



POLYCYSTIC OVARY SYNDROME (PCOS): HORMONAL IMBALANCE AND REPRODUCTIVE HEALTH

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Abstract: Polycystic Ovary Syndrome (PCOS) is a complex endocrine disorder that affects a significant proportion of women of reproductive age worldwide. Characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology, PCOS has broad systemic implications, including metabolic, reproductive, and psychological effects. This comprehensive review elaborates on the multifactorial etiology, pathophysiology, clinical phenotypes, advanced diagnostic methods, current and emerging treatment options, and the psychosocial impact of PCOS. Understanding the heterogeneous nature of PCOS is essential for personalized treatment and improving patient outcomes.

Keywords: Polycystic Ovary Syndrome, hormonal imbalance, reproductive dysfunction, hyperandrogenism, insulin resistance, ovulatory disorders, polycystic ovarian morphology, menstrual irregularities, infertility, metabolic syndrome, anti-androgen therapy, ovulation induction, metformin treatment, lifestyle modification, cardiovascular risk.

Introduction

PCOS is recognized as one of the most common endocrine disorders affecting women aged 15-44 years, with a prevalence estimated between 8% and 20%, varying by diagnostic criteria and population studied. It is a leading cause of female infertility and is associated with metabolic syndrome components such as insulin resistance, dyslipidemia, and increased cardiovascular risk. Despite extensive research, the precise pathogenesis of PCOS remains incompletely understood, given its heterogeneous clinical presentations.

The syndrome was first described in 1935 by Stein and Leventhal, but modern insights have vastly expanded knowledge of its hormonal, genetic, metabolic, and psychosocial dimensions. This article aims to provide an in-depth understanding of PCOS by discussing its pathogenesis, clinical features, diagnostic challenges, and therapeutic strategies.

Etiology and Pathogenesis. Genetic and Epigenetic Factors. PCOS has a strong familial aggregation, suggesting a genetic predisposition. Genome-wide association studies (GWAS) have identified several susceptibility loci related to metabolic and reproductive functions, such as the DENND1A, THADA, and FSHR genes. However, no single gene explains all cases,

indicating polygenic inheritance and gene-environment interactions.

Epigenetic mechanisms, including DNA methylation and histone modifications, also contribute to PCOS pathophysiology by affecting gene expression related to steroidogenesis and insulin signaling. Environmental factors during fetal development, such as androgen exposure in utero, may epigenetically program susceptibility to PCOS later in life.

Hormonal Dysregulation: The hallmark of PCOS is hyperandrogenism, caused by excessive ovarian and adrenal androgen production. Elevated luteinizing hormone (LH) pulsatility and altered LH to follicle-stimulating hormone (FSH) ratio disrupt follicular maturation, resulting in anovulation. Insulin resistance exacerbates hyperandrogenism by stimulating ovarian theca cells and decreasing sex hormone-binding globulin (SHBG) production, increasing free circulating androgens.

Increased anti-Müllerian hormone (AMH) levels, produced by granulosa cells, contribute to follicular arrest and polycystic ovarian morphology. Moreover, dysregulation of the hypothalamic-pituitary-ovarian axis plays a crucial role.

Metabolic Abnormalities

Insulin resistance, observed in approximately 50-70% of PCOS patients, is a central metabolic defect independent of obesity. It leads to compensatory hyperinsulinemia, which worsens androgen excess and increases cardiovascular risk factors such as dyslipidemia and hypertension.

Adipose tissue dysfunction, chronic low-grade inflammation, and altered adipokine profiles (e.g., decreased adiponectin) further exacerbate metabolic derangements in PCOS.

Clinical Phenotypes: The Rotterdam criteria define four phenotypes based on the presence or absence of hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology: Phenotype A: Hyperandrogenism + oligo/anovulation + polycystic ovaries (classic PCOS). Phenotype B: Hyperandrogenism + oligo/anovulation. Phenotype C: Hyperandrogenism + polycystic ovaries. Phenotype D: Oligo/anovulation + polycystic ovaries (non-hyperandrogenic). Phenotypes differ in metabolic risk, with Phenotype A showing the highest risk of insulin resistance and cardiovascular complications.

