approach enables a more precise analysis of ovarian morphology, particularly in cases where technical constraints or operator proficiency impede comprehensive visualization of the ovaries. In order to diagnose OPK, the presence of at least 10 follicles per ovarian slice, in at least one ovary, is necessary. The following text is intended to provide a comprehensive overview of the subject matter. In instances where a less powerful ultrasound scanner is employed, the presence of an ovarian volume exceeding 10 milliliters or the measurement of an ovarian surface area along its longest axis can facilitate the ultrasound diagnosis of OPK. With regard to the peripheral distribution of follicles and ovarian density, these have been excluded from the consensus definition because they are non-discriminatory and do not allow for a reliable diagnosis [33].

The initial step in diagnosing PCOS is to exclude other conditions that may present with comparable clinical, biological, and ultrasound manifestations. These include congenital adrenal hyperplasia, nonclassical 21-hydroxylase deficiency, thyroid disorders, Cushing's syndrome, hyperprolactinemia, and androgen-secreting tumors. It is imperative to consider the potential effects of medications that may mimic the symptoms of PCOS, including synthetic progestogens, anabolic steroids, and valproic acid (Depakine®), an anticonvulsant medication that is well-known for its hormonal implications [26].

Another factor that is not listed in the diagnostic criteria but is common in PCOS is insulin resistance [6] [34]-[36]. Insulin resistance and hyperinsulinism are two conditions found in at least 50% of PCOS cases [35].

Hyperinsulinism has been demonstrated to induce the activation of steroidogenesis in small follicles, resulting in elevated levels of ovarian androgens. Insulin has been demonstrated to impede SHBG, augment the bioavailability of testosterone in the circulation, and exacerbate the clinical manifestations of HA [35] [36]. When evaluating PCOS, the issue of insulin resistance is paramount, as it is often implicated in the pathophysiology of the syndrome. Among the tools available for assessing insulin resistance, the HOMA (Homeostasis Model Assessment) index appears to be the most widely used in clinical and epidemiological studies [19]. The HOMA index, a calculation derived from fasting blood glucose and insulin levels, offers a straightforward and cost-effective approach to estimating pancreatic function and insulin sensitivity. This approach is particularly valuable in the early identification of insulin resistance in adolescent girls with PCOS, even in the absence of overt clinical signs such as obesity [37].

Waist circumference measurement, in conjunction with the waist-to-height ra-

tio, serves as a crucial predictor of insulin resistance and metabolic risk. Waist circumference greater than 80 centimeters, or a waist-to-height ratio equal to or greater than 0.52, has been demonstrated to correlate well with an increased risk of insulin resistance and cardiometabolic complications. Moreover, it is imperative to assess glucose tolerance, commencing with a fasting blood glucose measurement, particularly in adolescents with a body mass index (BMI) greater than 25 kg/m^2. In the event of abnormalities or additional risk factors, an oral glucose tolerance test (OGTT) should be performed to detect possible glucose intolerance or type 2 diabetes [38].

In light of the considerable phenotypic variability observed among individuals diagnosed with PCOS, multiple criteria have been established by prominent scientific societies to streamline the diagnostic process. The inaugural expert conference on PCOS took place in 1990, under the auspices of the National Institutes of Health (NIH). By consensus, the association of HA with OA in the diagnosis of PCOS was retained, with no reference to OPK [11]. Subsequently, the Rotterdam criteria, established by the European Society of Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM 2003), included, in addition to the two aforementioned criteria, the presence of OPK on ultrasound examination. However, it was specified that the presence of two of the three criteria was sufficient to make the diagnosis, thus leaving open the possibility of diagnosing PCOS without HA [32]. In 2006, at a conference organized by the Androgen Excess Society and PCOS Society (AE-PCOS), experts convened to re-evaluate the conclusions reached in 2003. They concluded that HA was a prerequisite for diagnosing PCOS. The second criterion remained either OPK and/or OA [39]. The following text is intended to provide a comprehensive overview of the subject matter.

In 2012, the National Institutes of Health (NIH) convened a meeting to deliberate the merits and drawbacks of the prevailing diagnostic criteria, which were grounded in the principles of evidence-based medicine [40]. Two major recommendations were formulated as a result of this conference. The initial proposal pertained to a modification in the nomenclature of the syndrome. It was proposed that the nomenclature should incorporate terms reflecting the complexity of its pathophysiology and related complications. Among the various proposals put forth was the concept of "reproductive metabolic syndrome." Despite the fact that this designation suggested impaired reproductive and metabolic health, thereby alluding to the pathophysiology and clinical manifestation of PCOS, it was not adopted.

The second recommendation validated the utilization of the Rotterdam criteria for diagnosis, encompassing the 1990 NIH conference diagnosis and the 2006 AE-PCOS diagnosis, while also providing a comprehensive description of the four PCOS phenotypes, including one devoid of AH [26] [40]. The reemergence of PCOS in the absence of HA was substantiated by the inadequacy of clinical and biological assessment methodologies, which could result in false negatives [40].

The diagnostic criteria for PCOS, as established by consensus conferences and delineated according to the four established phenotypes of the syndrome, are delineated in Tables 1 and 2, respectively.

Table 1. Diagnostic criteria for PCOS according to consensus conferences. [16] [26] [41]

Conference	National Institutes of Health (NIH) 1990	Rotterdam (2003)	AE-PCOS Society 2006	NIH 2012/International PCOS Guidelines 2018
Criteria	Hyperandrogenism Oligo anovulation Both criteria are required.	Hyperandrogenism Oligo anovulation Polycystic ovaries 2 of the 3 criteria are required	Hyperandrogenism Oligo anovulation Both criteria are required.	Hyperandrogenism Oligo anovulation Polycystic ovaries 2 of the 3 criteria are required
Innovation	First criteria developed	Addition of ultrasound criteria	Excludes PCOS without hyperandrogenism	Identification of phenotypes

Table 2. PCOS phenotypes. (NIH 2012/International PCOS Guidelines 2018)

PCOS phenotypes	Diagnostic criteria in adults (Rotterdam)
Phenotype A **Classic PCOS**	Hyperandrogenism Oligo anovulation Polycystic ovaries
Phenotype B **(According to NIH 1990 criteria)**	Hyperandrogenism Oligo anovulation
Phenotype C **Ovulatory PCOS**	Hyperandrogenism Polycystic ovaries
Phenotype D **PCOS without hyperandrogenism**	Oligo anovulation Polycystic ovaries

PCOS = polycystic ovaries syndrome

In 2023, the International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome (IGAM-PCOS) proposed the most recent expert opinions and guidelines for PCOS [26]. A simplified three-step approach was described for diagnosing PCOS. The initial step in this process is to ascertain the regularity or irregularity of the cycles. In the event of irregular cycles, a clinical examination is indicated to ascertain the presence of AH. The presence of clinical AH is indicative of PCOS, provided that other conditions have been excluded [42]. In the absence of clinical hypothyroidism (HA), investigation of biological hypothyroidism (HA) is recommended, and if present, PCOS can be considered a likely diagnosis after ruling out other conditions. In instances where cycles are irregular in the absence of clinical and biological HA, an endovaginal ultrasound should be performed in sexually active women. In the case of sexually inactive adolescents, it is necessary to wait and reassess at a later date. However, it is imperative to consider these patients as potentially being at risk of PCOS until an ultrasound scan can be performed under optimal conditions [13] [16]. The Rotterdam criteria continue to be valid, albeit with some modifications to their

validation process [15]. Since 2023, the IGAM-PCOS has authorized the measurement of AMH as a diagnostic marker for PCOS in adults only, with the same value as the follicular count on ultrasound [26].

