

## POLYCYSTIC OVARY SYNDROME IN MODERN MEDICINE: FROM ETIOLOGY TO DIAGNOSIS AND EVIDENCE-BASED MANAGEMENT

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### ABSTRACT

#### BACKGROUND

Polycystic ovary syndrome is one of the most common endocrine disorders in women of reproductive age and is associated with reproductive dysfunction, metabolic disturbances, and significant psychological burden. The marked heterogeneity of clinical phenotypes and variability in diagnostic criteria complicate timely diagnosis, risk stratification, and long-term management, underscoring the need for an integrated and clinically oriented synthesis of current evidence.

#### AIMS

The aim of this narrative review is to summarize and integrate contemporary evidence on the epidemiology, pathophysiology, diagnostic approaches, and management of polycystic ovary syndrome, with particular emphasis on the interrelation of reproductive, metabolic, and psychological aspects relevant to clinical practice.

#### METHODS

A narrative review of the literature was conducted using the PubMed, Google Scholar, and ResearchGate databases. International clinical guidelines, consensus documents, systematic reviews, meta-analyses, randomized controlled trials, cohort and population-based studies, and clinically relevant review articles were considered. The analysis was descriptive in nature and did not involve a formal systematic review protocol or quantitative data synthesis.

## RESULTS

The reviewed evidence confirms that polycystic ovary syndrome should be regarded as a chronic, multisystem condition rather than a disorder limited to reproductive age. Insulin resistance, hormonal dysregulation, and metabolic abnormalities contribute to long term risks, including infertility, type 2 diabetes mellitus, cardiovascular disease, endometrial pathology, and impaired quality of life. Phenotypic heterogeneity and inconsistent application of diagnostic criteria remain major barriers to early diagnosis and individualized management. Lifestyle modification represents the cornerstone of therapy across phenotypes, while pharmacological and fertility directed interventions should be tailored to individual clinical profiles. Psychological comorbidities are common and frequently underrecognized.

## CONCLUSIONS

Effective management of polycystic ovary syndrome requires a patient centred and multidisciplinary approach that integrates reproductive, metabolic, and psychological care. Early identification of metabolic risk factors, long term follow up, and systematic attention to mental health are essential to improve clinical outcomes and quality of life.

**Keywords:** Polycystic Ovary Syndrome (PCOS), hyperandrogenism, anovulation, hormonal imbalance, metabolic syndrome, endocrine disorder, metformin, insulin.

## INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine disorder affecting women throughout their reproductive lifespan and is characterized by a variable combination of hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology [1]. The syndrome has significant implications for reproductive, metabolic, and psychological health, making it one of the most common endocrine conditions encountered in clinical practice [2].

Clinically, patients with PCOS often present with menstrual irregularities, hirsutism, acne, and infertility, while many also exhibit metabolic disturbances such as insulin resistance, obesity, dyslipidaemia, and non-alcoholic fatty liver disease [3]. Insulin resistance is increasingly recognized as a central pathophysiological mechanism linking obesity, hyperinsulinaemia, and ovarian androgen excess, contributing to both reproductive and metabolic manifestations of the syndrome [8].

Beyond physical morbidity, PCOS is associated with a substantial psychosocial burden. Women with PCOS frequently experience anxiety, depression, impaired body image, and reduced quality of life, highlighting the importance of comprehensive, multidisciplinary care [29]. Current international guidelines emphasize routine assessment of psychological well-being alongside reproductive and metabolic evaluation [1].

The prevalence of PCOS varies depending on the diagnostic criteria applied, with higher rates observed in populations selected for infertility or metabolic disorders [6,7]. Studies using the Rotterdam criteria report prevalence estimates between 6% and 20%, illustrating the influence of diagnostic definitions and population characteristics on epidemiological data [7].

The aetiology of PCOS is multifactorial, involving genetic predisposition, prenatal androgen exposure, neuroendocrine dysregulation, abnormal steroidogenesis, and chronic low-grade inflammation [5,29]. While substantial progress has been made in understanding these mechanisms, gaps remain in the identification of reliable biomarkers, phenotype-specific risk stratification, and individualized therapeutic strategies [1].

## RELEVANCE

Polycystic ovary syndrome is one of the most common endocrine disorders in women of reproductive age and represents a significant clinical problem. The condition is associated with menstrual cycle disturbances and impaired fertility, metabolic disorders, and psychoemotional disturbances, including anxiety and depressive states. The diversity of clinical manifestations and the involvement of multiple physiological systems substantially complicate timely diagnosis and patient management. This underscores the relevance of a comprehensive and multidisciplinary approach to the assessment and treatment of polycystic ovary syndrome in clinical practice.

