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Review Article

Polycystic Ovarian Disease (PCOD): A Comprehensive Review

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Polycystic Ovarian Disease (PCOD) is one of the most prevalent endocrine and metabolic disorders affecting women of reproductive age worldwide. It is characterized by hormonal imbalance, irregular menstrual cycles, ovarian cyst formation, hyperandrogenism, and metabolic disturbances such as insulin resistance and obesity. The exact etiology of PCOD remains multifactorial, involving genetic, environmental, hormonal, and lifestyle-related factors. Women with PCOD commonly present with symptoms including menstrual irregularities, infertility, acne, hirsutism, weight gain, and psychological disturbances such as anxiety and depression. Early diagnosis and appropriate management are essential to prevent long-term complications, including type 2 diabetes mellitus, cardiovascular disorders, metabolic syndrome, and endometrial abnormalities. Diagnostic approaches generally involve clinical evaluation, hormonal assessment, ultrasonography, and established criteria such as the Rotterdam criteria. Management strategies focus on lifestyle modifications, pharmacological interventions, hormonal therapies, insulin sensitizers, and fertility treatments depending on symptom severity and reproductive goals. Recent advancements in understanding the pathophysiology of PCOD have emphasized personalized treatment approaches and preventive healthcare strategies. This comprehensive review highlights the epidemiology, etiology, pathophysiology, clinical manifestations, diagnostic criteria, treatment modalities, complications, and recent therapeutic advances in PCOD, aiming to provide a better understanding of the disease and improve patient outcomes.

Keywords: PCOD, PCOS, Hyperandrogenism, Insulin resistance, Ovarian dysfunction, Herbal therapy, Nanotechnology, Drug delivery.

INTRODUCTION

Polycystic ovarian disease (PCOD), often interchangeably referred to in the literature as **Polycystic Ovary Syndrome**, represents one of the most common and complex endocrine-metabolic disorders affecting women during their reproductive years. It is characterized by a constellation of reproductive, endocrine, metabolic, and psychological abnormalities, including chronic anovulation, menstrual irregularities, hyperandrogenism, polycystic ovarian morphology, obesity, insulin resistance, infertility, and emotional disturbances. The condition is considered a heterogeneous syndrome due to the wide variation in clinical manifestations, severity, and long-term complications among affected individuals. This heterogeneity makes diagnosis and management particularly challenging for clinicians and researchers. The syndrome was first described in 1935 by Irving F. Stein Sr. and Michael L. Leventhal, who reported a series of women presenting with amenorrhea, infertility, and enlarged polycystic ovaries, subsequently termed Stein-Leventhal syndrome. Since this initial description, scientific understanding of the disorder has evolved substantially. What was once regarded as a purely gynecological condition is now recognized as a multisystem endocrine and metabolic disorder with lifelong implications extending beyond reproductive health. Globally, PCOD affects approximately 6–20% of women of reproductive age depending on the

diagnostic criteria applied, such as the European Society of Human Reproduction and Embryology/American Society for Reproductive Medicine Rotterdam criteria, the National Institutes of Health criteria, or the Androgen Excess and PCOS Society criteria [3]. The prevalence appears to be particularly high in South Asian populations, including India, where rapid urbanization, sedentary lifestyles, altered dietary patterns, and genetic susceptibility contribute significantly to disease incidence. The increasing prevalence among adolescent girls has emerged as a major public health concern due to its potential impact on future fertility and metabolic health. The pathophysiology of PCOD is multifactorial and incompletely understood, involving intricate interactions between genetic, epigenetic, hormonal, metabolic, and environmental factors. Central to its pathogenesis is dysfunction of the hypothalamic-pituitary-ovarian (HPO) axis, which leads to increased secretion of luteinizing hormone (LH) relative to follicle-stimulating hormone (FSH), promoting ovarian androgen overproduction. Hyperandrogenism disrupts normal follicular maturation and ovulation, resulting in the accumulation of immature follicles that appear as cysts on ultrasonography. Insulin resistance is another hallmark feature observed in a majority of women with PCOD, independent of obesity status. Hyperinsulinemia resulting from insulin resistance amplifies ovarian androgen synthesis and suppresses hepatic production of sex hormone-binding globulin (SHBG), thereby increasing circulating free androgen levels. This interaction between insulin resistance and hyperandrogenism establishes a vicious cycle that perpetuates disease progression. Additionally, chronic low-grade inflammation and oxidative stress have been implicated in the pathogenesis of PCOD, contributing to both reproductive and metabolic dysfunction.

2. Overview of Polycystic Ovarian Disease (PCOD)

Polycystic Ovarian Disease (PCOD) is a complex endocrine and metabolic disorder characterized by hormonal imbalance, ovarian dysfunction, and impaired ovulation. It primarily affects women during their reproductive years and is considered one of the leading causes of menstrual irregularities, infertility, and hyperandrogenism. The disorder results from abnormal ovarian function in which multiple immature follicles accumulate within the ovaries due to incomplete follicular maturation and failure of ovulation. These immature follicles appear as multiple small cyst-like structures on ultrasonographic examination, although they are not true pathological cysts. PCOD is regarded as a heterogeneous disorder because its clinical presentation varies considerably among affected individuals. Some women predominantly experience reproductive symptoms such as irregular menstruation and infertility, while others mainly exhibit metabolic abnormalities including obesity, insulin resistance, dyslipidemia, and impaired glucose tolerance. Dermatological manifestations such as acne, hirsutism, oily skin, and androgenic alopecia are also common due to excessive androgen production. The disorder develops through the interaction of multiple factors including genetic susceptibility, endocrine abnormalities, insulin resistance, environmental influences, and unhealthy lifestyle habits. Elevated androgen levels interfere with normal follicular development, preventing the release of mature ova from the ovaries. Simultaneously, insulin resistance and compensatory hyperinsulinemia further stimulate androgen production, creating a cycle that perpetuates hormonal imbalance and ovarian dysfunction. Normally, during each menstrual cycle, several ovarian follicles begin to mature under the influence of follicle-stimulating hormone (FSH). One dominant follicle eventually releases a mature ovum during ovulation. In women with PCOD, this maturation process is disrupted due to hormonal disturbances. As a result, ovulation either occurs infrequently or fails completely, causing immature follicles to accumulate around the ovarian cortex and giving the ovaries a characteristic "string of pearls" appearance on ultrasound imaging. PCOD not only affects reproductive health but also has significant metabolic and cardiovascular implications. Women with the condition have an increased risk of developing obesity, metabolic syndrome, hypertension, dyslipidemia, impaired glucose tolerance, type 2 diabetes mellitus, and cardiovascular diseases later in life. Chronic anovulation also increases the risk of endometrial hyperplasia and endometrial carcinoma due to prolonged exposure of the endometrium to unopposed estrogen. The disorder significantly impacts psychological well-being.