In instances of anovulation and hyperandrogenism, ultrasound and AMH testing are not necessary for diagnosis. Moreover, it is recommended that AMH testing and ultrasound imaging not be used concurrently to avoid overdiagnosis [26].

3.2. Polycystic Ovary Syndrome in Adolescents

3.2.1. Diagnosis of PCOS in Adolescents

The absence of a consensus on the definition of PCOS in adolescents hinders the establishment of diagnostic criteria and, consequently, the development of effective treatment strategies [22]. The diagnostic criteria employed for adult women may be subject to misinterpretation in adolescents due to transient physiological phenomena associated with their biological transition [23] [25]. Hyperandrogenism, cycle disorders, polycystic ovaries, insulin resistance, and weight gain are all common conditions associated with PCOS that are present in adolescence. However, these abnormalities, which are considered temporary, persist in some adolescents and develop into full-blown PCOS.

HA, which is one of the signs of PCOS, is found in 3% - 20% of adolescents [43]. It is possible that this HA is the result of the immaturity of the hypothalamic-pituitary-ovarian axis during adolescence (HHO) [26]. Hirsutism and moderate to severe acne are the most common skin signs of PCOS. They have a negative impact on the self-esteem and social life of adolescents at a time when physical appearance is of paramount importance for their integration into society. Acne is a physiological manifestation of puberty. It is linked to the relative physiological HA of this period. This functional HA is the result of a hormonal imbalance in favor of androgens.

During adrenarche, which occurs between the ages of 8 and 10 in girls, there is a tripling of adrenal androgen concentration. The increase in ovarian androgens contributes to the increase in circulating androgens. Conversely, the absence of estrogen and progesterone during the initial cycles, which frequently manifest as anovulatory, exacerbates this HA. However, this imbalance is counterbalanced as the hypothalamic-pituitary-ovarian axis attains maturity [26]. However, the clinical presentation of acne is pathological when it occurs before puberty or in the form of moderate to severe acne with comedones at the onset of puberty, or moderate to severe inflammatory acne during perimenarche. Alopecia, which is also a manifestation of hyperandrogenism, has not yet been studied in adolescent girls with PCOS [31].

In the majority of adolescent girls, androgen levels attain adult levels around the time of menarche, which occurs between the ages of 12 and 15. The upper limit of androgen levels in this age group is 0.5 ng/mL (1.7 nmol/L). It is important to acknowledge that the use of estrogen-progestogen pills, an increase in the free fraction of testosterone, and a decrease in sex hormone-binding globulin (SHBG) are all confounding factors. With regard to oligomenorrhea in adolescents, it is

considered physiological in the year following menarche. This phenomenon can be attributed to the immaturity of the hypothalamic-pituitary-ovarian axis, the hormonal regulation of which is a gradual process that precedes the establishment of regular ovulatory cycles [34]-[36]. However, it would be a mistake to consider all cycle irregularities as normal in adolescents. In the three-year period following menarche, cycle disorders are characterized by cycles that are either less than 21 days or more than 45 days in duration, or that occur with a frequency of fewer than four cycles per year. Indeed, the persistence of spaniomenorrhea for a period exceeding one year or more than two years following menarche, or primary amenorrhea after the age of 15 or 16, *i.e.*, three years after the onset of breast development, has been identified as a contributing factor to ovarian dysfunction, glucose regulation disorders, and PCOS [37] [44]. This should prompt diagnostic steps to determine the underlying cause.

With regard to the well-described ultrasound criteria for PCOS in adults, it is not recommended until after eight years of gynecological age in adolescents. Indeed, the ultrasound diagnosis of PCOS involving the use of a vaginal probe is not possible in sexually inactive adolescents. The suprapubic approach, however, poses challenges in the estimation of ovarian follicles due to its inherent low spatial resolution [25]. The micro-polycystic ultrasound appearance of the ovaries manifests with a high incidence during adolescence. Furthermore, an increase in gonadotropin physiological hyperstimulation results in increased volume and size of the ovaries, which are proportionally larger than in adults and thus become an additional confounding factor [39] [40]. However, the use of ultrasound can help rule out underlying uterine or ovarian pathologies [45]. In contrast to adults, AMH testing is not recommended for adolescents.

In adolescent girls diagnosed with metabolic syndrome, insulin resistance is frequently observed and results from compensatory hyperinsulinism. The latter results in a decrease of approximately 50% in insulin sensitivity, leading to increased insulin production to maintain glycemic homeostasis. However, this hyperinsulinemia appears to be transient and may normalize in adulthood, suggesting that hormonal changes associated with puberty influence the regulation of insulin sensitivity [25] [42]. Excess insulin potentiates stimulation of the hypothalamic-pituitary-ovarian axis, leading to increased androgen production by theca cells. This, in turn, disrupts follicular maturation and promotes the clinical signs of PCOS. Increased AMH levels are indicative of a high follicular reserve, which is associated with excessive recruitment of follicles without adequate maturation.

It has been demonstrated that certain anamnestic factors have the potential to serve as a catalyst for the diagnosis of PCOS in adolescence. These factors may include a family history of PCOS and/or metabolic diseases. Leibel *et al.* reported that the majority of adolescent girls with PCOS either have a mother with PCOS or a father with metabolic syndrome [46]. The diagnosis may also be considered in adolescents born with intrauterine growth retardation or macrosomia, as well as those who have experienced early onset of pubic and axillary hair growth [47].

However, the age at menarche appears to be later in thin adolescents with PCOS (body mass index [BMI] < 25 kg/m^2).

In adolescents, a diagnosis of PCOS is made on the basis of persistent clinical, biological, and ultrasound abnormalities, taking into account the physiological characteristics of this period of life. When these abnormalities persist for more than two years after menarche, a diagnosis of PCOS can be confirmed in the adolescent, while remaining vigilant about differential diagnoses and physiological variations in puberty.

The Paediatric Endocrine Society, ESHRE, the American Society for Reproductive Medicine (ASRM), and the Australian National Health Medical Research Council (NHMRC) have concluded that PCOS should be suspected in adolescents with irregular menstrual cycles associated with hyperandrogenism. However, in adolescents, the presence of regular cycles does not preclude the development of the condition. In such cases, the implementation of progesterone testing can facilitate the discernment of anovulation [47]. Additionally, as is the case for adult women, PCOS in adolescents remains a diagnosis of exclusion, and therefore, other differential diagnoses must be ruled out. Current recommendations advocate for the identification and management of the signs of PCOS in adolescents, even in the presence of a single presumptive symptom [24] [25]. The identification of adolescents at risk of PCOS will facilitate the preservation of their fertility and the prevention of the metabolic, cardiovascular, oncological, and psychiatric complications associated with this syndrome.