## NOVELTY

The novelty of this review is editorial and synthetic in nature. The article integrates current data on the pathogenesis, prevalence, clinical manifestations, diagnosis, and treatment of polycystic ovary syndrome within a unified narrative analysis. Particular attention is given to the interaction between hormonal disturbances, insulin resistance, and chronic low-grade inflammation, as well as to the need to consider reproductive, metabolic, and psychoemotional aspects in patient management. The novelty of the review lies not in the formulation of new pathogenetic concepts, but in the structured systematization of up-to-date data and an emphasis on a clinically oriented, patient centered

approach.

## AIM

The aim of this narrative review is to summarize and integrate current evidence on the epidemiology, pathophysiology, diagnostic approaches, and management of polycystic ovary syndrome, with particular attention to the interrelation of reproductive, metabolic, and psychological aspects relevant to clinical practice.

## RESEARCH OBJECTIVES

The objectives of this review are to describe the etiological and clinical features of polycystic ovary syndrome, to outline current diagnostic criteria and principles of differential diagnosis, and to review evidence based management strategies, including lifestyle interventions, pharmacological treatment, and fertility oriented care. In addition, the review addresses the psychological aspects of PCOS and highlights areas where further research is needed.

## METHODS

**Design.** This work was conducted as a narrative literature review. The review focuses on the etiology, epidemiology, clinical manifestations, diagnostics, differential diagnosis, complications, and therapeutic management of polycystic ovary syndrome. The methodology was not intended to meet the criteria of a systematic review.

**Sources of information.** The literature search was carried out using the PubMed, Scopus and Web of Science databases. In addition, reference lists from international clinical guidelines and key review articles included in the final list of references were examined.

**Search strategy.** Keywords and their combinations in English were used, corresponding to the content of the article and the list of keywords: polycystic ovary syndrome, PCOS, hyperandrogenism, anovulation, hormonal imbalance, metabolic syndrome, endocrine disorder, insulin resistance, metformin, insulin. The search was limited to publications in peer reviewed scientific sources.

**Inclusion criteria.** The review included international clinical guidelines and consensus documents on polycystic ovary syndrome, systematic reviews and meta-analyses, randomized controlled trials, cohort and population-based studies, as well as review articles directly relevant to the thematic scope of this work.

**Exclusion criteria.** Conference abstracts, non peer reviewed publications, and sources lacking clinically relevant information on the diagnosis, complications, or treatment of polycystic ovary syndrome were excluded.

**Study selection.** Sources were selected based on analysis of titles, abstracts, and full texts, with inclusion of publications that directly support the statements presented in the main sections of the article.

**Data analysis and synthesis.** The literature analysis was descriptive in nature and did not involve a formal systematic review protocol or quantitative data synthesis. The results were summarized and structured according to the clinical logic of managing patients with polycystic ovary syndrome. A total of 61 sources were included in the final analysis to support the key statements of the article.

## RESULTS

### ETIOLOGY

The etiology of polycystic ovary syndrome (PCOS) is complex and results from the interaction of genetic, metabolic, hormonal and environmental factors. Modern research indicates that PCOS is a consequence of overlapping metabolic and endocrine dysregulation, leading to hyperandrogenism and chronic anovulation [1,2,3]. One of the most important elements of the pathogenesis of PCOS is insulin resistance, which may occur regardless of body weight. Hyperinsulinemia stimulates thecal cells of the ovary to increase androgen production and lowers SHBG levels, which exacerbates hyperandrogenism. These phenomena are observed in various PCOS phenotypes, although their severity may vary [1,8]. Another key mechanism is dysregulation of the hypothalamic-pituitary-ovarian axis. Increased GnRH pulse frequency results in LH over FSH, which disrupts follicular maturation and promotes the development of functional ovarian hyperandrogenism [9,6].

There is also evidence of the involvement of inflammatory and immunological factors. Many patients experience chronic, low-grade inflammation, which may contribute to impaired insulin signaling and steroidogenesis. The literature also highlights the role of oxidative stress and glycation end products (AGEs) as factors exacerbating metabolic and hormonal disorders [3,11]. Genetic predisposition, which is polygenic in nature, also plays a significant role. Research has identified numerous loci related to the regulation of androgen production, glucose metabolism, and the functioning of the hypothalamic-pituitary-ovarian axis. Genetic susceptibility can manifest under the influence of environmental factors such as poor diet, excess body weight, or low levels of physical activity [3,6]. Research

indicates that PCOS is not a single disorder, but rather a syndrome with significant phenotypic heterogeneity resulting from interactions between metabolic, hormonal, and genetic factors. This complexity means that the etiology of PCOS remains an area of intense research, and its full understanding is crucial for developing more effective diagnostic and therapeutic methods [1,2,3].