Cosmetic concerns such as acne, obesity, excessive facial hair, and hair loss often lead to anxiety, depression, low self-esteem, emotional distress, and reduced quality of life. Infertility associated with chronic anovulation further contributes to psychological burden and social challenges in many affected women. Although PCOD and Polycystic Ovary Syndrome (PCOS) are frequently used interchangeably, they differ slightly in clinical interpretation. PCOD generally refers to ovarian dysfunction characterized by the presence of multiple immature follicles and hormonal imbalance, whereas PCOS is considered a broader endocrine syndrome involving reproductive, metabolic, and hormonal abnormalities. Nevertheless, both conditions share several clinical features and management strategies. The diagnosis of PCOD requires comprehensive clinical evaluation supported by laboratory investigations and imaging studies. Assessment includes menstrual history, physical examination, hormonal profiling, metabolic evaluation, and pelvic ultrasonography. Since symptoms may overlap with other endocrine disorders, differential diagnosis is essential to exclude conditions such as thyroid dysfunction, hyperprolactinemia, congenital adrenal hyperplasia, and androgen-secreting tumors. Management of PCOD focuses on correcting hormonal imbalance, restoring ovulation, improving metabolic health, alleviating symptoms, and preventing long-term complications. Lifestyle modification, including weight reduction, regular physical activity, balanced nutrition, stress management, and adequate sleep, remains the cornerstone of therapy. Pharmacological treatment is individualized based on the patient's age, symptoms, reproductive goals, and associated metabolic abnormalities. As research continues to advance, greater understanding of the molecular and genetic mechanisms underlying PCOD has facilitated the development of targeted therapeutic approaches. Early diagnosis, multidisciplinary management, patient education, and regular follow-up are essential for improving both reproductive outcomes and overall long-term health.

3. Epidemiology and Global Burden of Polycystic Ovarian Disease (PCOD)

Polycystic Ovarian Disease (PCOD) is among the most prevalent endocrine disorders affecting women of reproductive age worldwide. It represents a significant public health challenge because of its high prevalence, chronic nature, reproductive consequences, metabolic complications, and psychosocial impact. The disorder affects women across all ethnicities, socioeconomic groups, and geographical regions, although its prevalence varies depending on the diagnostic criteria used and the characteristics of the study population. Globally, PCOD is estimated to affect approximately 6–20% of women of reproductive age. Variations in prevalence are attributed to differences in genetic background, ethnicity, environmental influences, dietary habits, obesity rates, lifestyle patterns, and diagnostic approaches. Urbanization, sedentary lifestyles, unhealthy dietary practices, and increasing obesity have contributed to a steady rise in the number of affected individuals over recent decades. The condition commonly develops during adolescence, often becoming apparent soon after menarche when menstrual cycles fail to become regular. However, many women remain undiagnosed until adulthood when they seek medical attention for infertility, menstrual irregularities, or cosmetic concerns. Delayed diagnosis is common because early symptoms may be mild, nonspecific, or mistakenly considered part of normal pubertal development. The prevalence of PCOD is generally higher among overweight and obese women compared with those having normal body weight. Excess adipose tissue worsens insulin resistance and hormonal imbalance, thereby increasing disease severity and associated metabolic complications. Nevertheless, lean women may also develop PCOD, indicating that obesity is an aggravating rather than a primary causative factor. Ethnic differences influence both the prevalence and clinical presentation of PCOD. Women from South Asian, Middle Eastern, Hispanic, and certain Mediterranean populations tend to exhibit a higher frequency of insulin resistance, central obesity, and metabolic syndrome compared with women from other populations. Such variations emphasize the importance of considering ethnicity during diagnosis and treatment planning. Beyond reproductive health, PCOD contributes substantially to the global burden of chronic non-communicable diseases. Women with the disorder have an increased lifetime risk of

infertility, pregnancy-related complications, gestational diabetes mellitus, hypertension, type 2 diabetes mellitus, dyslipidemia, cardiovascular disease, non-alcoholic fatty liver disease, obstructive sleep apnea, and endometrial disorders. These associated conditions increase healthcare utilization and long-term medical costs. The psychosocial burden of PCOD is equally significant. Depression, anxiety, stress, eating disorders, body image dissatisfaction, reduced self-confidence, and impaired quality of life are frequently reported among affected women. These psychological issues often coexist with reproductive and metabolic complications, highlighting the need for comprehensive multidisciplinary care. Increasing awareness, early screening of high-risk individuals, patient education, lifestyle intervention programs, and improved access to healthcare services are essential strategies for reducing the global burden of PCOD. Continued epidemiological research is necessary to better understand regional variations, identify emerging risk factors, and develop effective preventive and management strategies.

4. Etiology and Risk Factors of Polycystic Ovarian Disease (PCOD)

Polycystic Ovarian Disease (PCOD) is a multifactorial disorder that develops through the interaction of genetic, hormonal, metabolic, environmental, and lifestyle factors. Although the exact cause remains unknown, current evidence suggests that multiple mechanisms contribute to ovarian dysfunction, hyperandrogenism, insulin resistance, and chronic anovulation. These factors act synergistically, resulting in hormonal imbalance and the characteristic clinical manifestations of the disease.

4.1 Genetic Factors

Genetic predisposition plays an important role in the development of PCOD. Women with a family history of PCOD, type 2 diabetes mellitus, obesity, or metabolic syndrome have a higher likelihood of developing the disorder. Several genes involved in steroid hormone synthesis, insulin signaling, gonadotropin regulation, inflammation, and ovarian follicular development have been implicated. The inheritance pattern is considered polygenic, meaning that multiple genes collectively influence disease susceptibility. Genetic abnormalities may alter ovarian steroidogenesis, insulin receptor function, and androgen metabolism, predisposing susceptible individuals to hormonal disturbances. However, genetic predisposition alone is insufficient to cause PCOD, and environmental triggers are often required for disease expression.

