



**A RETROSPECTIVE STUDY ON RISK FACTORS, LIFESTYLE MODIFICATIONS,
PHARMACOLOGICAL PROFILE AND ASSOCIATED CO-MORBIDITIES IN WOMENS
WITH POLYCYSTIC OVARIAN SYNDROME**

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a common hormonal disorder in women of reproductive age characterized by irregular periods, hormonal imbalance, and polycystic ovaries. Retrospective findings show that obesity, central fat accumulation, physical inactivity, unhealthy diet, chronic stress, and family history of diabetes or weight gain. Management mainly involves lifestyle modification like such as calorie controlled balanced diet and regular physical activity. Medication like oral contraceptives, metformin, anti- androgens, and ovulation - including drug are used based on symptoms. PCOS is often associated with insulin resistance, type -2 diabetes, dyslipidaemia, hypertension, metabolic syndrome, and thyroid disorder. Early diagnosis and multidisciplinary can improve long -term outcomes.

KEYWORDS: PCOS; Gut dysbiosis; hyperinsulinemia; hyperandrogenism; metabolic disorders.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine and metabolic disorder affecting many women of the reproductive age worldwide. it is one of the most common causes of female infertility and is characterized by chronic anovulation, hyper an drogenism, and polycystic ovarian morphology. The clinical presentation of polycystic ovary disease (PCOD), a disease related to the female reproductive system, is increasing day by day in reproductive system, aged women because of lifestyle, diet, obesity, insulin resistance and metabolic disturbances, other medical issues, etc. PCOD is a major

cause leading to infertility. PCOS is characterized by a chronic an ovulation means ovaries, the site of egg production, have tiny fluid-filled sacs called follicles or cysts. Ovulation refers to the release of an oocyte from the ovary, and disruption of this process results in menstrual irregularities and infertilities. This syndrome is often associated with enlarged and dysfunctional ovaries, excess androgen levels resistance to insulin etc. PCOD stays a complicated disease with a wide range of indications that affects not just females in the reproduce tivephase.

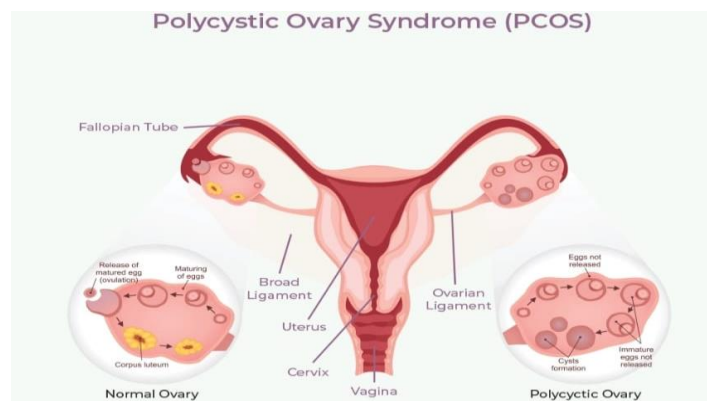


Fig. No. 1: Polycystic ovary syndrom.

but also, teenagers and postmenopausal females. Because of the disorder's nature, PCOD negatively impacts affected women's fertility and reproductive health. Polycystic ovarian disease is the most common female endocrine disorders, affecting approximately 6%-13% of the all females and 6%-8% of adolescent girls and young women. A burden that has significantly increased, with millions more cases emerging over the last three decades, reaching around prevalent from around 35 million cases in 1990 to over by 69 million by 2021, increase of about 28-89%. In recent WHO Guidelines research studies, they increased from about 0.8 million in 1990 to over 2.3 million in 2021, a rise of roughly 27-49%. PCOS although the high ratio of luteinizing hormone (LH) follicle-stimulating hormone (FSH) etiology involves a mix of genetics and environment, leading to complex pathogenesis centered on insulin resistance (IR), hyper androgenism, and abnormal and gonadotropin-releasing hormone (Gn. RH) creating a vicious cycle of hormonal imbalance, ovarian dysfunction underlying causes of PCOS. one of the hand, it's a well-known fact that root cause of PCOD has a substantial. Hereditary factors is often transmitted from mother to daughter. On the other hand, many studies have suggested that lifestyle modification and dietary treatment of women with PCOD was the best initial management for obese women seeking to improve their reproductive function. Study of lifestyle modifications by use of alteration of diet intake and exercise therapy to treat obese women with PCOD were successfully employed by Paloma. Various factors like genetics, epigenetics, dietary preference, lifestyle, and 01environmental factors play an essential role in the ethology of PCOS increases the risk for cardiovascular diseases, type-2 diabetes mellitus, gestational diabetes and other pregnancy, -related complications, venous throm boembolism, cerebrovascular and cardiovascular diseases and endometrial cancer. Treatment should be tailored to the complaints and of the patient and involves targeting metabolic abnormalities through lifestyle changes, medication and potentially sugary for the prevention and