## EPIDEMIOLOGY

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age and represents a significant public health problem. The prevalence of PCOS is estimated at 6-10% of the female population using the NIH criteria, while the more inclusive Rotterdam criteria may increase to 15-20% [1,2]. These differences are primarily due to diagnostic differences and the significant heterogeneity of PCOS phenotypes. PCOS affects women worldwide, but its prevalence may vary among populations. Population-based studies indicate a higher prevalence among women of South Asian and Latino origin, who are more likely to have insulin resistance and a more severe metabolic disease course [3,4]. European and North American populations, on the other hand, have comparable prevalence rates, typically ranging from 8% to 13% [3]. A significant element of PCOS epidemiology is the relationship between body weight. Although PCOS also occurs in women with a normal BMI, obesity can increase the risk of developing the disease by up to two-fold, while also exacerbating hyperandrogenism and metabolic disorders [1,5]. In countries with a high prevalence of obesity, such as the United States, a proportionally higher number of PCOS diagnoses is observed. PCOS often goes undiagnosed - it is estimated that up to 50% of cases are undiagnosed, primarily due to the variety of symptoms, lack of patient awareness, and differences in clinical practice [3]. This is important from a public health perspective, as PCOS is associated with an increased risk of developing type 2 diabetes, hypertension, infertility, and mental health problems. Globally, PCOS represents a growing epidemiological burden. This phenomenon is associated with the increasing prevalence of obesity, sedentary lifestyles, and environmental and metabolic changes that may favor the development of genetic predispositions. Therefore, PCOS is currently recognized as a key endocrine disorder requiring intensified population-based research and implementation of early detection programs [2,6].

## SYMPTOMS

The clinical presentation of polycystic ovary syndrome is highly diverse and encompasses reproductive, dermatological, metabolic, and psychological disorders. The occurrence of specific symptoms depends on the PCOS phenotype, the patient's age, and individual tissue sensitivity to steroid hormones. Despite significant heterogeneity, several groups of symptoms can be distinguished that are most frequently observed in clinical practice. One of the key manifestations of PCOS is menstrual cycle disruption, which results from chronic anovulation. Patients often report prolonged cycles, irregular bleeding, or a complete absence of menstrual periods [7]. These symptoms pose a significant problem for both quality of life and reproductive health, as they complicate conception and increase the risk of endometrial hyperplasia. For many women, the first symptom they notice is infrequent menstruation during adolescence, often leading to a late diagnosis of PCOS [16]. The second characteristic group of symptoms are the clinical manifestations of androgen excess. The most typical is hirsutism, which involves excessive hair growth in areas typical of male hair [15]. Acne, which appears not only on the face but also on the back and chest, and seborrhea, resulting from increased activity of the sebaceous glands, often coexist. Some patients also experience androgenetic alopecia, which manifests as thinning hair in the crown area [19]. Although these symptoms do not pose a health risk, they significantly impact well-being and psychological well-being [14]. Symptoms observed in many women with PCOS also include skin lesions associated with metabolic disorders, primarily acanthosis nigricans, which are dark, thickened skin patches around the creases. These are often accompanied by difficulty losing weight and a tendency to gain weight rapidly, which patients report as one of the most distressing symptoms of the disease [11]. Metabolic disorders also contribute significantly to the clinical picture of PCOS, manifesting as symptoms such as chronic fatigue, excessive sleepiness after meals, and a tendency to experience episodes of reactive hypoglycemia. In many cases, an increased tendency to accumulate fat tissue in the abdominal area is also observed, which affects the perception of one's body shape and motivation for treatment [11]. Psychological symptoms, which are an integral part of PCOS, are receiving increasing attention. Studies have shown an increased risk of depression, anxiety disorders, low self-esteem, and body image disturbances [12,18]. Patients also often report difficulties regulating emotions, chronic stress, and a sense of lack of control over their health, which intensifies the psychological burden [12,20]. It's worth noting that PCOS symptoms can change with age. Adolescents typically experience menstrual irregularities and acne, while older women are more likely to experience metabolic symptoms [16]. Hyperandrogenic symptoms, on the other hand, may improve over time [14]. This variability requires an individualized approach to clinical assessment, taking into account the patient's life stages.