4.2 Hormonal Imbalance

Hormonal dysregulation is the hallmark of PCOD. Increased secretion of luteinizing hormone (LH) stimulates excessive androgen production by ovarian theca cells. At the same time, relatively lower follicle-stimulating hormone (FSH) levels impair maturation of ovarian follicles, preventing normal ovulation. Elevated androgen concentrations inhibit follicular development and contribute to symptoms such as acne, hirsutism, androgenic alopecia, and menstrual irregularities. Increased insulin levels further enhance androgen production, thereby worsening endocrine dysfunction.

4.3 Insulin Resistance and Hyperinsulinemia

Insulin resistance is one of the most significant metabolic abnormalities associated with PCOD. Body tissues become less responsive to insulin, prompting the pancreas to produce higher amounts of insulin to maintain normal blood glucose levels. Hyperinsulinemia promotes ovarian androgen synthesis and suppresses hepatic production of sex hormone-binding globulin (SHBG), leading to increased circulating free testosterone. This hormonal imbalance contributes to anovulation, infertility, obesity, and metabolic syndrome. Insulin resistance may occur in both obese and lean women, although it is generally more severe in obese individuals.

4.4 Obesity and Lifestyle Factors

Obesity is not the primary cause of PCOD but significantly aggravates its clinical manifestations. Excess adipose tissue contributes to insulin resistance, chronic inflammation, hormonal imbalance, and increased androgen production. Central or abdominal obesity is particularly associated with metabolic complications. Lifestyle factors such as sedentary behavior, excessive consumption of calorie-rich

processed foods, irregular eating habits, inadequate sleep, and psychological stress further increase the risk of developing PCOD and worsen disease severity. Regular physical activity and healthy dietary habits are therefore essential components of prevention and management.

4.5 Environmental Factors

Environmental exposures are increasingly recognized as contributing factors in PCOD. Exposure to endocrine-disrupting chemicals, environmental pollutants, pesticides, plastics containing bisphenol A (BPA), and certain industrial chemicals may interfere with normal hormonal regulation and ovarian function. Urbanization, changing dietary patterns, reduced physical activity, and chronic psychosocial stress have also been associated with the increasing prevalence of PCOD worldwide.

4.6 Chronic Low-Grade Inflammation

Women with PCOD frequently exhibit chronic low-grade systemic inflammation characterized by increased production of inflammatory cytokines and oxidative stress. Persistent inflammation interferes with insulin signaling, ovarian steroidogenesis, and follicular maturation. Inflammatory mediators contribute to endothelial dysfunction, cardiovascular risk, and metabolic disturbances while further aggravating insulin resistance and hyperandrogenism.

4.7 Oxidative Stress

Oxidative stress results from an imbalance between reactive oxygen species (ROS) and antioxidant defense mechanisms. Increased oxidative stress damages ovarian tissue, disrupts follicular development, impairs oocyte quality, and contributes to infertility. It also promotes insulin resistance and chronic inflammation, creating a vicious cycle that accelerates disease progression.

4.8 Psychological Stress

Chronic psychological stress activates the hypothalamic-pituitary-adrenal (HPA) axis, leading to increased cortisol secretion. Elevated cortisol influences glucose metabolism, appetite regulation, fat accumulation, and reproductive hormone secretion. Stress-related hormonal disturbances may worsen menstrual irregularities, ovulatory dysfunction, and metabolic abnormalities while negatively affecting treatment adherence and quality of life.

Table 4.1: Major Etiological Factors Associated with PCOD

Etiological Factor	Mechanism	Clinical Consequences
Genetic predisposition	Altered hormone regulation and insulin signaling	Increased susceptibility to PCOD
Hormonal imbalance	Increased LH, decreased FSH, elevated androgens	Anovulation, infertility, acne, hirsutism
Insulin resistance	Hyperinsulinemia increases androgen production	Obesity, diabetes, metabolic syndrome
Obesity	Increased adipose tissue and inflammation	Worsened insulin resistance and hormonal imbalance
Environmental exposure	Endocrine disruption	Ovarian dysfunction
Chronic inflammation	Cytokine-mediated endocrine alterations	Metabolic complications
Oxidative stress	Cellular damage and impaired follicular maturation	Poor oocyte quality and infertility
Psychological stress	Increased cortisol secretion	Menstrual disturbances and metabolic dysfunction

Table 4.2: Risk Factors for Development of PCOD

Risk Factor	Contribution to Disease Development
Family history of PCOD	Strong genetic predisposition
Obesity	Increases insulin resistance and androgen production
Sedentary lifestyle	Promotes weight gain and metabolic dysfunction

High-calorie processed diet	Contributes to obesity and insulin resistance
Insulin resistance	Central mechanism in disease progression
Early puberty	Associated with hormonal abnormalities
Chronic psychological stress	Alters endocrine function
Poor sleep quality	Affects metabolic and reproductive hormones
Endocrine-disrupting chemicals	May interfere with ovarian hormone regulation
Type 2 diabetes mellitus in family	Indicates inherited metabolic susceptibility

Table 4.3: Interaction Between Major Pathogenic Factors in PCOD

Primary Factor	Secondary Effect	Final Clinical Outcome
Genetic susceptibility	Hormonal dysregulation	Development of PCOD
Insulin resistance	Hyperinsulinemia	Increased androgen synthesis
Hyperandrogenism	Arrested follicular maturation	Chronic anovulation
Chronic anovulation	Irregular menstruation	Infertility
Obesity	Increased inflammation	Metabolic syndrome
Oxidative stress	Cellular injury	Reduced fertility
Chronic inflammation	Endocrine dysfunction	Disease progression

The etiology of PCOD is complex and involves multiple interconnected pathways rather than a single causative factor. Genetic susceptibility combined with hormonal imbalance, insulin resistance, obesity, environmental influences, inflammation, and oxidative stress contributes to the onset and progression of the disorder. Understanding these mechanisms is essential for developing effective preventive strategies and individualized treatment approaches.

5. Pathophysiology of Polycystic Ovarian Disease (PCOD)

The pathophysiology of Polycystic Ovarian Disease (PCOD) is complex and involves interactions among the hypothalamic-pituitary-ovarian (HPO) axis, insulin resistance, hyperandrogenism, genetic susceptibility, chronic inflammation, and environmental factors. These mechanisms disrupt normal follicular growth and ovulation, resulting in the characteristic reproductive, metabolic, and endocrine abnormalities observed in affected women.