management of excess weight, endometrial protection, reproductive therapy and the detection and treatment of psychological features. First line management of PCOS is lifestyle interventions (LSI) as diet and /or exercise to achieve and maintain a healthy weight. eight loss of 5%-10% can result in significant disease process improvement like regular menstruation and decreased hyperandrogenism. Oxidative stress and chronic inflammation together play critical roles in the devolvement and progression of PCOS. Lifestyle changes, dietary patterns, physical activity, and stress management are crucial for controlling the symptoms of PCOS. Diet and exercise are two crucial areas that must be addressed for lifestyle change adjustments to be successful. Aerobic exercise is any activity that uses large muscle groups, is maintained continuously, and is rhythmic in nature. Studies have proven that exercise, particularly workout, multiple benefits for managing PCOS symptoms, such as improving insulin sensitivity, cardiovascular health, and hormonal balance. Aerobic exercise, such as walking, running cycling helps to enhance insulin sensitivity by improving how muscles absorb glucose from the blood. It may regulate menstrual periods by lowering insulin levels and enhancing ovarian function. In a study on women with PCOS, a significant decrease in BMI and fat mass was observed. Along with an increase in FSH, free testosterone, and sex- hormone-binding globulin (SHBG) levels, in the experimental group as compared to the control.

PATHOPHYSIOLOGY OF PCOS

The pathophysiology of PCOS is a complex interplay of between genetic and environment factors, primarily involving hyperandrogenism, insulin resistance, and dysfunction of the hypothalamic -pituitary-ovarian(HPO) axis leading to hormonal imbalance (High LH/FSH ratio, elevated androgen AMH), impaired folliculogenesis (anovulation, cysts), and metabolic issues like obesity and inflammation, contributing to reproductive, metabolic and psychological symptoms.

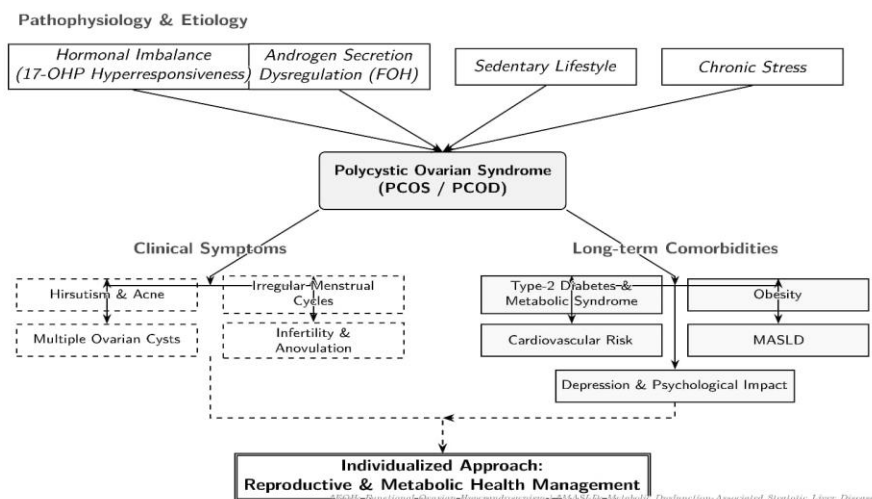


Fig. No. 2: Polycystic Ovarian Syndrome (PCOS/PCOD).

INSULIN RESISTANCES

Insulin resistance is a central pathophysiological feature of polycystic ovary syndrome (PCOS). Elevated insulin levels stimulate ovarian theca cells to produce excess androgens, which suppress ovulation and contribute to the clinical manifestations of PCOS. Insulin resistance and the associated compensatory hyperinsulinemia are common findings in women with PCOS and play a significant role in disease progression.

