

Polycystic Ovary Syndrome (PCOS): A Comprehensive Review of Pathophysiology, Clinical Manifestations, Diagnosis, and Management

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Abstract: Polycystic ovary syndrome (PCOS) is a common hormonal and metabolic disorder that affects women of reproductive age and can have a significant impact on their reproductive health, metabolic function, and overall quality of life. The condition is characterized by a wide range of clinical features, including irregular menstrual cycles, excess androgen levels, acne, hirsutism, and difficulties with ovulation and fertility. Although the exact cause of PCOS remains unclear, its development is associated with a complex interaction of genetic, hormonal, environmental, and metabolic factors, particularly insulin resistance and altered androgen production. This review provides an overview of the pathophysiology, clinical manifestations, risk factors, diagnostic approaches, and current management strategies for PCOS. It discusses commonly used diagnostic criteria, including the NIH, Rotterdam, and Androgen Excess and PCOS Society criteria, while highlighting the importance of clinical assessment and excluding other conditions with similar symptoms. Management approaches include lifestyle modifications, such as a balanced diet and regular physical activity, as well as pharmacological treatments, including oral contraceptive pills, insulin sensitizers, and antiandrogen medications. Surgical interventions and assisted reproductive technologies may also be considered in selected cases, particularly when fertility is a concern. Since PCOS presents differently among individuals, treatment should be tailored to each woman's symptoms, metabolic health, and reproductive goals. A better understanding of this multifaceted condition, together with early recognition and appropriate management, may help reduce long-term complications and improve the quality of life of affected women. Further research is needed to clarify its underlying mechanisms and establish the long-term effectiveness and safety of emerging treatment options.

Keywords: Polycystic ovary syndrome (PCOS), insulin resistance, hyperandrogenism, reproductive health, hormonal imbalance, infertility, diagnostic criteria, lifestyle modification, pharmacological management, metabolic disorders

I. INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting women of reproductive age, with an estimated prevalence ranging from 8% to 13%. [1]. It is a major contributor to female infertility and is commonly associated with irregular menstrual cycles, excessive hair growth, acne, increased sebum production, hair thinning or loss, and obesity [2]. In 2006, the Androgen Excess Society (AES) formed a group of experts to review the available research on PCOS and make its diagnosis easier and clearer [3]. The link between PCOS and infertility has been widely studied, and PCOS is believed to contribute to about 40% of infertility cases in women [4]. It is estimated



that about 1 in 10 women develop PCOS before menopause and may experience related health problems [5]. Women with PCOS are at greater risk of developing health problems such as type 2 diabetes, high insulin levels, high blood pressure, abnormal cholesterol levels, heart and blood vessel diseases, fatty liver, infertility, and mood disorders. These complications can also negatively affect their quality of life and increase healthcare costs and the use of medical resources [6]. The pathophysiology of PCOS is a combination of genetic, environmental, and inherited factors. Therefore, women with PCOS may experience a range of related metabolic, reproductive, and psychological problems [7]. Although the underlying mechanisms of polycystic ovary syndrome (PCOS) have not been completely elucidated, its development is thought to be associated with genetic and epigenetic influences, insulin resistance, and disruptions in hormonal regulation [8]. PCOS can affect women throughout different stages of life and may lead to various health problems that negatively impact their quality of life. It can also contribute to significant health complications and increased risk of death among women of reproductive age [9]. A healthy diet and regular physical activity are important for making successful lifestyle changes. For women with PCOS, the amount of calories consumed, the types of nutrients in the diet, and the quality of food choices can affect body weight, insulin sensitivity, and levels of inflammation [10].

HISTORY

Over the past 170 years, scientific knowledge of polycystic ovary syndrome (PCOS) has advanced considerably, leading to a better understanding of its underlying mechanisms, clinical features, and management approaches. In 1844, doctors in France first described ovaries that were enlarged, had many small cysts, and were covered by a smooth outer layer [11]. From 1935 to the late 1970s, scientists mainly studied the hormonal causes of PCOS. In the last 20 years of the 20th century, researchers began to focus more on metabolic problems linked to PCOS, such as how the body processes sugar and insulin [12].