3.2.2. Strategies for Managing PCOS in Adolescents

In the case of adolescent females exhibiting clinical indications of PCOS, the necessity for symptomatic treatment is paramount. For those whose diagnosis is confirmed, the initial management consists of informing and educating the patient and her guardians about the disease, its risks, and its complications to ensure better compliance with treatment. Healthcare providers are obliged to ensure that explanations are clear and comprehensive, taking into account the patient's social and cultural background. Addressing concerns regarding future fertility is imperative to ensure patient and family reassurance regarding a matter that is particularly sensitive in sub-Saharan culture.

In light of the current paucity of high-quality data, the optimal treatment protocols for PCOS must be customized to align with the clinical presentation, needs, and preferences of each patient, while also considering the potential adverse effects. Indeed, the management of PCOS comprises two components. A symptomatic component is defined as the treatment of the signs of the condition with the objective of enhancing patients' quality of life. A prophylactic component, on the other hand, is intended to reduce the incidence of complications.

A holistic therapeutic approach encompasses lifestyle and dietary measures, pharmacological interventions, and surgical procedures, particularly in cases of infertility. Surgical interventions are not addressed in this literature review, as they are of minimal relevance to adolescents. The management of comorbidities and

regular follow-up of patients are integral components of the care of adolescents with PCOS.

a) Dietary and hygiene measures

The health and dietary aspect of treatment involves implementing dietary measures and promoting regular physical activity [48], while introducing lifestyle changes that will slow down or prevent the onset of complications. This is the first therapeutic option to be applied in overweight or obese adolescents [49]. For slender adolescents, health and dietary measures should promote a healthy lifestyle and prevent excessive weight gain.

In numerous countries within the sub-Saharan region of Africa, the prevalence of obesity among women does not invariably result in adverse consequences for their mental well-being. In some instances, obesity is even regarded as an aesthetic criterion of physical attractiveness. It is therefore imperative to elucidate to patients and their guardians the benefits of weight loss and physical exercise. A 5% weight reduction has been demonstrated to regulate menstrual cycle disorders, reduce hyperandrogenism and insulin resistance, and limit cardiovascular risks [48]. To date, no study has demonstrated the superiority of one diet over another or of one form of physical exercise over another. However, extant studies have reported high relapse rates and suboptimal treatment compliance [49] [50]. The following text is intended to provide a comprehensive overview of the subject matter.

Finally, various dietary supplements may be recommended, including those containing vitamin D and L-carnitine, as well as probiotics.

b) Pharmacological treatment.

The pharmacological treatment of PCOS in adolescents encompasses the use of estrogen-progestogen combinations, metformin, antiandrogens, and cosmetic interventions for acne and hirsutism. In the contemporary scientific literature, there is an increasing prevalence of reports concerning novel molecules that demonstrate variable efficacy in the metabolic management of PCOS. These include inositols, N-acetylcysteine, dipeptidyl peptidase-IV (DPP-IV) inhibitors, sodium-glucose cotransporter-2 (SGLT-2) inhibitors, and glucagon-like peptide-1 (GLP-1) agonists.

Estrogen-progestins pills: In the medical management of cycle disorders in adolescents, estrogen-progestogen therapy is considered the standard of care. Beyond the regulation of menstrual cycles, these medications have been demonstrated to impede abnormal functional bleeding associated with anovulation and to ameliorate the clinical manifestations of hyperandrogenism. A notable advantage of these medications is their capacity to serve as a contraceptive method for sexually active adolescents. This attribute justifies their prescription as a primary treatment option for this demographic [51]. Furthermore, estrogen-progestogen combinations have been observed to elevate serum SHBG levels, thereby reducing excess androgens [52].

The combination of cyproterone acetate and ethinyl estradiol has also been

demonstrated to reduce the skin symptoms associated with HA. The primary limitation of estrogen-progestogen therapy pertains to the potential risks of vascular and thromboembolic complications associated with its use. Estrogen-progestogen combinations containing third-generation progestogens (gestodene, desogestrel, or norgestimate) combined with ethinyl estradiol are preferred because they exhibit low androgenicity and present a minimal thrombogenic risk. In instances where estrogen-progestogen contraceptives are contraindicated, progestogen-only pills may be prescribed, given their low systemic side effects and very high contraceptive efficacy. However, these hormones do not increase serum SHBG levels and may cause weight gain [48] [53].

In adolescent girls who do not require contraception and who have oligomenorrhea, it is imperative to prescribe sequential progestogens (Duphaston®) every three months, for example, for ten days, to create artificial cycles. This approach is intended to circumvent the potential for relative hyperestrogenism and thereby mitigate the risk of endometrial cancer. Prolonged use of estrogen-progestogen combinations has been associated with deficiencies in essential vitamins and minerals, primarily due to alterations in liver metabolism, reduced intestinal absorption, and increased excretion. The effects are particularly pronounced on vitamins B (B6, B9, B12), vitamin C, and vitamin E. These deficiencies may result in a range of health implications, including low energy levels, mood disorders, and diminished antioxidant protection. Furthermore, mineral imbalances, such as calcium and magnesium, have been observed to be impacted, thereby increasing the likelihood of developing bone and muscle disorders due to their augmented filtration by the kidneys. It is recommended that patients who are prescribed oral contraceptives adhere to a balanced diet in order to compensate for the aforementioned deficiencies.

Metformin: Metformin has been demonstrated to enhance the responsiveness of target cells to insulin. It has been demonstrated to reduce glucose intolerance and hyperandrogenism. In cases where the objective of treatment is to regulate menstrual cycles, estrogen-progestogen therapy is the preferred option [54]. Metformin is indicated as a first-line treatment for obese adolescents, those with glucose metabolism disorders that do not respond to lifestyle and dietary interventions, or in cases where estrogen-progestogen use is contraindicated [55]. The efficacy of metformin in adolescent girls diagnosed with PCOS and a thin body type remains to be substantiated. A recent meta-analysis of randomized controlled trials has been conducted to evaluate the efficacy of metformin and COCs in the treatment of PCOS in adolescent girls. The analysis revealed that metformin exhibited a comparable effectiveness to COCs in addressing hirsutism. Metformin was found to be superior to COCs for weight loss and improved blood glucose control; however, COCs were preferable for menstrual regulation [56].

Antiandrogens: Antiandrogens have been demonstrated to ameliorate the cutaneous manifestations associated with HA [57]. These medications function by impeding the binding of dihydrotestosterone to androgen receptors and by sup-

pressing the activity of type 2 5α-reductase, the enzyme that catalyzes the conversion of testosterone to dihydrotestosterone in the periphery. This results in a reduction of circulating androgen levels. These hormones have been demonstrated to reduce acne and hirsutism, while also regulating menstrual cycles. In cases where estrogen-progestogen therapy has been ineffective or is contraindicated, or when patients exhibit poor tolerance to this treatment, antiandrogens are recommended as a second-line treatment option. In sexually active adolescents, the prescription of antiandrogens must be accompanied by the recommendation of contraception due to the teratogenic effects associated with these medications. The pharmaceutical agents prescribed for this group include spironolactone, cyproterone acetate, flutamide, and finasteride. Antiandrogens are generally recommended as a complementary treatment to estrogen-progestogen pills for cases of severe hirsutism, or in instances where the latter are deemed contraindicated [48].