5.1 Normal Ovarian Physiology

Under normal physiological conditions, the hypothalamus secretes gonadotropin-releasing hormone (GnRH), which stimulates the anterior pituitary gland to release follicle-stimulating hormone (FSH) and luteinizing hormone (LH). FSH promotes the growth and maturation of ovarian follicles, while LH stimulates theca cells to produce androgens. These androgens are converted into estrogens by granulosa cells under the influence of FSH. During each menstrual cycle, one dominant follicle matures and releases a mature ovum through ovulation. After ovulation, the corpus luteum secretes progesterone, which prepares the uterus for implantation. This tightly regulated hormonal balance is disrupted in PCOD.

5.2 Dysfunction of the Hypothalamic–Pituitary–Ovarian (HPO) Axis

One of the earliest abnormalities in PCOD is altered secretion of GnRH from the hypothalamus. Increased frequency of GnRH pulses stimulates preferential release of LH over FSH from the anterior pituitary gland. The elevated LH/FSH ratio leads to excessive androgen production by ovarian theca cells while inadequate FSH prevents complete maturation of ovarian follicles. Consequently, follicles remain arrested at the early developmental stage and fail to ovulate. Persistent anovulation results in menstrual irregularities, infertility, and accumulation of multiple immature follicles within the ovaries.

Table 5.1: Normal HPO Axis vs PCOD

Parameter	Normal Physiology	PCOD
GnRH secretion	Regular pulsatile release	Increased pulse frequency
LH secretion	Normal	Elevated
FSH secretion	Normal	Relatively decreased
Follicular development	Complete maturation	Arrested development
Ovulation	Regular	Absent or infrequent
Menstrual cycle	Regular	Irregular

5.3 Hyperandrogenism

Hyperandrogenism is one of the defining features of PCOD. Elevated LH stimulates ovarian theca cells to produce excessive amounts of testosterone and other androgens. Hyperinsulinemia further enhances androgen synthesis and decreases hepatic production of sex hormone-binding globulin (SHBG), increasing circulating free testosterone. Excess androgen levels interfere with normal follicular maturation and contribute to various clinical manifestations, including:

- Hirsutism
- Acne vulgaris
- Oily skin
- Androgenic alopecia
- Irregular menstruation
- Chronic anovulation

Persistent hyperandrogenism also aggravates insulin resistance, creating a self-perpetuating cycle.

5.4 Insulin Resistance and Hyperinsulinemia

Insulin resistance is present in a significant proportion of women with PCOD. Reduced sensitivity of muscle, liver, and adipose tissues to insulin results in compensatory hyperinsulinemia. High circulating insulin levels exert several pathological effects:

- Stimulate androgen production by ovarian theca cells.
- Reduce hepatic synthesis of SHBG.
- Increase free androgen concentrations.
- Enhance LH-mediated steroidogenesis.
- Promote adipose tissue accumulation.
- Increase inflammatory mediator production.

These metabolic abnormalities contribute to obesity, impaired glucose tolerance, dyslipidemia, and type 2 diabetes mellitus.

Table 5.2: Effects of Insulin Resistance in PCOD

Effect of Hyperinsulinemia	Clinical Outcome
Increased ovarian androgen production	Hyperandrogenism
Reduced SHBG synthesis	Increased free testosterone
Increased adipose tissue deposition	Obesity
Impaired glucose utilization	Prediabetes and diabetes
Increased inflammatory cytokines	Chronic inflammation
Enhanced ovarian steroidogenesis	Follicular arrest

5.5 Follicular Arrest

Normal ovarian follicles grow through several developmental stages before one becomes dominant and undergoes ovulation. In PCOD, elevated androgen levels and inadequate FSH prevent selection of a dominant follicle.

Consequently:

- Follicles stop developing at approximately 6–9 mm diameter.
- Ovulation fails to occur.
- Numerous immature follicles accumulate around the ovarian cortex.

- Ovaries become enlarged with increased stromal tissue.

This arrested follicular development is responsible for chronic anovulation and infertility.

5.6 Ovarian Morphological Changes

Ultrasonographic examination of PCOD ovaries typically demonstrates characteristic structural abnormalities, including:

- Enlarged ovarian volume.
- Increased stromal echogenicity.
- Multiple small peripheral follicles.
- Thickened ovarian capsule.
- Increased stromal vascularity.

These changes reflect prolonged follicular arrest and excessive androgen production within ovarian tissue.

Table 5.3: Morphological Changes in PCOD Ovaries

Normal Ovary	PCOD Ovary
Single dominant follicle	Multiple immature follicles
Regular ovulation	Chronic anovulation
Normal ovarian size	Enlarged ovaries
Thin ovarian cortex	Thickened cortex
Normal stromal tissue	Increased stromal volume

5.7 Chronic Low-Grade Inflammation

Women with PCOD often exhibit persistent low-grade inflammation characterized by elevated inflammatory mediators.

Inflammation contributes to:

- Insulin resistance
- Endothelial dysfunction
- Ovarian steroid abnormalities
- Cardiovascular risk
- Follicular dysfunction

Inflammatory cytokines also impair ovarian follicle maturation and worsen reproductive outcomes.

5.8 Oxidative Stress

Oxidative stress occurs when the production of reactive oxygen species exceeds the body's antioxidant capacity.

In PCOD, oxidative stress causes:

- Damage to ovarian cells.
- Poor oocyte quality.
- Mitochondrial dysfunction.
- Increased apoptosis.
- Reduced fertility potential.

Oxidative stress also enhances inflammatory pathways and insulin resistance.

5.9 Role of Adipose Tissue

Adipose tissue acts as an endocrine organ by secreting adipokines and inflammatory mediators.

Excess body fat contributes to:

- Increased aromatase activity.
- Elevated inflammatory cytokines.
- Leptin resistance.
- Reduced adiponectin levels.
- Worsening insulin resistance.
- Increased androgen production.

Central obesity therefore significantly aggravates PCOD severity.

5.10 Molecular Mechanisms

Recent research has identified several molecular pathways involved in PCOD pathogenesis.

Major mechanisms include:

- Altered insulin receptor signaling.
- PI3K/Akt pathway dysfunction.
- Increased androgen receptor activity.

- Mitochondrial dysfunction.
- Oxidative stress-mediated DNA damage.
- Chronic activation of inflammatory pathways.
- Epigenetic modifications affecting reproductive hormones.

These molecular alterations contribute to ovarian dysfunction and metabolic abnormalities.