## DIAGNOSTICS

The diagnosis of PCOS is based on the Rotterdam criteria, which require the presence of at least two of three elements: oligo- or anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology (PCOM) [21]. The AE-PCOS Society criteria require the presence of hyperandrogenism as a necessary condition, as well as ovulatory dysfunction and/or PCOM [22]. International guidelines from 2018 and 2023 recommend the use of the

Rotterdam criteria, along with standardization of androgen testing and cautious use of AMH and imaging studies [1,23].

Table 1. Diagnostic criteria for polycystic ovary syndrome

Diagnostic component	Rotterdam criteria 2003	NIH criteria 1990	AE PCOS Society criteria 2006
Hyperandrogenism	Clinical and or biochemical	Mandatory	Mandatory
Oligo ovulation or anovulation	One of the criteria	Mandatory	May be present
Polycystic ovarian morphology on ultrasound	One of the criteria	Not included	Additional criterion
Minimum requirements for diagnosis	Two out of three criteria	Both criteria required	Hyperandrogenism plus one additional criterion
Exclusion of other causes of hyperandrogenism	Mandatory	Mandatory	Mandatory
Clinical characteristics	Broad phenotype spectrum with high heterogeneity	More restrictive definition with limited phenotypes	Emphasis on hyperandrogenic phenotype

Note. Diagnostic criteria are presented according to the NIH definition, the Rotterdam ESHRE ASRM Consensus 2003, and the Androgen Excess and PCOS Society criteria [61,21,22].

## DIAGNOSIS IN ADOLESCENTS

In adolescent patients, PCOS can only be diagnosed if two factors are present: menstrual disturbances persisting for  $\geq 2$  years after menarche and clinical or biochemical hyperandrogenism [26]. Ultrasonography should not be the key diagnostic criterion in this group due to the physiologically high number of follicles in the ovaries of adolescents [26]. AMH is not recommended as a standalone diagnostic marker [23].

## HISTORY AND PHYSICAL EXAMINATION

The history should include regularity of cycles, signs of hyperandrogenism, body weight, body fat distribution, and metabolic risk factors [1]. Hirsutism is assessed using the modified Ferriman-Gallway scale [21]. The physical examination includes assessment of BMI, waist circumference, blood pressure, and the presence of signs of insulin resistance [1]. AMH can support the assessment of PCOM, but it should not replace ultrasound or be used as a standalone criterion [1,23]. Metabolic assessment includes fasting glucose, OGTT, lipid profile, and HbA1c, due to the increased risk of insulin resistance and metabolic disorders in women with PCOS [24].

## IMAGING TESTS:

Transvaginal ultrasound (TVUS) is the primary method for assessing PCOM [21]. Technological advances are increasing the number of follicles observed, requiring regular updates to the criteria used in clinical practice [24]. Routine ultrasound is not recommended in adolescents [1].

## DIAGNOSTIC ALGORITHM:

1. Clinical assessment - menstrual irregularities, symptoms of hyperandrogenism, body weight, and metabolic parameters [21,1].
2. Hormonal testing - androgens measured using a highly sensitive method (preferably LC-MS/MS) [21,24].
3. Metabolic assessment - OGTT or fasting glucose, lipid profile, HbA1c [1,24].

4. TVUS - PCOM assessment according to updated criteria [21,24].
5. AMH - supportive, not conclusive [1,23].
6. Exclusion of other causes of hyperandrogenism - androgenic tumors, congenital adrenal hyperplasia (17-OH-progesterone), thyroid disorders, hyperprolactinemia [22,1].

## DIFFERENTIAL DIAGNOSIS OF PCOS

The diagnosis of polycystic ovary syndrome (PCOS) requires careful exclusion of other endocrine and metabolic disorders that may mimic its clinical and biochemical features [1]. Several conditions can present with hyperandrogenism, menstrual irregularities, or infertility, making differential diagnosis essential for accurate diagnosis and appropriate management [2].

Endocrine disorders, such as Cushing’s syndrome and hyperprolactinemia, should be considered in the diagnostic work-up of women with suspected PCOS [1]. Cushing’s syndrome may present with menstrual disturbances and features including central obesity, purple striae, easy bruising, and proximal muscle weakness, while biochemical evaluation reveals cortisol excess, distinguishing it from PCOS [32]. Hyperprolactinemia, most commonly caused by pituitary adenomas, typically manifests as amenorrhea, galactorrhea, and elevated serum prolactin concentrations, features not characteristic of PCOS [33].