EPIDERMIOLOGY

A systematic review of 13 studies reported a slightly higher prevalence of polycystic ovarian syndrome among Black and Middle Eastern populations compared with Chinese and White populations [13]. PCOS is also common among Indian women of reproductive age, affecting approximately 9.13% of them [4]. The first international guidelines based on scientific evidence, published in 2018, highlighted several problems in diagnosing PCOS and understanding its etiology and epidemiology [14]. Insulin resistance is a common metabolic feature of polycystic ovary syndrome (PCOS), affecting up to 80% of women with the condition and reducing the body's ability to respond effectively to insulin [6]. 40% of teenage girls with irregular menstrual periods show polycystic ovaries on an ultrasound scan [15]. Studies show that about 1 in 10 women have PCOS before menopause. In the past, PCOS was thought to affect only adult women. However, recent research suggests that PCOS may have its origins before birth and can affect a person throughout their life [16].

CLINICAL MANIFESTITATIONS

The clinical manifestations of PCOS are diverse and vary among individuals, with patients presenting different combinations of signs and symptoms [17]. The intensity and presentation of PCOS-related symptoms can change over time, and individual women may experience different combinations of symptoms, with some not developing all the characteristic features of the condition [23].





- Menstrual periods may be heavy or prolonged, occur intermittently, follow an unpredictable pattern, or be completely absent for certain periods of time [18].
- Hyperandrogenism may manifest as excessive hair growth in areas such as the face, chest, and abdomen, a condition known as hirsutism [9].
- Oligomenorrhea (having periods less often than normal) is a clinical manifestation of PCOS [17].
- Impaired blood glucose regulation caused by insulin resistance [19].
- Women with PCOS are more likely to experience depression, anxiety, low self-esteem, negative feelings about their body, and difficulties with sexual health and relationships [11].
- Sleep Disturbances: Women with PCOS may experience sleep-related difficulties, such as insomnia and obstructive sleep apnea, which can reduce sleep quality and negatively influence overall health and well-being [23].
- Some women may develop excess body weight, which can be associated with hormonal imbalances and may worsen PCOS symptoms [25].

PCOS-Associated Risk Factors

- Women with PCOS are mainly classified into two groups: lean PCOS and obese PCOS. A small number of women with PCOS have a normal body mass index ($BMI \leq 25 \text{ kg/m}^2$) and are known as having lean PCOS. Recent research suggests that these women may also experience metabolic, hormonal, and hematological abnormalities like those observed in women with obesity-related PCOS, although these changes are generally less pronounced [11].
- Women with PCOS have a higher risk of developing impaired glucose tolerance (IGT), type 2 diabetes mellitus (T2DM), abnormal blood lipid levels (dyslipidemia), cardiovascular diseases, high blood pressure (hypertension), and metabolic syndrome later in life [4].
- Women with PCOS may have increased abdominal fat, which raises their risk of developing non-alcoholic fatty liver disease (NAFLD), a condition that can cause fat buildup, inflammation, and scarring in the liver [6].
- Sleep apnea, high cholesterol, and endometrial cancer are some health problems linked to PCOS. If not treated, PCOS can lead to serious health complications [2].
- Excessive consumption of sugary drinks, fructose-rich foods, trans fats, animal fats, and processed foods worsens pcod [18].
- In addition to causing hormonal imbalances, thyroid issues may raise the risk of PCOD or PCOS [23].



DIAGNOSIS

PCOS cannot be diagnosed through a single specific test. It is diagnosed by evaluating symptoms, medical history, physical examination, blood tests to check hormone levels, and ultrasound findings. Other medical conditions that may present with similar symptoms should be excluded before confirming a diagnosis of PCOS [5].

An ovary is considered polycystic when it contains 12 or more small follicles, each measuring 2–9 mm and has an ovarian volume greater than 10 mL. Some experts use 25 or more follicles as the criteria for better accuracy. Some women may have polycystic ovaries without experiencing any noticeable symptoms or clinical signs. Ultrasound is used to examine the ovaries, and an experienced ultrasonographer is required for accurate assessment. However, the presence of polycystic ovaries alone is not sufficient to diagnose PCOS [9].

PCOS is a complex hormonal disorder, and its symptoms vary from woman to woman.

Therefore, different criteria have been developed to diagnose the condition.