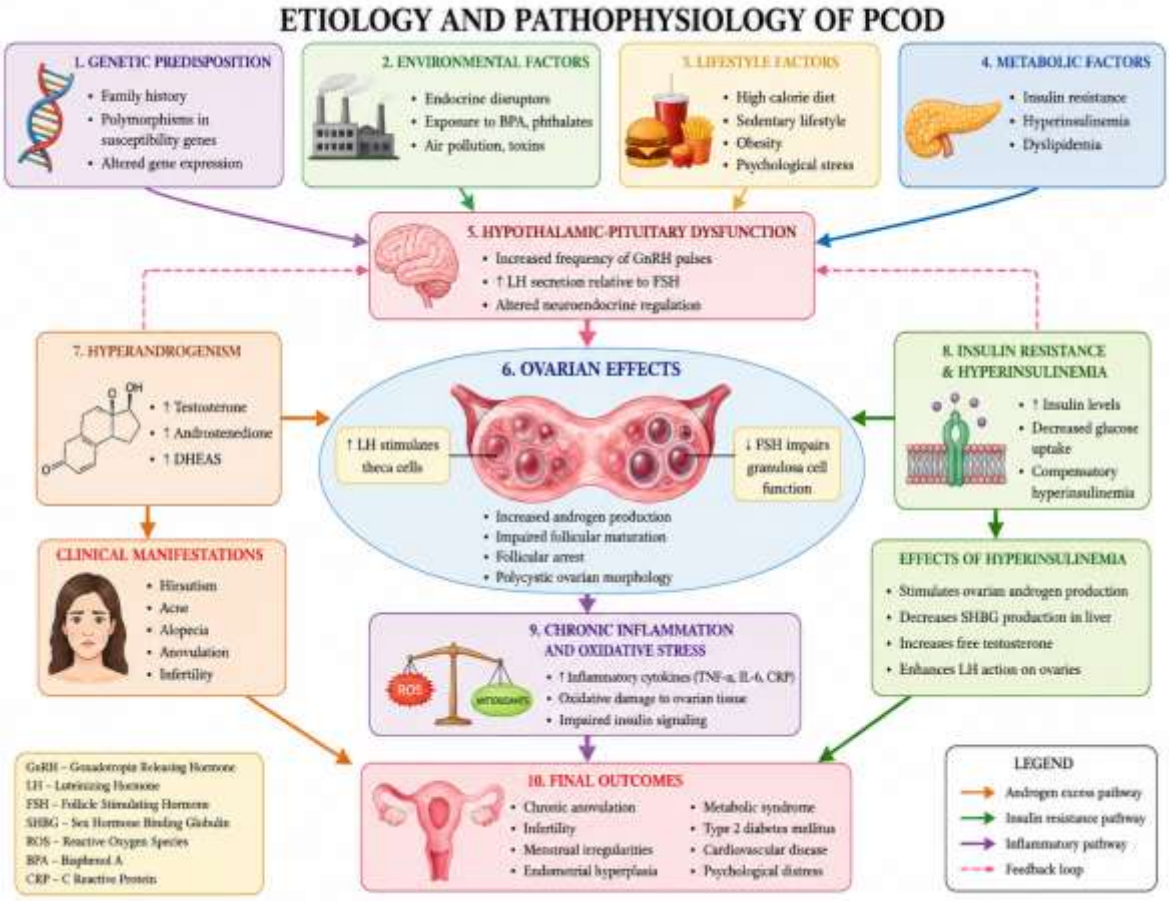

Figure 1. Etiology and Pathophysiological Mechanisms of Polycystic Ovarian Disease (PCOD): Integrated Overview of Genetic, Environmental, Metabolic, and Endocrine Factors

6. Clinical Manifestations and Symptoms of Polycystic Ovarian Disease (PCOD)

The clinical presentation of Polycystic Ovarian Disease (PCOD) varies considerably among affected women due to differences in hormonal imbalance, insulin resistance, genetic predisposition, and lifestyle factors. Some women present with mild menstrual disturbances, while others experience severe reproductive, metabolic, dermatological, and psychological complications. Symptoms generally begin during adolescence but may become more pronounced during the reproductive years. The severity of symptoms depends on the degree of hyperandrogenism, obesity, insulin resistance, and ovarian dysfunction. Since PCOD is a multisystem disorder, its manifestations extend beyond the reproductive system and significantly affect the patient's physical, emotional, and social well-being.

6.1 Reproductive Manifestations

Reproductive abnormalities are the most common clinical features of PCOD. Hormonal imbalance interferes with normal follicular development, leading to irregular or absent ovulation.

Common reproductive manifestations include:

- Irregular menstrual cycles (oligomenorrhea)
- Complete absence of menstruation (amenorrhea)
- Heavy or prolonged menstrual bleeding
- Delayed ovulation

- Chronic anovulation
- Difficulty in conception
- Infertility
- Recurrent pregnancy loss
- Subfertility

Menstrual irregularities are often the earliest sign of PCOD and usually appear within a few years after menarche.

6.2 Hyperandrogenic Manifestations

Hyperandrogenism results from increased production of ovarian androgens and reduced levels of sex hormone-binding globulin (SHBG). Elevated free androgen levels produce several characteristic physical changes.

Common manifestations include:

- Hirsutism (excessive facial and body hair)
- Acne vulgaris
- Oily skin (seborrhea)
- Male-pattern hair loss (androgenic alopecia)
- Thick, coarse body hair
- Increased facial hair growth
- Darkening of skin folds due to insulin resistance (acanthosis nigricans)

These symptoms often affect self-esteem and body image.

Table 6.1: Hyperandrogenic Manifestations in PCOD

Manifestation	Underlying Cause	Clinical Significance
Hirsutism	Elevated testosterone	Most common androgenic symptom
Acne	Increased sebaceous gland activity	Common during adolescence
Oily skin	Excess androgen stimulation	Persistent skin problems
Alopecia	Hair follicle miniaturization	Cosmetic concern
Acanthosis nigricans	Hyperinsulinemia	Marker of insulin resistance

6.3 Metabolic Manifestations

Metabolic abnormalities are increasingly recognized as an important component of PCOD. Insulin resistance plays a central role in the development of obesity, dyslipidemia, impaired glucose tolerance, and metabolic syndrome.

Common metabolic manifestations include:

- Central obesity
- Weight gain
- Difficulty losing weight
- Insulin resistance
- Prediabetes
- Type 2 diabetes mellitus
- Dyslipidemia
- Hypertension
- Metabolic syndrome

These complications increase the long-term risk of cardiovascular disease.

