

POLYCYSTIC OVARY SYNDROME: MODERN INSIGHTS INTO PATHOGENESIS AND CLINICAL MANAGEMENT

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Abstract: Polycystic Ovary Syndrome (PCOS) is a complex chronic endocrine disorder characterized by ovulatory dysfunction, hyperandrogenism, and polycystic ovarian morphology. It affects approximately 5–20% of women of reproductive age worldwide, making it one of the most common causes of infertility and metabolic disturbances in women. PCOS is associated not only with reproductive dysfunction but also with metabolic, cardiovascular, and psychological complications. This paper discusses the latest insights into the pathogenesis, classification, clinical manifestations, and management of PCOS, emphasizing the multifactorial nature of the syndrome and its long-term health implications.

Introduction

Polycystic Ovary Syndrome (PCOS), also known as Stein–Leventhal Syndrome, remains a major public health issue due to its high prevalence and complex pathophysiology. The syndrome is clinically heterogeneous, and its diagnosis is typically based on the **Rotterdam criteria (2003)**, which require the presence of at least two of the following features:

1. Clinical or biochemical hyperandrogenism,
2. Ovulatory dysfunction (oligo- or anovulation),
3. Polycystic ovarian morphology on ultrasound.

In recent years, research has focused on the interaction between **genetic, metabolic, and neuroendocrine** factors contributing to the onset and progression of PCOS.

Pathogenesis of PCOS

The pathogenesis of PCOS is multifactorial, involving disturbances in the **hypothalamic–pituitary–ovarian axis, insulin resistance, and genetic predisposition**.

1. Neuroendocrine Regulation

Abnormal secretion of gonadotropin-releasing hormone (GnRH) leads to increased luteinizing hormone (LH) pulsatility and decreased follicle-stimulating hormone (FSH) levels. This imbalance enhances ovarian androgen production, which disrupts follicular development and prevents normal ovulation.

2. Insulin Resistance and Metabolic Factors

Approximately 70–80% of women with PCOS exhibit varying degrees of insulin resistance, regardless of body mass index. Hyperinsulinemia promotes ovarian androgen synthesis and reduces the production of sex hormone-binding globulin (SHBG) in the liver, leading to elevated free testosterone

levels. Insulin resistance also contributes to the development of metabolic syndrome, type 2 diabetes mellitus, and cardiovascular diseases.

3. Genetic and Epigenetic Factors

Recent genome-wide association studies (GWAS) have identified several genes associated with PCOS, including **FSHR**, **LHCGR**, **DENND1A**, and **INSR**. These genes are involved in gonadotropin signaling, androgen biosynthesis, and insulin receptor function. Family studies show that the risk of PCOS is 30–50% higher among first-degree relatives, confirming its hereditary component.

Clinical Features

The clinical presentation of PCOS varies among patients but commonly includes:

- **Menstrual irregularities** (oligomenorrhea or amenorrhea),
- **Hyperandrogenic symptoms** such as hirsutism, acne, and androgenic alopecia,
- **Obesity or central adiposity**,
- **Infertility** due to chronic anovulation,
- **Psychological disturbances**, including depression, anxiety, and eating disorders.

Notably, up to 20% of women with PCOS may have regular menstrual cycles but still lack ovulation, highlighting the importance of hormonal assessment and ultrasound for accurate diagnosis.

Classification of PCOS Phenotypes

According to the Rotterdam criteria, PCOS can be divided into four main phenotypes:

1. **Classic phenotype (A):** Hyperandrogenism + ovulatory dysfunction + polycystic ovaries,
2. **Ovulatory phenotype (B):** Hyperandrogenism + polycystic ovaries,
3. **Non-hyperandrogenic phenotype (C):** Ovulatory dysfunction + polycystic ovaries,
4. **Anovulatory phenotype (D):** Hyperandrogenism + ovulatory dysfunction.

Each phenotype may have distinct metabolic and reproductive outcomes, requiring individualized management strategies.

Complications and Long-Term Consequences

PCOS is associated with a wide range of complications:

- **Metabolic syndrome and type 2 diabetes mellitus**,
- **Dyslipidemia and hypertension**,
- **Non-alcoholic fatty liver disease (NAFLD)**,
- **Endometrial hyperplasia and carcinoma**,
- **Obstructive sleep apnea**,
- **Cardiovascular disease**,

- **Depression and anxiety disorders.**

Insulin resistance is a central mechanism linking PCOS to these metabolic and cardiovascular complications. Moreover, chronic anovulation and unopposed estrogen exposure increase the risk of endometrial hyperplasia and cancer.

Modern Approaches to Management

The management of PCOS requires a **multidisciplinary approach** aimed at controlling hyperandrogenism, restoring ovulation, and preventing metabolic complications.

1. Lifestyle Modification

- Weight reduction through a balanced diet and regular physical activity remains the cornerstone of PCOS management.
- Even a 5–10% reduction in body weight can improve insulin sensitivity, menstrual regularity, and fertility outcomes.

2. Pharmacological Treatment

- **Combined oral contraceptives (COCs)** are used to regulate menstrual cycles and reduce androgenic symptoms.
- **Metformin** improves insulin sensitivity and restores ovulatory function.
- **Anti-androgenic agents** (e.g., spironolactone) may be used to reduce hirsutism and acne.
- **Clomiphene citrate** or **letrozole** are first-line agents for ovulation induction in women seeking pregnancy.

3. Psychological and Reproductive Support

- Given the high prevalence of anxiety and depressive disorders, psychological counseling and cognitive-behavioral therapy (CBT) should be part of the management plan.
- Assisted reproductive technologies (ART), including IVF, are recommended for cases resistant to medical ovulation induction.

Conclusion

PCOS remains one of the most common and multifactorial endocrine disorders in women, with significant reproductive, metabolic, and psychological implications. Recent advances in molecular biology and endocrinology have improved our understanding of its pathogenesis, yet early diagnosis and personalized management remain critical for reducing long-term complications. Integrating lifestyle interventions, pharmacotherapy, and mental health support offers the best outcomes for women with PCOS.

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