1. NIH/NICHD Criteria (1990)

According to these criteria, PCOS is diagnosed when the following conditions are present:

- Elevated androgen levels or clinical signs of androgen excess, such as excessive body or facial hair growth.
- Irregular or absent menstrual periods.
- Ruling out other endocrine disorders that may present with similar clinical symptoms.

2. Rotterdam Criteria (2003)

These criteria are widely used for diagnosing PCOS. A diagnosis requires the presence of at least two of the following three characteristics in a woman:

- Ovulatory Dysfunction: Abnormal or absent ovulation that can result in irregular menstrual periods or a complete absence of menstruation.
- Hyperandrogenism: Increased androgen levels in the blood or visible signs of excess androgens, such as excessive facial and body hair growth (hirsutism).
- Polycystic ovaries: An ultrasound showing an increased number of small follicles or enlarged ovarian volume.

Other disorders that can produce similar symptoms should be ruled out before establishing a diagnosis of PCOS.

3. Androgen Excess and PCOS Society (AE-PCOS) Criteria (2006)

According to these criteria, PCOS diagnosis requires:

- Hyperandrogenism: Increased androgen levels in the blood or physical signs of androgen excess, such as excessive facial and body hair growth (hirsutism).
- Ovarian dysfunction: Irregular ovulation or polycystic ovaries.
- Exclusion of other related hormonal disorders.

Among these criteria, the Rotterdam criteria are widely used because they consider the different ways PCOS can present in women. However, diagnosis requires proper clinical assessment, as symptoms vary from person to person [11].

Table: Comparison of Diagnostic Criteria for PCOS

Features	NIH Criteria (1990)	Rotterdam Criteria (2003)	AE-PCOS Criteria (2006)
Hyperandrogenism (HA)	Required; may be clinical or biochemical	One of the three diagnostic features	Required; may be clinical or biochemical
Ovulatory dysfunction (OD)	Required; irregular or absent ovulation	One of the three diagnostic features	Required as an alternative to polycystic ovarian morphology
Polycystic ovarian morphology (PCO)	Not required	One of the three diagnostic features; assessed by ultrasound	Required as an alternative to ovulatory dysfunction
Diagnostic requirements	Both HA and OD must be	At least two of the three	HA plus at least one of the



	present	features: HA, OD, or PCO.	following: OD or PCO
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Abbreviations: HA = Hyperandrogenism; OD = Ovulatory Dysfunction; PCO = Polycystic Ovarian Morphology.

MANAGEMENT

The management and choice of treatment depend on the patient and her needs. Goals of treatment may include improving fertility, regulating menstrual cycles, reducing weight, or managing symptoms of high androgen levels, such as acne, hirsutism, and androgenic alopecia. Therefore, treatment should be personalized to each individual to achieve the best results. Since no single treatment is suitable for all women with PCOS, treatment mainly focuses on managing individual symptoms [5].

Polycystic ovary syndrome has no known cure; meaning treatment focuses on ongoing management. The typical presentation often involves a combination of hirsutism, oligomenorrhea, and obesity.

To guide initial treatment, selecting a primary metabolic parameter is often effective. Because glucose intolerance significantly increases the risk of diabetes and serves as an independent cardiovascular risk factor for these individuals, it frequently serves as a key focus. Once initial therapy is established, additional targeted interventions for hirsutism or oligomenorrhea can be introduced based on individual response. Furthermore, contraception should be evaluated if pregnancy is not currently desired [18].

NON- PHARMACOLOGICAL TREATMENT

PCOS is a complex condition linked to poor lifestyle habits, genetics, and epigenetic elements, standing as a primary cause of female infertility, and it is no longer viewed as an isolated ovarian disorder [19].

Adopting healthy lifestyle changes serves as the foundational approach for effectively treating and managing Polycystic Ovary Syndrome (PCOS) [18].

A balanced diet, mindful eating, and regular physical activity are crucial parts. Striving for a minimum of 150 minutes of moderate-intensity workouts weekly matches the Physical Activity Guidelines for Americans, supporting heart health and symptom control in PCOS [8].

Carbohydrate Limitation: Excessive consumption of carbohydrate-rich foods can cause a rapid increase in blood glucose levels, stimulating the release of insulin. In contrast, complex carbohydrates are generally digested more slowly, helping to regulate blood sugar levels. Good sources of complex carbohydrates include fruits, whole grains, vegetables, peas, and cooked dried beans [19].