A. approximately 60%-70% of women with PCOS exhibits insulin resistance, independent of obesity. PCOS is widely recognized as both a metabolic and reproductive disorder, conferring a substantially increased risk of type-2 diabetes mellitus and other metabolic complications. Although insulin resistance has long been associated with metabolic abnormalities in PCOS, increasing evidence highlights its significant contribution to endocrine dysfunction and reproductive abnormalities. Studies using cell culture models and insulin-target tissue biopsies from women with PCOS have been conducted to elucidate the underlying mechanisms and spectrum of insulin resistance associated with the syndrome.

HYPERANDROGENISM

Hyperandrogenism is a multifactorial feature. PCOS pathology is influenced by a combination of genetic, environmental, and endocrine factors. It is primarily a result of dysregulation of the hypothalamic-pituitary-ovarian (HPO) axis, leading to excess secretion of androgens. Increased luteinizing hormone relative to follicle-stimulating hormone (FSH) stimulates ovarian theca cells, resulting in enhanced androgen production and disruption of normal follicular maturation, ultimately causing chronic anovulation. Elevated levels of circulating androgens, including testosterone, and dehydroepiandrosterone sulfate (DHEA-S), are hallmark biochemical features of hyperandrogenism in PCOS. Increase in anti-Müllerian hormone (AMH) levels further reflect impaired folliculogenesis and increased ovarian follicle number.

Central to its pathophysiology is hyperandrogenism, marked by. Another cause can be theca cell intrinsic dysfunction or diminished levels of cortisol that stimulate negative feedback on the hypothalamic-pituitary axis and elevate the synthesis of the hypothalamic adrenocorticotropic hormone after adrenal steroidogenesis stimulation, a leading factor in adrenal hyperandrogenism. However, calibration studies have not been conducted to develop a female androgen assay. In addition, biochemical evaluation is unreliable in the case of women on hormonal contraceptives, as alterations in sex hormone-binding globulin (SHBG) levels can affect the interpretation of circulating androgen concentrations. Collectively, hyperandrogenism plays a pivotal role in reproductive, metabolic, and clinical manifestation of PCOS.

ROLE OF OBESITY AND LIFESTYLE FACTORS

Obesity plays a significant role in worsening the clinical features of polycystic ovary syndrome (PCOS), primarily by increasing insulin resistance. Enhanced insulin resistance stimulates ovarian androgen production, leading to hyperandrogenism, irregular ovulation, and metabolic disturbances such as type-2 diabetes mellitus. Lifestyle factors, including poor diet habits and physical inactivity, further exacerbate this pathological cycle. Evidence suggests that modest weight loss (5-10%) achieved through dietary modification and regular physical activity can result in significant improvements in insulin sensitivity, hormonal balance, menstrual regularity, fertility outcomes, and long-term metabolic health in some cases. Pharmacological therapy or bariatric surgery may be considered to achieve sustained metabolic benefits... Overweight and obesity are common findings among women with PCOS, with central obesity being particularly associated with insulin resistance, a core feature of the syndrome. The prevalence of obesity has reached epidemic proportions globally, including among adolescent females, thereby increasing the risk and severity of PCOS. Obesity adversely affects both the metabolic and endocrine profiles of women with PCOS and may also reduce

responsiveness to therapeutic intervention.

RISK FACTORS

ROLE OF GENES AND GENETICS

PCOS is a polygenic, multifactorial disorder influenced by complex interactions between genetic and environmental factors. Gene-gene and gene-environmental interactions may significantly affect an individual's susceptibility to developed PCOD. Genetic studies have identified multiple candidate genes associated with the pathogenesis of PCOS. These genes primarily regulate pathways involved in steroidogenesis, gonadotropin secretion regulation, insulin action, energy metabolism, and chronic inflammation. Variations such as single nucleotide polymorphisms (SNPs) may alter gene expression or protein function, contributing to the heterogeneity of clinical phenotypes observed in PCOS. Identification of genetic markers may enhance early diagnosis, allow better risk stratifications of associated comorbidities, and support the development of personalized therapeutic strategies.