Table 6.2: Metabolic Manifestations

Manifestation	Clinical Features
Obesity	Increased body mass index and abdominal fat
Insulin resistance	Reduced insulin sensitivity
Prediabetes	Elevated fasting blood glucose
Type 2 diabetes mellitus	Chronic hyperglycemia
Dyslipidemia	Increased triglycerides and LDL cholesterol
Hypertension	Elevated blood pressure
Metabolic syndrome	Combination of obesity, hypertension, dyslipidemia, and hyperglycemia

6.4 Psychological Manifestations

Women with PCOD frequently experience psychological disturbances resulting from chronic illness, infertility, obesity, acne, and excessive hair growth.

Common psychological manifestations include:

- Anxiety
- Depression
- Mood swings
- Emotional stress
- Reduced self-esteem
- Poor body image
- Social withdrawal
- Decreased quality of life
- Sleep disturbances

Psychological symptoms may negatively influence treatment adherence and overall health outcomes.

6.5 Dermatological Manifestations

Skin changes occur mainly because of hyperandrogenism and insulin resistance.

Common dermatological features include:

- Persistent acne
- Oily skin
- Hirsutism
- Acanthosis nigricans
- Skin tags
- Scalp hair thinning
- Increased facial pigmentation

6.6 Gynecological Manifestations

Long-standing anovulation affects reproductive health and increases the risk of gynecological complications.

Important manifestations include:

- Enlarged ovaries
- Multiple immature follicles
- Endometrial hyperplasia
- Abnormal uterine bleeding
- Infertility
- Recurrent miscarriage
- Pregnancy complications

Table 6.3: Reproductive and Gynecological Manifestations

Clinical Feature	Cause	Possible Outcome
Irregular menstruation	Chronic anovulation	Infertility
Amenorrhea	Hormonal imbalance	Endometrial changes
Heavy menstrual bleeding	Endometrial hyperplasia	Anemia
Enlarged ovaries	Multiple immature follicles	Pelvic discomfort
Infertility	Failure of ovulation	Need for fertility treatment

6.7 Long-Term Clinical Consequences

If left untreated, PCOD may lead to several chronic complications.

These include:

- Type 2 diabetes mellitus
- Cardiovascular disease
- Hypertension
- Dyslipidemia
- Endometrial hyperplasia
- Endometrial carcinoma
- Non-alcoholic fatty liver disease
- Obstructive sleep apnea
- Chronic infertility
- Pregnancy-related complications

Regular monitoring and early intervention are essential to reduce these risks.

6.8 Clinical Classification of PCOD

The severity and presentation of PCOD differ among individuals. Clinically, patients may be grouped according to their predominant manifestations.

Table 6.4: Clinical Classification of PCOD

Clinical Type	Predominant Features
Reproductive type	Menstrual irregularities and infertility
Hyperandrogenic type	Hirsutism, acne, alopecia
Metabolic type	Obesity, insulin resistance, diabetes
Mixed type	Combination of reproductive, metabolic, and androgenic manifestations

6.9 Impact on Quality of Life

PCOD affects multiple aspects of daily life. Persistent symptoms can interfere with education, employment, relationships, and emotional well-being.

Areas commonly affected include:

- Physical health
- Emotional health
- Reproductive health
- Sexual health
- Social relationships
- Self-confidence
- Occupational productivity

Patient counseling, lifestyle modification, and multidisciplinary management play an important role in improving overall quality of life.

7. Diagnosis and Diagnostic Criteria of Polycystic Ovarian Disease (PCOD)

Accurate diagnosis of Polycystic Ovarian Disease (PCOD) is essential for initiating appropriate treatment, preventing long-term complications, and improving reproductive and metabolic outcomes. Since no single laboratory test can definitively diagnose PCOD, the diagnosis is based on a combination of clinical features, medical history, physical examination, laboratory investigations, and imaging studies. The evaluation also aims to exclude other disorders that may present with similar clinical manifestations. Early diagnosis is particularly important in adolescents and young women because timely intervention through lifestyle modification and medical therapy can reduce disease progression and improve quality of life.

7.1 Clinical Evaluation

Clinical evaluation forms the first step in the diagnosis of PCOD. A detailed history helps identify menstrual abnormalities, reproductive problems, metabolic risk factors, and family history of endocrine disorders.

Important aspects of clinical evaluation include:

- Age at onset of symptoms
- Menstrual history
- History of infertility or recurrent miscarriage
- Weight gain and obesity
- Acne and excessive facial or body hair
- Hair loss or scalp thinning
- Family history of PCOD, diabetes mellitus, obesity, or cardiovascular disease
- Dietary habits and physical activity
- Psychological symptoms such as anxiety or depression

A comprehensive history assists in identifying the severity of the disease and planning further investigations.

7.2 Physical Examination

Physical examination provides valuable information regarding hormonal imbalance and metabolic abnormalities.

The examination includes:

- Measurement of height, weight, and Body Mass Index (BMI)
- Waist circumference
- Blood pressure
- Assessment of acne severity
- Evaluation of hirsutism
- Examination for androgenic alopecia
- Detection of acanthosis nigricans
- Thyroid examination
- General gynecological examination when indicated

Table 7.1: Physical Findings in PCOD

Clinical Finding	Significance
Increased BMI	Indicates obesity
Increased waist circumference	Suggests central obesity
Acne	Hyperandrogenism
Hirsutism	Elevated androgen levels
Alopecia	Androgen excess
Acanthosis nigricans	Marker of insulin resistance
Elevated blood pressure	Cardiovascular risk

7.3 Laboratory Investigations

Laboratory investigations are performed to assess hormonal imbalance, metabolic abnormalities, and to exclude other endocrine disorders.

Hormonal Investigations

Important hormonal tests include:

- Luteinizing hormone (LH)
- Follicle-stimulating hormone (FSH)
- LH/FSH ratio
- Total testosterone
- Free testosterone
- Dehydroepiandrosterone sulfate (DHEAS)
- Sex hormone-binding globulin (SHBG)
- Estradiol
- Progesterone
- Prolactin
- Thyroid-stimulating hormone (TSH)

Elevated LH levels, increased androgen concentrations, and reduced SHBG are commonly observed in women with PCOD.

Metabolic Investigations

Because metabolic abnormalities are common in PCOD, the following tests are recommended:

- Fasting blood glucose
- Oral glucose tolerance test (OGTT)
- Glycated hemoglobin (HbA1c)
- Fasting insulin level
- Lipid profile
- Liver function tests
- Kidney function tests

These investigations help identify insulin resistance, diabetes, dyslipidemia, and associated metabolic disorders.