Spironolactone, a diuretic that conserves potassium, exhibits an anti-androgenic effect, which is a therapeutic advantage in the treatment of PCOS. The mechanism of action of this pharmaceutical agent involves the inhibition of androgen receptors in target tissues, such as the skin and hair follicles. Consequently, this results in a reduction of the clinical manifestations of hyperandrogenism, including hirsutism and acne. Furthermore, it has been demonstrated to inhibit certain enzymes involved in androgen production, thereby limiting the conversion of testosterone to dihydrotestosterone (DHT). DHT is the biologically active form responsible for many androgenic effects. While spironolactone has been demonstrated to assist in the regulation of menstrual cycles by decreasing circulating androgen levels, it does not possess a direct impact on the metabolic disorders associated with PCOS, including insulin resistance and lipid imbalance. Consequently, its application must be integrated with other therapeutic modalities to ensure a comprehensive management strategy for the syndrome. It is the most frequently prescribed antiandrogen in the United States, typically following a six-month course of estrogen-progestin therapy. However, the available literature offers scant evidence to support its use in adolescents [58]-[60].

Cyproterone acetate (Androcur®) is a potent progestogen with intrinsic androgenic activity. It is primarily indicated for severe forms of HA [61]. It has been associated with an increased risk of meningioma, and therefore, it is recommended that it be replaced by another estrogen-progestogen after a maximum of 12 months of use [62]. Flutamide has demonstrated efficacy in treating hirsutism, with optimal dosages ranging from 250 to 500 milligrams administered in two divided doses per day. Its use is not widely recommended due to its high risk of hepatotoxicity compared to other antiandrogens [63]. The following text is intended to provide a comprehensive overview of the subject matter.

Finasteride, a 5α-reductase inhibitor, has been demonstrated to reduce dihydrotestosterone levels and ameliorate symptoms of hyperandrogenism. The efficacy of the treatment is restricted to cases of hirsutism or alopecia. It is classified as a second-line treatment following the failure of estrogen-progestogen and cy-

proterone therapies. The impact of this medication on adolescents remains underexplored, and as such, its recommendation for this demographic is not supported by substantial evidence [11].

Dermatological and cosmetic treatments

It has been documented that among adolescent patients diagnosed with PCOS; a common complaint is the presence of moderate to severe acne and hirsutism. These conditions have been demonstrated to exert a detrimental influence on patients' quality of life, both in terms of their physical well-being and their psychological well-being. The therapeutic approach entails a multifaceted strategy aimed at reducing circulating androgen levels systemically. This involves the use of estrogen-progestogens or antiandrogens, in conjunction with lifestyle modifications and dietary interventions. However, it should be noted that these treatments have their limitations and must be accompanied by specific treatment. The therapeutic approach to acne encompasses a range of interventions, including topical treatments. In certain cases, systemic treatment may be employed. The following text is intended to provide a comprehensive overview of the subject matter.

The treatment of moderate acne has been shown to be effective with benzoyl peroxide concentrations ranging from 0.1% to 2.5% [64]. The application of this solution should be performed twice daily, following the cleansing of the face with a mild soap. For certain forms of severe inflammatory acne, cyclins, such as doxycycline, are employed as therapeutic agents [65]. It is imperative to exercise caution when considering the use of doxycycline. It is recommended that the treatment be administered in the evening, given its photosensitizing properties, and at least one hour prior to bedtime [66].

The anti-inflammatory and healing properties of zinc have been utilized in the treatment of acne. Its pharmaceutical properties make it suitable for use in the treatment of moderate acne, either as a standalone medication or in conjunction with macrolides for cases of severe acne [67]. In cases of severe, recalcitrant nodular acne, isotretinoin (Roaccutane®), a natural retinoid derived from tretinoin (or retinoic acid/vitamin A), is an anti-acne medication that is prescribed as a last resort [68]. It is imperative to note that retinoids cannot be combined with cyclins and zinc. In addition to pharmaceutical interventions, mechanical cosmetic treatments, including laser therapy, electrolysis, depilation, and hair removal, can be utilized as standalone modalities or in conjunction with medication to address hirsutism [69].

Other treatments

Myo-inositol and D-chiro-inositol

The most recent guidelines concerning PCOS, as outlined by ESHRE and ASRM, now incorporate myo-inositol and D-chiro-inositol as preferred therapeutic options for addressing infertility associated with PCOS [26]. These molecules have demonstrated encouraging results in terms of regulating menstrual cycles, enhancing ovarian function, and even increasing the chances of pregnancy in women with PCOS. Clinical studies have demonstrated the efficacy of the treat-

ment in reducing clinical symptoms such as hirsutism and acne, which are frequently associated with hyperandrogenism.

Furthermore, the administration of myo-inositol and D-chiro-inositol has demonstrated particular efficacy in adolescent girls and young women, as it facilitates early treatment of PCOS symptoms, thereby reducing the risk of long-term complications such as infertility and metabolic disorders. However, while these molecules offer numerous advantages, it is imperative to acknowledge that their efficacy is often maximized when employed as a component of a multifaceted therapeutic strategy that incorporates a balanced diet, regular physical activity, and continuous monitoring of metabolic parameters [70] [71].

N-acetylcysteine (NAC)

The use of N-acetylcysteine (NAC) in the treatment of PCOS is attracting growing interest due to its antioxidant properties and beneficial effects on the management of oxidative stress, hyperandrogenism, and insulin resistance. The restoration of balance between antioxidants and reactive oxygen species (ROS) is a critical factor in the beneficial effects of NAC. This balance is crucial for the improvement of ovarian function and the reduction of high androgen levels, as well as the enhancement of insulin sensitivity.

These effects may potentially reduce the risk of metabolic complications, such as type 2 diabetes and cardiovascular disease, which are common in patients with PCOS [72]-[74]. Recent guidelines from prominent gynecology and endocrinology societies, including ESHRE and ASRM, have recommended NAC for the management of PCOS, particularly to promote ovulation in anovulatory patients and alleviate symptoms such as hirsutism and acne [26].

A substantial corpus of clinical studies has demonstrated the efficacy of this treatment in regulating menstrual cycles and reducing free testosterone levels. While the extant evidence is encouraging, further research is necessary to confirm the long-term benefits of NAC and to refine treatment strategies, particularly with regard to dosage and the patients most likely to benefit [73] [74].

Glucocorticoids

Glucocorticoids, including dexamethasone and prednisolone, are occasionally employed in the management of PCOS to mitigate hyperandrogenism by suppressing androgen production by the adrenal glands. However, their utilization is constrained by substantial adverse effects, including weight gain, hypertension, and metabolic disturbances, which renders their prolonged use less advisable [75].