GUT MICROBIOTA DYSBIOSIS

The gut microbiota comprises approximately 10^{13} – 10^{14} microorganisms and functions as a metabolically active "organ" possessing a gene pool significantly larger than the human genome. Under physiological conditions, a balanced interaction exists between the host and gut microbiota contributing to metabolic regulation, immune modulation and disease prevention. Disruption of this balance referred to as gut dysbiosis has been implicated in increased intestinal permeability, systemic inflammation, metabolic dysfunction. Emerging evidence indicates a strong association between gut microbiota alterations and polycystic ovary syndrome (PCOS). Comparative studies demonstrate significant differences in microbial composition between PCOS patients and healthy controls, typically characterized by reduced microbial diversity, depletion of beneficial bacteria (e.g., *Lactobacilli* and *Bifidobacteria*), and an increase in pathogenic taxa such as *Escherichia* and *Shigella*. These microbial alterations are closely linked to insulin resistance, hyperandrogenism, obesity, and metabolic disturbances commonly observed in PCOS. Altered gut microbial metabolites—including secondary bile acids, short-chain fatty acids (SCFAs), and trimethylamine (TMA)—further contribute to systemic metabolic imbalance. Both human and animal studies report shifts in major bacterial phyla, particularly changes in the Firmicutes/Bacteroidetes ratio, along with reduced α - and β -diversity in PCOS populations. The Dysbiosis of Gut Microbiota (DOGMA) theory proposes that diet-induced dysbiosis increases intestinal

permeability, facilitating translocation of lipopolysaccharides (LPS) into systemic circulation. This endotoxemia triggers chronic low-grade inflammation, impairs insulin receptor signalling, elevates circulating insulin levels, and enhances ovarian androgen production, thereby contributing to anovulation, menstrual irregularities, and cyst formation.

Overall, gut microbiota dysbiosis represents a significant mechanistic link between metabolic dysfunction and reproductive abnormalities in PCOS, highlighting its potential as a therapeutic target in future management strategies.

CLINICAL FEATURES

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic disorder in women of reproductive age. It presents with a combination of reproductive, hyperandrogenic, and metabolic features.

CLINICAL MANIFESTATIONS

Clinical manifestation of polycystic ovary syndrome (PCOS) includes menstrual irregularities such as oligomenorrhea or amenorrhea, clinical signs of hyperandrogenism including hirsutism (excess facial and body hair), severe acne, and androgenic alopecia. Many patients experience weight gain, particularly central obesity. Metabolic abnormalities such as insulin resistance may lead to dermatological changes, including acanthosis nigricans, characterized by dark, velvety skin patches in body folds. These clinical features collectively contribute to reproductive dysfunction and infertility in affected women.

LIFESTYLE MANAGEMENT IN POLYCYSTIC OVARY SYNDROME

DIETARY MODIFICATIONS

Lifestyle management is a cornerstone in the treatment of polycystic ovary syndrome (PCOS) and primarily focuses on dietary modification, physical activity, weight management, sleep quality, and stress reduction. These interventions are aimed at improving insulin sensitivity and restoring hormonal balance. A diet rich in low-glycemic index (GI) food and high in dietary fiber such as whole grains, veggies, lean protein, healthy fats are recommended, while excessive, including both metabolic health. Maintaining a healthy weight, ensuring adequate sleep (7–8 hours per night), and managing stress through relaxation techniques such as mindfulness and journaling have been shown to significantly alleviate symptoms and reduce long-term metabolic and reproductive risk associated with PCOS.

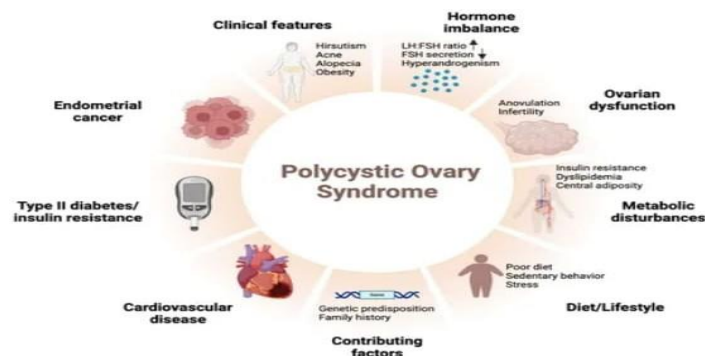


Fig. No. 2 : Polycystic ovarian syndrome.