Congenital adrenal hyperplasia (CAH), particularly non-classic 21-hydroxylase deficiency, represents another important differential diagnosis, as it may present with hirsutism, acne, and ovulatory dysfunction similar to PCOS [34]. Measurement of basal and ACTH-stimulated 17-hydroxyprogesterone levels is essential for differentiation, as elevated concentrations are diagnostic for CAH [34]. Early identification is critical to avoid misdiagnosis and to ensure appropriate long-term management [34].

Hormone-secreting tumors of the adrenal glands or ovaries should be suspected in women presenting with rapid-onset hyperandrogenism or signs of virilization, such as deepening of the voice, clitoromegaly, or rapid progression of hirsutism [35]. These tumors are typically associated with markedly elevated androgen levels, including testosterone or dehydroepiandrosterone sulfate (DHEAS), and require prompt imaging studies for localization and management [35].

In clinical practice, a structured diagnostic approach incorporating detailed medical history, physical examination, targeted biochemical testing, and selective imaging enables effective differentiation between PCOS and alternative causes of hyperandrogenism and menstrual dysfunction [30,31]. Accurate differential diagnosis is crucial to guide appropriate therapy and to address potential underlying conditions with distinct prognostic and therapeutic implications [2].

## COMPLICATIONS OF POLYCYSTIC OVARY SYNDROME

Polycystic ovary syndrome is associated with a wide range of short- and long-term complications that extend beyond reproductive dysfunction and significantly affect overall health and quality of life [1]. These complications encompass reproductive, metabolic, cardiovascular, oncological, and psychological domains, underscoring the systemic nature of the disorder [2].

Phenotypic classification of polycystic ovary syndrome and associated clinical features are summarized in the Table 2 based on review data and international diagnostic approaches [7,16,52], taking into account the classification principles of the Rotterdam criteria and the Androgen Excess and PCOS Society [21,22].

*Table 2. Clinical phenotypes of polycystic ovary syndrome and associated risks*

PCOS phenotype	Reproductive manifestations	Metabolic risks	Psychological features	Clinical comments
Classic hyperandrogenic anovulatory phenotype	Chronic anovulation, marked menstrual irregularities, infertility	High prevalence of insulin resistance, obesity, increased risk of type 2 diabetes mellitus and cardiovascular disease	Frequent anxiety and depressive disorders, pronounced reduction in quality of life	The most severe clinical phenotype, requiring early detection and long term multidisciplinary follow up

Ovulatory hyperandrogenic phenotype	Relatively preserved ovulation, possible fertility impairment	Moderate metabolic disturbances, with risk increasing in the presence of weight gain	Psychological disturbances may occur but are usually less pronounced	Diagnosis is often delayed due to preserved menstrual cyclicity
Non hyperandrogenic anovulatory phenotype	Ovulatory dysfunction and reduced fertility	Variable metabolic risk, often associated with obesity	Psychological manifestations are nonspecific	Requires careful differential diagnosis to exclude other causes of anovulation
Phenotype with isolated polycystic ovarian morphology	Generally preserved fertility and regular menstrual cycles	Minimal or absent metabolic disturbances	Psychological disorders are not typical	Often an incidental ultrasound finding without independent clinical significance

## INFERTILITY

Infertility is one of the most prominent complications of PCOS and is primarily related to chronic anovulation and disordered folliculogenesis [1]. Women with PCOS account for a substantial proportion of cases of anovulatory infertility, although many retain good ovarian reserve and may respond favorably to ovulation induction when appropriately managed [36].

## METABOLIC DISORDERS

Metabolic complications are highly prevalent in women with PCOS and include insulin resistance, impaired glucose tolerance, type 2 diabetes mellitus, and dyslipidaemia [37]. Compared with age- and body mass index-matched controls, women with PCOS have a significantly increased risk of developing type 2 diabetes, independent of obesity, suggesting an intrinsic metabolic component of the syndrome [37,38]. Dyslipidaemia in PCOS is characterized by elevated triglycerides and low-density lipoprotein cholesterol, along with reduced high-density lipoprotein cholesterol, further contributing to cardiometabolic risk [39].

## CARDIOVASCULAR DISEASE

The clustering of metabolic abnormalities in PCOS translates into an increased burden of cardiovascular risk factors, including hypertension, endothelial dysfunction, and subclinical atherosclerosis [40]. While definitive evidence linking PCOS to increased cardiovascular mortality remains limited, observational studies consistently demonstrate an adverse cardiovascular risk profile in affected women, particularly with advancing age [40,41]. Consequently, early identification and management of modifiable risk factors are recommended in current clinical guidelines [2].