Reproductive Manifestations

Menstrual irregularities: oligomenorrhea or amenorrhea.

Anovulatory infertility.

Polycystic ovarian morphology on ultrasound: ≥ 12 follicles measuring 2-9 mm or increased ovarian volume $> 10 \text{ cm}^3$. Increased miscarriage rates and pregnancy complications such as gestational diabetes

Hyperandrogenic Signs: Hirsutism, assessed by the modified Ferriman-Gallwey score. Acne vulgaris, Androgenic alopecia, Metabolic and Cardiovascular Features

Central obesity and increased waist-to-hip ratio, Insulin resistance and impaired glucose tolerance. Dyslipidemia (elevated triglycerides, decreased HDL cholesterol)

Hypertension and endothelial dysfunction, Increased risk of type 2 diabetes mellitus and cardiovascular disease

Psychological Impact

Women with PCOS have increased prevalence of mood disorders, including anxiety, depression, and eating disorders. The chronic nature of symptoms and cosmetic concerns can significantly reduce quality of life.

Diagnostic Approach

Diagnosis involves excluding other causes of hyperandrogenism and ovulatory dysfunction.

1. Biochemical Tests
2. Total and free testosterone
3. Androstenedione, dehydroepiandrosterone sulfate (DHEAS)
4. LH and FSH ratio
5. SHBG: Fasting glucose, insulin, and lipid profile

Imaging: Transvaginal ultrasound remains the gold standard for assessing polycystic ovarian morphology.

1. Differential Diagnoses
2. Thyroid dysfunction
3. Hyperprolactinemia
4. Non-classic congenital adrenal hyperplasia
5. Cushing's syndrome
6. Androgen-secreting tumors
7. Treatment Modalities
8. Lifestyle Modifications

First-line therapy for overweight and obese women with PCOS includes dietary changes, weight loss, and increased physical activity. Even modest weight loss (5-10%) improves menstrual regularity, insulin sensitivity, and androgen levels.

Pharmacological Interventions

Combined Oral Contraceptives (COCs): Suppress LH secretion, reduce ovarian androgen production, and increase SHBG.

Insulin Sensitizers: Metformin improves insulin sensitivity and may restore ovulation. Inositols (myo-inositol, D-chiro-inositol) show promise as adjunctive treatments.

Anti-androgens: Spironolactone, flutamide, and finasteride treat hirsutism and acne but require contraception due to teratogenicity. Ovulation Induction: Letrozole is now preferred over clomiphene citrate for ovulation induction due to higher pregnancy rates. Gonadotropins or laparoscopic ovarian drilling may be used in resistant cases.

Assisted Reproductive Technologies: In vitro fertilization (IVF) is reserved for women who do not respond to medical ovulation induction or have additional infertility factors.

Psychological Support.

Cognitive behavioral therapy and counseling help manage anxiety, depression, and improve body image and adherence to treatment.

Long-Term Health Risks.

PCOS is associated with an increased risk of: Type 2 diabetes mellitus (requiring regular glucose monitoring), Endometrial hyperplasia and carcinoma (due to chronic anovulation and unopposed estrogen exposure)

Cardiovascular disease:

Sleep apnea, particularly in obese patients.

Emerging Research and Future Directions.

Ongoing research aims to: Define PCOS phenotypes for personalized medicine approaches, Explore genetic and epigenetic therapies Identify novel biomarkers for early diagnosis and treatment response

Understand the role of gut microbiota and inflammation in PCOS pathogenesis.

Conclusion

PCOS is a heterogeneous syndrome with complex endocrine, metabolic, and psychological components. Comprehensive understanding and multidisciplinary management are vital for improving reproductive outcomes and reducing long-term health risks. Tailored interventions, combining lifestyle, pharmacological, and psychological therapies, optimize patient care.

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