A lack of physical activity and a sedentary lifestyle may contribute to the worsening of PCOS symptoms. Excess body weight can also affect many women with PCOS by increasing insulin resistance and disturbing hormonal balance. Therefore, regular exercise and maintaining an active lifestyle are important for improving metabolic function, supporting hormonal balance, and promoting reproductive health in women with PCOS [24].

PHARMACOLOGICAL TREATMENT

ORAL CONTRACEPTIVE PILLS

For women who do not want to get pregnant, birth control pills are a common treatment option [20]. OCPs are safer due to lower endometrial cancer risks. They combine estrogen and progestogen to raise SHBG, lower LH and FSH, and decrease free testosterone and ovarian androgen production, making low-dose progestogen recommended. Reported side effects include hyperglycemia, impaired glucose metabolism, insulin resistance, and diabetes mellitus [4].

INSULIN SENSITIZERS

Metformin helps manage weight and metabolic health in adult women diagnosed with polycystic ovary syndrome who have a body mass index of 25.3 or higher. It may also enhance ovulation and live birth rates, although it proves less effective than letrozole or clomifene citrate. Nevertheless, to its affordable price and widespread accessibility,



metformin remains useful for boosting reproductive success among women with polycystic ovary syndrome, particularly within healthcare systems where fertility treatments are restricted [13].

Thiazolidinediones trigger fluid retention resulting in weight gain; meanwhile, metformin can result in weight loss [9].

SURGICAL INTERVENTION

Surgical intervention remains an alternative treatment for polycystic ovary syndrome (PCOS), although it is less commonly used. Laparoscopic ovarian drilling (LOD) and transvaginal hydrolaparoscopy (THL) are among the procedures performed to improve ovulation and increase the likelihood of pregnancy [21].

SUPPLEMENTS

Besides FDA-approved medications, various dietary supplements have been studied for their potential role in managing polycystic ovary syndrome (PCOS) and improving related symptoms. These include vitamin D, resveratrol, alpha-lipoic acid, omega-3 fatty acids, berberine, folic acid, myo-inositol (MI), and D-chiro-inositol (DCI). The effectiveness of these supplements may vary among individuals, and further research is needed to establish their safety and clinical benefits [5].

ANTIADROGENS

Medications containing cyproterone acetate (CPA) are used in the treatment of conditions associated with excessive androgen activity. CPA acts as an anti-androgen by blocking androgen receptors and reducing the effects of male hormones. It also has progestogenic properties, which help regulate the menstrual cycle and protect the endometrium when used appropriately. CPA is commonly combined with an estrogen in certain treatments to enhance therapeutic effects and help maintain hormonal balance [22].

ASSISTED REPRODUCTIVE TECHNOLOGY

Assisted Reproductive Technology (ART) is commonly used to help women with PCOS who have difficulty becoming pregnant. In this treatment, hormones called gonadotropins are given to stimulate the ovaries to produce multiple follicles. However, this treatment may cause a condition called ovarian hyperstimulation syndrome (OHSS), in which the ovaries become overstimulated. To reduce this risk, in-vitro maturation (IVM) may be used, in which immature eggs are matured outside the body. Studies comparing IVM with traditional in vitro fertilization (IVF) have shown comparable results with both methods [4].

II. CONCLUSION

Polycystic ovary syndrome (PCOS) is a complex hormonal and metabolic condition that can affect women throughout their reproductive years and may have long-term implications for their overall health. PCOS can present differently in different women, with symptoms that may include irregular menstrual cycles, excess androgen levels, metabolic abnormalities, and problems with ovulation and fertility. Because of this variability, early recognition, appropriate diagnosis, and individualized management are important for improving health outcomes. Management strategies may include lifestyle modifications, pharmacological treatment, and fertility-related interventions, depending on the individual's symptoms, metabolic status, and reproductive goals. Although several treatment options are available, no single approach is suitable for every patient. Further research is needed to clarify the underlying mechanisms of PCOS and evaluate the long-term effectiveness and safety of emerging therapies. A comprehensive approach that combines evidence-based medical care, ongoing monitoring, and patient education can help address the diverse needs of women living with PCOS and support better long-term health and quality of life.



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