## RISK OF ENDOMETRIAL CANCER

Women with PCOS are at increased risk of endometrial hyperplasia and endometrial cancer, largely due to prolonged unopposed estrogen exposure resulting from chronic anovulation [42]. This risk is further amplified by obesity, insulin resistance, and hyperinsulinaemia, which exert proliferative effects on the endometrium [42,43]. Regular menstrual cycle regulation and endometrial protection are therefore key components of long-term management in women with PCOS [1].

## PSYCHOLOGICAL DISORDERS

Psychological and psychiatric complications represent an often under-recognized but clinically significant aspect of PCOS [44]. Women with PCOS exhibit higher prevalence rates of depression, anxiety disorders, eating disorders, and reduced health-related quality of life compared with the general population [44,45]. These disturbances are influenced by both biological factors, such as hyperandrogenism and insulin resistance, and psychosocial stressors related to body image, infertility, and chronic disease burden [2].

Overall, the diverse complications associated with PCOS highlight the importance of a comprehensive, lifelong approach to care that addresses reproductive, metabolic, cardiovascular, and psychological health in an integrated

## **THERAPEUTIC MANAGEMENT OF POLYCYSTIC OVARY SYNDROME**

The management of polycystic ovary syndrome (PCOS) is individualized and should be guided by the patient's primary concerns, including reproductive goals, metabolic risk, and symptoms of hyperandrogenism [1]. Current guidelines emphasize a comprehensive, long-term approach that integrates lifestyle interventions, pharmacological treatment, and fertility-directed therapies when indicated [2].

### **LIFESTYLE MODIFICATION**

Lifestyle modification represents the cornerstone of PCOS management, particularly in women with overweight or obesity [1]. Weight reduction through dietary interventions, regular physical activity, and behavioral strategies has been shown to improve insulin sensitivity, menstrual regularity, ovulation rates, and metabolic parameters, even with modest weight loss of 5–10% [46]. In addition to weight-related benefits, lifestyle interventions positively affect cardiovascular risk factors and overall quality of life [2].

### **PHARMACOLOGICAL TREATMENT**

Pharmacological therapy is tailored to specific symptoms and comorbidities and is frequently used in conjunction with lifestyle modification [1]. The choice of medication depends on the presence of menstrual dysfunction, hyperandrogenic symptoms, metabolic abnormalities, and fertility intentions [2].

### **HORMONAL THERAPY**

Combined oral contraceptives (COCs) are considered first-line pharmacological treatment for menstrual irregularities and hyperandrogenism in women not seeking pregnancy [1]. COCs suppress gonadotropin secretion, reduce ovarian androgen production, and increase sex hormone-binding globulin levels, thereby lowering free androgen concentrations [47]. Careful assessment of cardiometabolic risk is recommended prior to initiation, particularly in women with obesity or additional risk factors [2].

### **METFORMIN**

Metformin is widely used in PCOS, particularly in women with insulin resistance, impaired glucose tolerance, or type 2 diabetes mellitus [48,49]. Its primary mechanism involves improvement of insulin sensitivity, which may lead to secondary reductions in androgen levels and improvements in menstrual cyclicality [48]. Although metformin is not considered first-line therapy for hyperandrogenic symptoms, it plays an important role in metabolic risk reduction and may be beneficial in selected patients [1].

### **ANTIANDROGEN THERAPY**

Antiandrogen agents, such as spironolactone, are commonly used as adjunctive therapy for the treatment of hirsutism and acne when response to COCs is inadequate [50]. These agents inhibit androgen action at the receptor level or reduce androgen production but must be used with effective contraception due to the risk of teratogenicity [50]. Regular monitoring for adverse effects is recommended during long-term use [2].

### **INFERTILITY TREATMENT**

Management of infertility in women with PCOS primarily targets ovulation induction [36]. Letrozole is currently recommended as first-line pharmacological treatment for ovulation induction, as it has been shown to result in higher ovulation, pregnancy, and live birth rates compared with clomiphene citrate [36,51]. In cases of treatment resistance, gonadotropin therapy or assisted reproductive technologies may be considered, with careful monitoring to minimize the risk of ovarian hyperstimulation [36].

### **EMERGING AND NOVEL THERAPIES**

Emerging therapeutic strategies for PCOS focus on addressing underlying pathophysiological mechanisms, including insulin resistance, inflammation, and gut microbiota dysregulation [52]. Novel agents such as inositols, glucagon-like peptide-1 receptor agonists (GLP-1 RAs), and combination therapies have shown promise in improving metabolic and reproductive outcomes, although further high-quality trials are needed before widespread clinical adoption [52,53].