Table 7.2: Common Laboratory Investigations

Investigation	Purpose
LH	Evaluate gonadotropin levels
FSH	Assess follicular function
Testosterone	Detect hyperandrogenism
DHEAS	Evaluate adrenal androgen production
SHBG	Estimate free androgen levels
TSH	Exclude thyroid disorders
Prolactin	Exclude hyperprolactinemia
Fasting glucose	Screen for diabetes
HbA1c	Assess long-term glucose control
Lipid profile	Evaluate cardiovascular risk

7.4 Ultrasonographic Evaluation

Pelvic ultrasonography is an important imaging modality for diagnosing PCOD. It helps visualize ovarian morphology and assess follicular development.

Typical ultrasound findings include:

- Enlarged ovaries
- Multiple peripheral follicles
- Increased ovarian volume
- Thickened ovarian stroma
- "String of pearls" appearance

Transvaginal ultrasonography provides better resolution in sexually active women, whereas transabdominal ultrasonography is preferred in adolescents and unmarried women.

Table 7.3: Ultrasonographic Features of PCOD

Ultrasound Finding	Clinical Importance
Enlarged ovaries	Characteristic feature
Multiple immature follicles	Indicates follicular arrest
Peripheral arrangement of follicles	Typical "string of pearls" appearance
Increased stromal volume	Associated with hyperandrogenism
Increased ovarian volume	Supports diagnosis

7.5 Rotterdam Diagnostic Criteria

The Rotterdam criteria are the most widely accepted diagnostic criteria for PCOD/PCOS. According to these criteria, the diagnosis is established when **any two of the following three features** are present after excluding other disorders:

1. Oligo-ovulation or anovulation.
2. Clinical and/or biochemical signs of hyperandrogenism.
3. Polycystic ovarian morphology on ultrasonography.

These criteria recognize the heterogeneity of the disorder and allow diagnosis even when all features are not present.

Table 7.4: Rotterdam Diagnostic Criteria

Criterion	Description
Oligo-ovulation or anovulation	Irregular or absent ovulation
Hyperandrogenism	Clinical (hirsutism, acne) or biochemical evidence
Polycystic ovaries	Multiple follicles with increased ovarian volume on ultrasound

Diagnosis: Presence of **any two** of the above three criteria after excluding other causes.

7.6 Differential Diagnosis

Several endocrine disorders may mimic the clinical features of PCOD. Therefore, careful evaluation is necessary to exclude these conditions.

Common differential diagnoses include:

- Thyroid disorders
- Hyperprolactinemia
- Congenital adrenal hyperplasia
- Cushing's syndrome
- Androgen-secreting ovarian tumors
- Adrenal tumors
- Premature ovarian insufficiency
- Hypothalamic amenorrhea

Excluding these disorders ensures accurate diagnosis and appropriate treatment.

8. Management and Treatment of Polycystic Ovarian Disease (PCOD)

Management of Polycystic Ovarian Disease (PCOD) aims to relieve symptoms, restore regular ovulation, improve fertility, correct hormonal imbalance, prevent metabolic complications, and enhance the patient's quality of life. Since PCOD presents differently among individuals, treatment should be individualized based on age, symptoms, body weight, metabolic status, and reproductive goals. A multidisciplinary approach involving gynecologists, endocrinologists, dietitians, and mental health professionals is often required.

8.1 Lifestyle Modification

Lifestyle modification is the first-line treatment for all women with PCOD, particularly those who are overweight or obese. Even modest weight loss can improve insulin sensitivity, regulate menstrual cycles, reduce androgen levels, and increase the chances of spontaneous ovulation.

Recommended lifestyle measures include:

- Balanced, nutrient-rich diet
- Regular physical exercise
- Weight management
- Stress reduction techniques
- Adequate sleep
- Avoidance of smoking and excessive alcohol intake

8.2 Dietary Management

A healthy diet plays an important role in managing PCOD by improving insulin sensitivity and supporting weight control.

General dietary recommendations include:

- High-fiber foods such as fruits, vegetables, and whole grains
- Lean protein sources
- Healthy fats from nuts and seeds
- Limiting refined carbohydrates and sugary beverages
- Adequate water intake

8.3 Pharmacological Management

Drug therapy is selected according to the patient's symptoms and reproductive plans.

a) Combined Oral Contraceptive Pills (COCs)

COCs are commonly prescribed for women who do not wish to conceive. They help:

- Regulate menstrual cycles
- Reduce androgen levels
- Improve acne and hirsutism
- Prevent endometrial hyperplasia

b) Insulin Sensitizers

Metformin is widely used to improve insulin sensitivity. It helps:

- Lower blood glucose levels
- Improve ovulation
- Promote weight reduction
- Reduce the risk of type 2 diabetes

c) Ovulation Induction Agents

For women with infertility, ovulation may be induced using:

- Letrozole
- Clomiphene citrate
- Gonadotropins (in selected cases)

d) Anti-androgen Therapy

Anti-androgen drugs may be used to reduce symptoms of hyperandrogenism, such as:

- Hirsutism
- Acne
- Androgenic alopecia

Table 8.1: Pharmacological Treatment of PCOD

Drug/Class	Main Purpose
Combined oral contraceptives	Regulate menstruation and reduce androgen levels
Metformin	Improve insulin sensitivity
Letrozole	Induce ovulation
Clomiphene citrate	Stimulate ovulation
Anti-androgens	Treat hirsutism and acne

8.4 Surgical Management

Surgical treatment is considered only when medical therapy is unsuccessful. The most commonly

performed procedure is **laparoscopic ovarian drilling (LOD)**, which reduces androgen production and may restore ovulation in selected women with infertility.

8.5 Fertility Management

Women wishing to conceive may require fertility treatment if lifestyle modification and medications are ineffective.

Available options include:

- Ovulation induction
- Intrauterine insemination (IUI)
- In vitro fertilization (IVF) for resistant cases

8.6 Psychological Support

Psychological counseling is an important component of PCOD management. Counseling can help patients cope with:

- Anxiety
- Depression
- Body image concerns
- Infertility-related stress

Support groups and patient education programs also improve treatment adherence and overall well-being.

9. Complications and Prognosis of Polycystic Ovarian Disease (PCOD)

Polycystic Ovarian Disease (PCOD) is a chronic endocrine disorder that can lead to several short-term and long-term complications if left untreated. Persistent hormonal imbalance, insulin resistance, and chronic anovulation increase the risk of reproductive, metabolic, cardiovascular, and psychological disorders. Early diagnosis, appropriate treatment, and regular follow-up are essential to minimize these complications and improve long-term health outcomes.