Recent recommendations from prominent societies such as ESHRE and ASRM suggest that glucocorticoids should not be used as a first-line treatment. Instead, these medications should be reserved for specific cases, such as patients with congenital adrenal hyperplasia or severe insulin resistance. In such cases, they should be accompanied by comprehensive PCOS management, including lifestyle measures and other more targeted treatments.

Gonadotropin-releasing hormone agonists (GnRH-A)

GnRH agonists have been utilized in the induction of medical oophorectomy

and the treatment of refractory hirsutism caused by ovarian hyperandrogenism. However, the occurrence of hypoestrogenic side effects generally necessitates the utilization of oral contraceptive pills [32] [76]. Despite its efficacy, this treatment is intricate and costly.

3.2.3. Management of Comorbidities

In light of the high prevalence of these comorbidities, the ACOG, the Endocrine Society, and the European Society of Endocrinology advocate for screening for cardiovascular risk factors, performing an OGTT with 75 g of glucose (every 3 to 5 years), and evaluating for lipid abnormalities (every two years), irrespective of the patient's age [22].

Other comorbidities may appear in adolescents with PCOS, such as depression, anxiety, eating disorders, and body dysmorphia. The presence of insulin resistance, hyperinsulinemia, and obesity should prompt investigations to rule out the onset of glucose regulation disorders or dyslipidemia. The management of PCOS must be multidisciplinary, and the care of adolescents must give way to adult care, which has its own objectives. The treatment of adolescents diagnosed with PCOS should also include the involvement of psychologists and/or psychiatrists to monitor mental health and screen for any neuropsychological complications that may arise. Consequently, further research is necessary to ascertain the frequency of mental health monitoring.

4. Conclusions

PCOS is a complex, multifactorial disorder with variable manifestations that can appear as early as puberty. A conspicuous lacuna persists within the extant diagnostic criteria concerning the adolescent population. The consensus applied to adult women cannot be used in adolescents due to the similarity between the syndrome and the physiological signs of biological transition in adolescents.

Two distinct signs are identified in adolescents: hyperandrogenism and menstrual cycle disorders that meet specific definitions. The combination of these two criteria enables a diagnosis of PCOS in adolescents who present with the relevant symptoms, subsequent to the exclusion of other endocrine disorders. However, when these signs are isolated, the adolescent is said to be "at risk" of developing PCOS and should therefore receive appropriate monitoring.

To date, no single treatment has been demonstrated to effectively address and cure all the symptoms associated with PCOS. Consequently, treatment plans must be customized to address the unique characteristics and needs of each individual patient. The preliminary stage of the treatment process involves the education of the patient and her family members regarding the condition and its potential complications. Subsequent to this, the provision of counsel on lifestyle modifications and dietary interventions ensues. Treatment options include estrogen-progestogen therapy, metformin, aldosterone antagonists, and topical treatments for acne and hirsutism. The long-term follow-up of the patient is intended to mitigate the impact of comorbidities and to curtail the incidence of long-term complications.

This review underscores the necessity for extensive longitudinal studies to establish diagnostic criteria and appropriate treatment for PCOS in adolescents.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Deswal, R., Narwal, V., Dang, A. and Pundir, C.S. (2020) The Prevalence of Polycystic Ovary Syndrome: A Brief Systematic Review. Wolters Kluwer Medknow Publications.

[2] Akpata, C.B., Uadia, P.O. and Okonofua, F.E. (2018) Prevalence of Polycystic Ovary Syndrome in Nigerian Women with Infertility: A Prospective Study of the Three Assessment Criteria. *Open Journal of Obstetrics and Gynecology*, **8**, 1109-1120. https://doi.org/10.4236/ojog.2018.812112

[3] Rosenfield, R.L. (2015) The Polycystic Ovary Morphology-Polycystic Ovary Syndrome Spectrum. *Journal of Pediatric and Adolescent Gynecology*, **28**, 412-419. https://doi.org/10.1016/j.jpag.2014.07.016

[4] Dursun, F., Güven, A. and Yıldız, M. (2016) Assessment of Anti-Müllerian Hormone Level in Management of Adolescents with Polycystic Ovary Syndrome. *Journal of Clinical Research in Pediatric Endocrinology*, **8**, 55-60. https://doi.org/10.4274/jcrpe.2338

[5] Shahid, M. and Wajid, M. (2024) Polycystic Ovary Syndrome in North America. In: Rehman, R. and Sheikh, A., Eds., *Polycystic Ovary Syndrome*, Elsevier, 229-236. https://doi.org/10.1016/b978-0-323-87932-3.00039-6

[6] Imaouen, M., Ameziane Hassani, F. and El Ouahabi, H. (2017) Le syndrome des ovaires polykystiques (SOPK): Caractéristiques cliniques, hormonales et métaboliques (à propos de 63 cas). *Annales d'Endocrinologie*, **78**, 380-381. https://doi.org/10.1016/j.ando.2017.07.535

[7] Sanchez-Garrido, M.A. and Tena-Sempere, M. (2020) Metabolic Dysfunction in Polycystic Ovary Syndrome: Pathogenic Role of Androgen Excess and Potential Therapeutic Strategies. *Molecular Metabolism*, **35**, Article ID: 100937. https://doi.org/10.1016/j.molmet.2020.01.001

[8] Palomba, S., Santagni, S., Falbo, A. and La Sala, G.B. (2015) Complications and Challenges Associated with Polycystic Ovary Syndrome: Current Perspectives. *International Journal of Women's Health*, **7**, 745-763. https://doi.org/10.2147/ijwh.s70314

[9] Frétel, M. (2023) SOPK: Trait Pharmaco et Cosme Fretel 2023. Université de Bordeaux. https://dumas.ccsd.cnrs.fr/dumas-04187737

[10] Rosenfield, R.L. (2007) Identifying Children at Risk for Polycystic Ovary Syndrome. *The Journal of Clinical Endocrinology & Metabolism*, **92**, 787-796. https://doi.org/10.1210/jc.2006-2012

[11] Hajam, Y.A., Rather, H.A., Neelam, Kumar, R., Basheer, M. and Reshi, M.S. (2024) A Review on Critical Appraisal and Pathogenesis of Polycystic Ovarian Syndrome. *Endocrine and Metabolic Science*, **14**, Article ID: 100162. https://doi.org/10.1016/j.endmts.2024.100162

[12] Trimèche, S., Thuan Dit Dieudonne, J., Jeandel, C., Paris, F., Simoni-Brum, I., Orio, F., *et al*. (2004) Le syndrome des ovaires polykystiques en période péri-pubertaire: Polymorphisme clinique, biologique, métabolique et génétique. *Gynécologie Obstétrique*

& Fertilité, **32**, 3-17. https://doi.org/10.1016/j.gyobfe.2003.10.027

[13] Rothenberg, S.S., Beverley, R., Barnard, E., Baradaran-Shoraka, M. and Sanfilippo, J.S. (2018) Polycystic Ovary Syndrome in Adolescents. *Best Practice & Research Clinical Obstetrics & Gynaecology*, **48**, 103-114. https://doi.org/10.1016/j.bpobgyn.2017.08.008