Overall, optimal management of PCOS requires a patient-centred, multidisciplinary approach that evolves over time in response to changing clinical priorities and life stages [30,31].

## **PCOS AND QUALITY OF LIFE**

Polycystic ovary syndrome significantly affects health-related quality of life (HRQoL), often to a greater extent than many other chronic endocrine disorders [1]. The impact of PCOS extends beyond physical symptoms and encompasses psychological well-being, social functioning, sexual health, and self-perception [54].

## **IMPACT ON MENTAL HEALTH**

Women with PCOS have a markedly increased prevalence of mood disorders, including depression and anxiety, compared with women without the condition [45]. Meta-analyses demonstrate that these associations persist even after adjustment for body mass index, suggesting that psychological distress in PCOS is not solely attributable to obesity [45,55]. Neuroendocrine abnormalities, insulin resistance, and hyperandrogenism may contribute biologically to altered mood regulation, while chronic disease burden further exacerbates mental health vulnerability [54].

## **PSYCHOSOCIAL ASPECTS**

Psychosocial stressors play a critical role in shaping the lived experience of PCOS [1]. Symptoms such as hirsutism, acne, weight gain, and infertility often lead to social stigma, reduced self-confidence, and impaired interpersonal relationships [56]. Delayed diagnosis and inconsistent information provided by healthcare professionals may further contribute to frustration, feelings of invalidation, and reduced trust in medical care [54].

## **SEXUALITY AND SELF-ESTEEM**

Sexual dysfunction and reduced sexual satisfaction have been reported more frequently in women with PCOS than in the general population [57]. Altered body image, low self-esteem, and concerns related to femininity and fertility can negatively affect sexual well-being and intimate relationships [57,58]. Addressing sexual health and self-esteem as part of routine PCOS care is therefore increasingly recognized as an essential component of patient-centred management [1].

## **CONTROVERSIES AND FUTURE DIRECTIONS IN PCOS RESEARCH**

Despite decades of research, PCOS remains a subject of ongoing debate regarding its definition, classification, and optimal management strategies [7]. These controversies reflect the syndrome's marked heterogeneity and the evolving understanding of its underlying mechanisms [5].

## **DIFFERENCES IN DIAGNOSTIC APPROACHES**

One of the most persistent controversies concerns the use of differing diagnostic criteria, particularly the Rotterdam criteria versus those emphasizing hyperandrogenism as a core feature [7]. Variability in diagnostic thresholds contributes to heterogeneity in research populations, complicates epidemiological comparisons, and may influence clinical decision-making [5]. Ongoing efforts aim to refine diagnostic frameworks to better reflect pathophysiological subtypes and long-term risk profiles [1].

## **PCOS AS A METABOLIC VERSUS REPRODUCTIVE DISORDER**

Traditionally considered a reproductive disorder, PCOS is increasingly recognized as a lifelong metabolic condition with reproductive manifestations [61]. This conceptual shift emphasizes the importance of early metabolic screening and long-term risk reduction, even in adolescents and women not seeking pregnancy [61,62]. However, balancing metabolic and reproductive priorities in clinical practice remains a challenge and a topic of active debate [5].

## **PERSONALIZED MEDICINE**

Advances in genomics, metabolomics, and phenotyping have renewed interest in personalized approaches to PCOS diagnosis and treatment [63]. Stratifying patients based on metabolic risk, androgen profile, and reproductive goals may enable more targeted interventions and improve treatment outcomes [63,64]. Nevertheless, translating these approaches into routine clinical practice requires robust validation and cost-effective implementation strategies [5].

## **FUTURE RESEARCH DIRECTIONS**

Future research priorities include the identification of reliable biomarkers, long-term prospective studies assessing cardiovascular outcomes, and high-quality trials evaluating novel therapeutic agents [64]. Greater emphasis on patient-reported outcomes and quality-of-life measures is also essential to ensure that research findings translate into meaningful clinical benefit [1]. Addressing these gaps will be critical for advancing the understanding and management of PCOS across the lifespan [59,64].