9.1 Reproductive Complications

Chronic anovulation is one of the major consequences of PCOD and is responsible for several reproductive problems.

Common reproductive complications include:

- Infertility due to failure of ovulation
- Delayed conception
- Recurrent miscarriage
- Pregnancy complications such as gestational diabetes and pregnancy-induced hypertension
- Endometrial hyperplasia due to prolonged exposure to unopposed estrogen
- Increased risk of endometrial carcinoma

9.2 Metabolic Complications

Insulin resistance and obesity significantly increase the likelihood of metabolic disorders in women with PCOD.

Major metabolic complications include:

- Impaired glucose tolerance
- Type 2 diabetes mellitus
- Metabolic syndrome
- Dyslipidemia
- Obesity
- Non-alcoholic fatty liver disease (NAFLD)

These conditions increase long-term morbidity and require regular monitoring.

9.3 Cardiovascular Complications

Women with PCOD have a higher risk of developing cardiovascular diseases due to associated metabolic abnormalities.

Potential cardiovascular complications include:

- Hypertension
- Atherosclerosis
- Endothelial dysfunction
- Coronary artery disease
- Increased risk of cardiovascular events later in life

Adopting a healthy lifestyle and controlling metabolic risk factors can significantly reduce cardiovascular risk.

9.4 Psychological Complications

The chronic nature of PCOD and its visible symptoms can have a significant impact on mental health.

Common psychological complications include:

- Anxiety
- Depression
- Low self-esteem
- Body image dissatisfaction
- Emotional stress
- Reduced quality of life

Early psychological assessment and counseling are beneficial for improving emotional well-being.

Table 9.1: Major Complications of PCOD

Category	Complications
Reproductive	Infertility, recurrent miscarriage, endometrial hyperplasia
Metabolic	Insulin resistance, type 2 diabetes, dyslipidemia, obesity
Cardiovascular	Hypertension, atherosclerosis, coronary artery disease
Psychological	Anxiety, depression, poor self-esteem
Pregnancy-related	Gestational diabetes, preeclampsia, preterm delivery

9.5 Prognosis

The prognosis of PCOD depends on the severity of symptoms, early diagnosis, adherence to treatment, and lifestyle modifications. Although PCOD cannot be completely cured, its symptoms and complications can be effectively controlled through appropriate management. Women who maintain a healthy body weight, engage in regular physical activity, follow a balanced diet, and receive timely medical treatment generally have better reproductive and metabolic outcomes. Advances in pharmacological therapy and assisted reproductive techniques have also improved fertility rates in women with PCOD. Regular follow-up is important to monitor menstrual function, metabolic health, cardiovascular risk factors, and psychological well-being. Long-term management helps reduce complications and improves overall quality of life.

10. Recent Advances and Future Perspectives in PCOD Management

Advances in research have significantly improved the understanding of the pathogenesis and management of Polycystic Ovarian Disease (PCOD). Recent studies emphasize personalized treatment approaches that consider individual hormonal profiles, metabolic status, reproductive goals, and lifestyle factors. Modern diagnostic techniques, novel pharmacological agents, and digital healthcare technologies are expected to improve disease management and patient outcomes.

10.1 Personalized Medicine

Personalized medicine is an emerging approach in PCOD management, where treatment is tailored according to the patient's clinical presentation, metabolic profile, and fertility requirements. Individualized therapy helps improve treatment effectiveness while minimizing adverse effects.

10.2 Advances in Pharmacological Therapy

Several newer therapeutic options are being explored to improve insulin sensitivity, reduce androgen levels, and promote ovulation.

Recent therapeutic approaches include:

- Improved insulin-sensitizing agents
- Inositol supplements (Myo-inositol and D-chiro-inositol)
- Glucagon-like peptide-1 (GLP-1) receptor agonists for obesity management
- Combination drug therapy for enhanced symptom control

These therapies show promising results, particularly in women with obesity and metabolic syndrome.

10.3 Role of Nutritional Supplements

Various nutritional supplements are being investigated as supportive therapies in PCOD.

Common supplements include:

- Vitamin D
- Omega-3 fatty acids
- Myo-inositol

- D-chiro-inositol
- Antioxidants

These supplements may help improve insulin sensitivity, ovarian function, and metabolic health when used alongside lifestyle modification.

10.4 Digital Health and Telemedicine

Digital healthcare technologies have improved long-term disease management by enabling remote consultation, symptom tracking, medication reminders, and lifestyle monitoring.

Mobile health applications and wearable devices can assist patients in monitoring:

- Menstrual cycles
- Body weight
- Physical activity
- Blood glucose levels
- Dietary habits

These technologies promote better treatment adherence and patient engagement.

10.5 Gut Microbiome Research

Recent evidence suggests that alterations in the gut microbiota may contribute to insulin resistance, chronic inflammation, and hormonal imbalance in PCOD. Modulation of the gut microbiome through diet, probiotics, and prebiotics is being explored as a potential therapeutic strategy, although further clinical studies are needed.

FUTURE PERSPECTIVES

Future research is focused on identifying reliable biomarkers for early diagnosis, understanding the genetic and molecular mechanisms of PCOD, and developing targeted therapies with improved efficacy and safety. Greater emphasis is also being placed on preventive strategies, early screening in high-risk individuals, and multidisciplinary care to improve long-term health outcomes.

CONCLUSION

Polycystic Ovarian Disease (PCOD) is a complex endocrine and metabolic disorder that affects multiple aspects of a woman's reproductive, metabolic, and psychological health. The disease is characterized by hormonal imbalance, insulin resistance, chronic anovulation, and hyperandrogenism, leading to menstrual irregularities, infertility, obesity, and various metabolic complications. Its multifactorial nature requires a comprehensive approach to diagnosis and management. Early identification of symptoms, appropriate diagnostic evaluation, and individualized treatment are essential for preventing long-term complications. Lifestyle modification remains the cornerstone of management, while pharmacological therapy, fertility treatment, and psychological support play important roles depending on the patient's clinical presentation and reproductive goals. Recent advances in personalized medicine, novel therapeutic agents, nutritional interventions, digital health technologies, and molecular research have expanded the possibilities for more effective and targeted management of PCOD. Continued research and increased awareness are expected to improve early diagnosis, optimize treatment strategies, and enhance the overall quality of life of affected women. A multidisciplinary approach involving healthcare professionals and active patient participation remains essential for achieving successful long-term outcomes.

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