[14] Baldauff, N.H. and Witchel, S.F. (2017) Polycystic Ovary Syndrome in Adolescent Girls. *Current Opinion in Endocrinology, Diabetes & Obesity*, **24**, 56-66. https://doi.org/10.1097/med.0000000000000309

[15] Dason, E.S., Koshkina, O., Chan, C. and Sobel, M. (2024) Diagnostic et prise en charge du syndrome des ovaires polykystiques. *Canadian Medical Association Journal*, **196**, E449-E459. https://doi.org/10.1503/cmaj.231251-f

[16] Reyss, A.C., Proust-Richard, C., Catteau-Jonard, S. and Dewailly, D. (2006) Le consensus de Rotterdam appliqué à l'adolescente: Quels examens prescrire et comment les interpréter pour établir le diagnostic de SOPK? *Gynécologie Obstétrique & Fertilité*, **34**, 341-346. https://doi.org/10.1016/j.gyobfe.2006.02.017

[17] Mboloko, E., Mbangama, M.A., Lokengo, L.D., Nzau, N.E., Bikuelo, B. and Mboloko, M. (2012) Infertilité en cas de syndrome des ovaires micropolykystiques dans une population kinoise. *Annals of African Medicine*, **6**, 855-864. https://anafrimed.net/rubrique/volume-6-n2-mars-2013/

[18] Mbuyamba, M., Kalenda, N., Biayi, J., Mwembo Tambwe, A.N. and Kalenga, P.M. (2014) Study of Clinical, Sonographic and Nutritional Aspects of Polycystic Ovary Syndrome (PCOS) in Mbuji-Mayi, DR Congo. *Pan African Medical Journal*, **19**, Article No. 267.

[19] Amisi, C., Mputu, L., Mboloko, E., Bieleli, E. and Pozzili, P. (2013) L'insulinorésistance biologique chez la femme congolaise avec syndrome des ovaires polymicrokystiques (SOPK). *Gynécologie Obstétrique & Fertilité*, **41**, 707-710. https://doi.org/10.1016/j.gyobfe.2013.08.002

[20] Saracci, C., Mahamat, M. and Jacquérioz, F. (2019) Comment rédiger un article scientifique de type revue narrative de la littérature? *Revue Médicale Suisse*, **15**, 1694-1698. https://doi.org/10.53738/revmed.2019.15.664.1694

[21] Baethge, C., Goldbeck-Wood, S. and Mertens, S. (2019) SANRA—A Scale for the Quality Assessment of Narrative Review Articles. *Research Integrity and Peer Review*, **4**, Article No. 5. https://doi.org/10.1186/s41073-019-0064-8

[22] Stein, I.F. and Leventhal, M.L. (1935) Amenorrhea Associated with Bilateral Polycystic Ovaries. *American Journal of Obstetrics and Gynecology*, **29**, 181-191. https://doi.org/10.1016/s0002-9378(15)30642-6

[23] Roe, A.H., *et al*. (2013) Using the Androgen Excess—PCOS Society Criteria to Diagnose Polycystic Ovary Syndrome and the Risk of Metabolic Syndrome in Adolescents. *The Journal of Pediatrics*, **162**, 937-941. https://www.sciencedirect.com/science/article/abs/pii/S0022347612013133

[24] Azziz, R., Carmina, E., Dewailly, D., Diamanti-Kandarakis, E., Escobar-Morreale, H.F., Futterweit, W., *et al*. (2006) Criteria for Defining Polycystic Ovary Syndrome as a Predominantly Hyperandrogenic Syndrome: An Androgen Excess Society Guideline. *The Journal of Clinical Endocrinology & Metabolism*, **91**, 4237-4245. https://doi.org/10.1210/jc.2006-0178

[25] Akgül, S., Düzçeker, Y., Kanbur, N. and Derman, O. (2018) Do Different Diagnostic Criteria Impact Polycystic Ovary Syndrome Diagnosis for Adolescents? *Journal of Pediatric and Adolescent Gynecology*, **31**, 258-262. https://doi.org/10.1016/j.jpag.2017.12.002

[26] Teede, H.J., Tay, C.T., Laven, J.J.E., Dokras, A., Moran, L.J., Piltonen, T.T., *et al*. (2023) Recommendations from the 2023 International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. *The Journal of Clinical Endocrinology & Metabolism*, **108**, 2447-2469. https://doi.org/10.1210/clinem/dgad463

[27] Özdemir, S., Özdemir, M., Görkemli, H., Kiyici, A. and Bodur, S. (2010) Specific Dermatologic Features of the Polycystic Ovary Syndrome and Its Association with Biochemical Markers of the Metabolic Syndrome and Hyperandrogenism. *Acta Obstetricia et Gynecologica Scandinavica*, **89**, 199-204. https://doi.org/10.3109/00016340903353284

[28] Ferriman, D. and Gallwey, J.D. (1961) Clinical Assessment of Body Hair Growth in Women. *The Journal of Clinical Endocrinology & Metabolism*, **21**, 1440-1447. https://doi.org/10.1210/jcem-21-11-1440

[29] Azziz, R., Woods, K.S., Reyna, R., Key, T.J., Knochenhauer, E.S. and Yildiz, B.O. (2004) The Prevalence and Features of the Polycystic Ovary Syndrome in an Unselected Population. *The Journal of Clinical Endocrinology & Metabolism*, **89**, 2745-2749. https://doi.org/10.1210/jc.2003-032046

[30] Kamboj, M.K. and Bonny, A.E. (2017) Polycystic Ovary Syndrome in Adolescence: Diagnostic and Therapeutic Strategies. *Translational Pediatrics*, **6**, 248-255. https://doi.org/10.21037/tp.2017.09.11

[31] Chang, W.Y., Knochenhauer, E.S., Bartolucci, A.A. and Azziz, R. (2005) Phenotypic Spectrum of Polycystic Ovary Syndrome: Clinical and Biochemical Characterization of the Three Major Clinical Subgroups. *Fertility and Sterility*, **83**, 1717-1723. https://doi.org/10.1016/j.fertnstert.2005.01.096

[32] Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group (2004) Revised 2003 Consensus on Diagnostic Criteria and Long-Term Health Risks Related to Polycystic Ovary Syndrome. *Fertility and Sterility*, **81**, 19-25.