# **DISCUSSION**

Polycystic ovary syndrome remains a complex and heterogeneous condition that challenges traditional disease classifications and clinical management strategies [7]. The broad range of reproductive, metabolic, psychoemotional, and long term health consequences highlights the need to consider PCOS as a lifelong disorder rather than a condition limited to the reproductive period [2]. Accumulating evidence indicates that the syndrome evolves dynamically over time, with clinical priorities shifting from reproductive concerns in early adulthood to metabolic and cardiovascular risks later in life [61]. Taken together, this points to the need to move from an episodic, symptom oriented approach toward a long term follow up strategy that accounts for changing risks throughout a patient's life.

One of the key issues emphasized in contemporary literature is the pronounced phenotypic variability of polycystic ovary syndrome, which complicates diagnosis, risk stratification, and therapeutic decision making [59,60]. Differences in diagnostic criteria contribute to heterogeneity across clinical studies and population data, limit comparability of results, and may lead to under evaluation or delayed diagnosis in certain patient groups, particularly adolescents and women with normal body weight [5]. These factors underscore the importance of using standardized diagnostic approaches while maintaining the clinical flexibility required to account for individual patient characteristics [2]. From a practical perspective, phenotypic heterogeneity has direct clinical implications, as it is associated with differences in reproductive outcomes, metabolic risk, and the need for prolonged dynamic follow up.

From a therapeutic standpoint, current evidence supports an individualized and symptom oriented approach, in which lifestyle modification represents the foundation of management regardless of phenotype [1]. However, despite the availability of international evidence based guidelines, their implementation in routine clinical practice remains inconsistent, particularly with respect to long term metabolic monitoring and systematic assessment of psychoemotional status [2]. This gap between evidence and real world practice may contribute to suboptimal clinical outcomes and persistent patient dissatisfaction with treatment [45]. In this context, the formal application of diagnostic criteria without clinical interpretation that takes into account age, body composition, and metabolic characteristics appears insufficient.

Emerging data increasingly emphasize the importance of early intervention, especially in adolescents and young women, to reduce long term metabolic and cardiovascular risk [62]. At the same time, growing recognition of the psychosocial burden of polycystic ovary syndrome points to the need to integrate mental health assessment and appropriate support into standard care pathways, an area that remains insufficiently implemented in many healthcare systems [45]. Inadequate attention to psychoemotional aspects may negatively affect treatment adherence and long term outcomes. Taken together, these data highlight the necessity of a multidisciplinary model of care that addresses the full spectrum of disorders associated with polycystic ovary syndrome and reflects the realities of clinical practice [59,64].

This review has several limitations related to its narrative nature. The selection and analysis of sources were not conducted according to a formal systematic review protocol and did not include quantitative data synthesis, which limits the ability to objectively compare results across individual studies. The use of heterogeneous sources, including clinical studies, reviews, and guidelines, reflects the variability of the existing evidence base and may contribute to differences in interpretation. In addition, variations in diagnostic criteria and study design among the included publications limit the generalizability of certain conclusions. These limitations should be considered when interpreting the findings of this review and applying them in clinical practice.

## CONCLUSIONS

Polycystic ovary syndrome is a common and multifaceted endocrine disorder characterized by reproductive dysfunction, metabolic abnormalities, and significant psychological impact, with manifestations that extend across the lifespan. Accumulating evidence indicates that PCOS should no longer be regarded solely as a reproductive disorder but rather as a chronic condition associated with increased risks of infertility, type 2 diabetes mellitus, cardiovascular disease, endometrial pathology, and impaired quality of life. The marked heterogeneity of clinical phenotypes and variability in diagnostic criteria continue to pose challenges for timely diagnosis, effective risk stratification, and individualized management.

Effective care for women with PCOS requires a patient centred and multidisciplinary approach that integrates lifestyle modification as the cornerstone of therapy, supported by pharmacological treatment and fertility directed interventions when appropriate. Early identification of metabolic risk factors, regular monitoring of cardiometabolic health, and proactive prevention strategies are essential to reduce long term morbidity and improve overall outcomes. Equally important is recognition of the substantial psychological and psychosocial burden associated with PCOS, which necessitates routine screening for mood disorders and incorporation of mental health support into standard clinical practice.

Advances in understanding the pathophysiology of PCOS have highlighted the complex interplay between genetic susceptibility, hormonal dysregulation, insulin resistance, and environmental influences, yet many underlying mechanisms remain incompletely elucidated. Future research should focus on refining diagnostic frameworks,

improving phenotypic stratification, and identifying clinically reliable biomarkers, as well as on longitudinal evaluation of cardiometabolic outcomes, psychological trajectories, and long term treatment safety.

## DISCLOSURE

### AUTHORS' CONTRIBUTIONS

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Authors declare no conflicts of interest.

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