[33] Zhu, R.Y., Wong, Y.C. and Yong, E.L. (2016) Sonographic Evaluation of Polycystic Ovaries. *Best Practice & Research Clinical Obstetrics & Gynaecology*, **37**, 25-37. https://doi.org/10.1016/j.bpobgyn.2016.02.005

[34] Chang, R.J. and Cook-Andersen, H. (2013) Disordered Follicle Development. *Molecular and Cellular Endocrinology*, **373**, 51-60. https://doi.org/10.1016/j.mce.2012.07.011

[35] Dumesic, D.A., Abbott, D.H., Sanchita, S. and Chazenbalk, G.D. (2020) Endocrine-Metabolic Dysfunction in Polycystic Ovary Syndrome: An Evolutionary Perspective. *Current Opinion in Endocrine and Metabolic Research*, **12**, 41-48. https://doi.org/10.1016/j.coemr.2020.02.013

[36] Trikudanathan, S. (2015) Polycystic Ovarian Syndrome. *Medical Clinics of North America*, **99**, 221-235. https://doi.org/10.1016/j.mcna.2014.09.003

[37] Fulghesu, A., Magnini, R., Portoghese, E., Angioni, S., Minerba, L. and Melis, G.B. (2010) Obesity-Related Lipid Profile and Altered Insulin Incretion in Adolescents with Polycystic Ovary Syndrome. *Journal of Adolescent Health*, **46**, 474-481. https://doi.org/10.1016/j.jadohealth.2009.10.008

[38] Ma, Y.L., Jin, C.H., Zhao, C.C., *et al*. (2022) Waist-to-Height Ratio Is a Simple and Practical Alternative to Waist Circumference to Diagnose Metabolic Syndrome in Type 2 Diabetes. *Frontiers in Nutrition*, **9**, Article ID: 986090. https://doi.org/10.3389/fnut.2022.986090

[39] Azziz, R., Carmina, E., Dewailly, D., Diamanti-Kandarakis, E., Escobar-Morreale, H.F., Futterweit, W., *et al*. (2009) The Androgen Excess and PCOS Society Criteria

for the Polycystic Ovary Syndrome: The Complete Task Force Report. *Fertility and Sterility*, **91**, 456-488. https://doi.org/10.1016/j.fertnstert.2008.06.035

[40] Dumesic, D.A., Oberfield, S.E., Stener-Victorin, E., Marshall, J.C., Laven, J.S. and Legro, R.S. (2015) Scientific Statement on the Diagnostic Criteria, Epidemiology, Pathophysiology, and Molecular Genetics of Polycystic Ovary Syndrome. *Endocrine Reviews*, **36**, 487-525. https://doi.org/10.1210/er.2015-1018

[41] Teede, H.J., *et al*. (2018) Recommendations from the International Evidence-Based Guideline for the Assessment and Management of Polycystic Ovary Syndrome. *Fertility and Sterility*, **110**, 364-379.

[42] Kocaay, P., Siklar, Z., Buyukfirat, S. and Berberoglu, M. (2018) The Diagnostic Value of Anti-Müllerian Hormone in Early Post Menarche Adolescent Girls with Polycystic Ovarian Syndrome. *Journal of Pediatric and Adolescent Gynecology*, **31**, 362-366. https://doi.org/10.1016/j.jpag.2018.02.126

[43] Esquivel-Zuniga, M.R., Kirschner, C.K., McCartney, C.R. and Burt Solorzano, C.M. (2022) Non-PCOS Hyperandrogenic Disorders in Adolescents. *Seminars in Reproductive Medicine*, **40**, 042-052. https://doi.org/10.1055/s-0041-1742259

[44] Humayun, K.N., Arif, M. and Memon, F. (2024) Polycystic Ovary Syndrome in Adolescents. In: Rehman, R. and Sheikh, A., Eds., *Polycystic Ovary Syndrome*, Elsevier, 11-22. https://doi.org/10.1016/b978-0-323-87932-3.00012-8

[45] Dewailly, D., Lujan, M.E., Carmina, E., Cedars, M.I., Laven, J., Norman, R.J., *et al*. (2013) Definition and Significance of Polycystic Ovarian Morphology: A Task Force Report from the Androgen Excess and Polycystic Ovary Syndrome Society. *Human Reproduction Update*, **20**, 334-352. https://doi.org/10.1093/humupd/dmt061

[46] Leibel, N.I., Baumann, E.E., Kocherginsky, M. and Rosenfield, R.L. (2006) Relationship of Adolescent Polycystic Ovary Syndrome to Parental Metabolic Syndrome. *The Journal of Clinical Endocrinology & Metabolism*, **91**, 1275-1283. https://doi.org/10.1210/jc.2005-1707

[47] Chang, W.Y., Knochenhauer, E.S., Bartolucci, A.A. and Azziz, R. (2005) Phenotypic Spectrum of Polycystic Ovary Syndrome: Clinical and Biochemical Characterization of the Three Major Clinical Subgroups. *Fertility and Sterility*, **8**, 1717-1723. https://doi.org/10.1016/j.fertnstert.2005.01.096

[48] Manique, M.E.S. and Ferreira, A.M.A.P. (2022) Polycystic Ovary Syndrome in Adolescence: Challenges in Diagnosis and Management. *Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics*, **44**, 425-433. https://doi.org/10.1055/s-0042-1742292

[49] Pkhaladze, L., Barbakadze, L. and Kvashilava, N. (2016) Myo-Inositol in the Treatment of Teenagers Affected by PCOS. *International Journal of Endocrinology*, **2016**, Article ID: 1473612. https://doi.org/10.1155/2016/1473612

[50] Wong, J.M.W., Gallagher, M., Gooding, H., Feldman, H.A., Gordon, C.M., Ludwig, D.S., *et al*. (2015) A Randomized Pilot Study of Dietary Treatments for Polycystic Ovary Syndrome in Adolescents. *Pediatric Obesity*, **11**, 210-220. https://doi.org/10.1111/ijpo.12047

[51] Vine, D., Ghosh, M., Wang, T. and Bakal, J. (2024) Increased Prevalence of Adverse Health Outcomes across the Lifespan in Those Affected by Polycystic Ovary Syndrome: A Canadian Population Cohort. *CJC Open*, **6**, 314-326. https://doi.org/10.1016/j.cjco.2023.12.010

[52] Mastorakos, G., Koliopoulos, C. and Creatsas, G. (2002) Androgen and Lipid Profiles in Adolescents with Polycystic Ovary Syndrome Who Were Treated with Two Forms of Combined Oral Contraceptives. *Fertility and Sterility*, **77**, 919-927.

https://doi.org/10.1016/s0015-0282(02)02993-x

[53] Ibáñez, L., Oberfield, S.E., Witchel, S., Auchus, R.J., Chang, R.J., Codner, E., *et al.* (2017) An International Consortium Update: Pathophysiology, Diagnosis, and Treatment of Polycystic Ovarian Syndrome in Adolescence. *Hormone Research in Paediatrics*, **88**, 371-395. https://doi.org/10.1159/000479371

[54] Bird, S.T., Hartzema, A.G., Brophy, J.M., Etminan, M. and Delaney, J.A.C. (2012) Risk of Venous Thromboembolism in Women with Polycystic Ovary Syndrome: A Population-Based Matched Cohort Analysis. *Canadian Medical Association Journal*, **185**, E115-E120. https://doi.org/10.1503/cmaj.120677

[55] Legro, R.S., Arslanian, S.A., Ehrmann, D.A., Hoeger, K.M., Murad, M.H., Pasquali, R., *et al.* (2013) Diagnosis and Treatment of Polycystic Ovary Syndrome: An Endocrine Society Clinical Practice Guideline. *The Journal of Clinical Endocrinology & Metabolism*, **98**, 4565-4592. https://doi.org/10.1210/jc.2013-2350

[56] Al Khalifah, R.A., Florez, I.D., Dennis, B., Thabane, L. and Bassilious, E. (2016) Metformin or Oral Contraceptives for Adolescents with Polycystic Ovarian Syndrome: A Meta-Analysis. *Pediatrics*, **137**, e20154089. https://doi.org/10.1542/peds.2015-4089

[57] Gariani, K., Hugon-Rodin, J., Philippe, J., Righini, M. and Blondon, M. (2020) Association between Polycystic Ovary Syndrome and Venous Thromboembolism: A Systematic Review and Meta-analysis. *Thrombosis Research*, **185**, 102-108. https://doi.org/10.1016/j.thromres.2019.11.019

[58] Fitzgerald, S., DiVasta, A. and Gooding, H. (2018) An Update on PCOS in Adolescents. *Current Opinion in Pediatrics*, **30**, 459-465. https://doi.org/10.1097/mop.0000000000000636

[59] Trent, M. and Gordon, C.M. (2020) Diagnosis and Management of Polycystic Ovary Syndrome in Adolescents. *Pediatrics*, **145**, S210-S218. https://doi.org/10.1542/peds.2019-2056j

[60] Soares-Jr, J.M., Sá, M.F.S.d. and Baracat, E.C. (2019) New Criteria for the Clinical Diagnosis of Hyperandrogenism in Polycystic Ovarian Syndrome and the Risk of Overdiagnosis. *Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics*, **41**, 361-362. https://doi.org/10.1055/s-0039-1693530

[61] Glueck, C.J., Woo, J.G., Khoury, P.R., Morrison, J.A., Daniels, S.R. and Wang, P. (2015) Adolescent Oligomenorrhea (Age 14-19) Tracks into the Third Decade of Life (Age 20-28) and Predicts Increased Cardiovascular Risk Factors and Metabolic Syndrome. *Metabolism*, **64**, 539-553. https://doi.org/10.1016/j.metabol.2015.01.005

[62] Samarut, E., Lugat, A., Amelot, A., Scharbarg, E., Hadjadj, S., Primot, C., *et al.* (2021) Meningiomas and Cyproterone Acetate: A Retrospective, Monocentric Cohort of 388 Patients Treated by Surgery or Radiotherapy for Intracranial Meningioma. *Journal of Neuro-Oncology*, **152**, 115-123. https://doi.org/10.1007/s11060-020-03683-6

[63] Zulian, E., Sartorato, P., Benedini, S., Baro, G., Armanini, D., Mantero, F., *et al.* (2005) Spironolactone in the Treatment of Polycystic Ovary Syndrome: Effects on Clinical Features, Insulin Sensitivity and Lipid Profile. *Journal of Endocrinological Investigation*, **28**, 49-53. https://doi.org/10.1007/bf03345529

[64] Kawashima, M., Nagare, T. and Doi, M. (2017) Clinical Efficacy and Safety of Benzoyl Peroxide for Acne Vulgaris: Comparison between Japanese and Western Patients. *The Journal of Dermatology*, **44**, 1212-1218. https://doi.org/10.1111/1346-8138.13996

[65] Kircik, L.H. (2019) Anti-Inflammatory Dose Doxycycline plus Adapalene 0.3% and Benzoyl Peroxide 2.5% Gel for Severe Acne. *Journal of Drugs in Dermatology*, **18**, 924-927.

[66] Eichenfield, L.F., Krakowski, A.C., Piggott, C., Del Rosso, J., Baldwin, H., Friedlander, S.F., *et al*. (2013) Evidence-Based Recommendations for the Diagnosis and Treatment of Pediatric Acne. *Pediatrics*, **131**, S163-S186. https://doi.org/10.1542/peds.2013-0490b

[67] Dhaliwal, S., Nguyen, M., Vaughn, A.R., Notay, M., Chambers, C.J. and Sivamani, R.K. (2019) Effects of Zinc Supplementation on Inflammatory Skin Diseases: A Systematic Review of the Clinical Evidence. *American Journal of Clinical Dermatology*, **21**, 21-39. https://doi.org/10.1007/s40257-019-00484-0

[68] Millikan, L.E. (2003) The Rationale for Using a Topical Retinoid for Inflammatory Acne. *American Journal of Clinical Dermatology*, **4**, 75-80. https://doi.org/10.2165/00128071-200304020-00001

[69] Mwanthi, M. and Zaenglein, A.L. (2018) Update in the Management of Acne in Adolescence. *Current Opinion in Pediatrics*, **30**, 492-498. https://doi.org/10.1097/mop.0000000000000649

[70] Fitz, V., Graca, S., Mahalingaiah, S., Liu, J., Lai, L., Butt, A., *et al*. (2024) Inositol for Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis to Inform the 2023 Update of the International Evidence-Based PCOS Guidelines. *The Journal of Clinical Endocrinology & Metabolism*, **109**, 1630-1655. https://doi.org/10.1210/clinem/dgad762

[71] Unfer, V., Facchinetti, F., Orrù, B., Giordani, B. and Nestler, J. (2017) Myo-Inositol Effects in Women with PCOS: A Meta-Analysis of Randomized Controlled Trials. *Endocrine Connections*, **6**, 647-658. https://doi.org/10.1530/ec-17-0243

[72] Liu, J., Su, H., Jin, X., Wang, L. and Huang, J. (2023) The Effects of N-Acetylcysteine Supplement on Metabolic Parameters in Women with Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis. *Frontiers in Nutrition*, **10**, Article ID: 1209614. https://doi.org/10.3389/fnut.2023.1209614

[73] Thakker, D., Raval, A., Patel, I. and Walia, R. (2015) N-Acetylcysteine for Polycystic Ovary Syndrome: A Systematic Review and Meta-Analysis of Randomized Controlled Clinical Trials. *Obstetrics and Gynecology International*, **2015**, Article ID: 817849. https://doi.org/10.1155/2015/817849

[74] Viña, I., Viña, J.R., Carranza, M. and Mariscal, G. (2025) Efficacy of N-Acetylcysteine in Polycystic Ovary Syndrome: Systematic Review and Meta-Analysis. *Nutrients*, **17**, Article No. 284. https://doi.org/10.3390/nu17020284

[75] Nikolić, M., Macut, D., Djordjevic, A., Veličković, N., Nestorović, N., Bursać, B., *et al*. (2015) Possible Involvement of Glucocorticoids in 5α-Dihydrotestosterone-Induced PCOS-Like Metabolic Disturbances in the Rat Visceral Adipose Tissue. *Molecular and Cellular Endocrinology*, **399**, 22-31. https://doi.org/10.1016/j.mce.2014.08.013

[76] Fulghesu, A.M., Canu, E., Casula, L., Melis, F. and Gambineri, A. (2021) Polycystic Ovarian Morphology in Normocyclic Non-Hyperandrogenic Adolescents. *Journal of Pediatric and Adolescent Gynecology*, **34**, 610-616. https://doi.org/10.1016/j.jpag.2021.02.004