PHYSICAL ACTIVITY

Physical activity is a cornerstone of PCOS management, contributing to improving insulin sensitivity, hormonal balance, weight regulations and mental health. Current reviews recommending 150-300 min per week of moderate intensity aerobic activity, combined with strength training, although the optimal intensity remains debated. Vigorous exercise shows great promising effects on cardiometabolic marks; however, long term success depends on consistency and addressing barriers limited access to supportive environment. Different types of exercise have demonstrated benefits in women with PCOS. Aerobic activities such as walking or swimming improve insulin sensitivity and reduce visceral fat, while high intensity interval training (HIIT) may further enhance insulin resistance and body mass index (BMI). Resistance training contributes to increased muscle mass, thereby support metabolic rate and insulin sensitivity. Additionally, mind-body practices such as yoga may help alleviate stress and improve overall well-being.

WEIGHT MANAGEMENT

Weight management plays a crucial role in the management polycystic ovary syndrome (PCOS), with lifestyle modifications including dietary intervention, physical activity, behavioral therapy recommended as first-line treatment. A modest weight reduction of approximately 5-10% has been shown to significantly improve metabolic, reproductive, and psychological outcomes. However, achieving and maintaining weight loss remains challenging due to underlying hormonal disturbances, particularly insulin resistance. Recent review articles emphasize the effectiveness of balanced dietary patterns, such as low glycemic index and, high-Fiber diets, combined with regular physical activity, stress management strategies. In selected cases pharmacological agents (e.g., metformin, orlistat) or bariatric surgery may be considered. Multidisciplinary approaches have been associated with improving adherence, reduced dropout rates, and better long-term outcomes.

IMPORTANCE OF WEIGHT REDUCTION

- Excess adipose tissue worsens insulin resistance, hyperandrogenism, and chronic inflammation.

- Recent evidence highlights personalized weight-loss approaches including calorie-restricted diets, low-glycemic index diets, and intermittent fasting.
- Weight loss improves glucose metabolism, lipid profile, and reduces cardiovascular risk.

EFFECTS ON OVULATION AND HORMONAL BALANCE

- Weight reduction lowers circulating androgen levels by improving insulin sensitivity.
- Restores hypothalamic-pituitary-ovarian axis function.
- Improves ovulation frequency, menstrual regularity, and fertility outcomes.
- Recent trials show better response to ovulation-inducing agents after lifestyle-based weight loss.

BEHAVIORAL AND STRESS MANAGEMENT

In recent years there has been a shift in PCOS management toward holistic, non-pharmacological approaches, emphasizing lifestyle modifications to tackle high stress and cortisol levels. Key strategies include mindfulness-based stress reduction (MBSR), yoga, regular exercise and cognitive behavioral therapy (CBT) to reduce anxiety and improve metabolic health.

ROLE OF STRESS IN PCOS

- Stress is linked with irregular menstruation, emotional eating, poor sleep, anxiety, and depression in PCOS patients.
- Chronic psychological stress increases cortisol, which aggravates insulin resistance and androgen excess.
- Recent research recognizes PCOS as a condition with both endocrine and psychosocial components.

YOGA AND MINDFULNESS

- Recent studies show yoga improves menstrual cyclicity, insulin sensitivity, and hormonal balance.
- Yoga improves neuroendocrine balance by reducing sympathetic activity.
- Mindfulness-based interventions reduce stress, anxiety, and improve quality of life.
- practices such as pranayama, meditation, and restorative yoga are increasingly recommended as

adjunct therapy.

- This approach uses poses, breathwork, and medications to connect mind and body, promoting relaxations, enhanced focus and improved mental health.
- It is a holistic tool for cultivating inner peace and physical well-being.

PHARMACOLOGICAL MANAGEMENT OF PCOS

Recent pharmacological of PCOS is individualized and

targets insulin resistance, hyperandrogenism, menstrual irregularities, and infertility. First-line therapies remain combined oral contraceptives (COCs) for cycle regulation/hirsutism and metformin for metabolic issue. Emerging trends include GLP-1 receptors agonists (e.g., liraglutides, semaglutide) for weight loss, inositol's (myo-inositol's) for insulin sensitivity, and aromatase inhibitors (letrozole) as a preferred ovulation inducer.

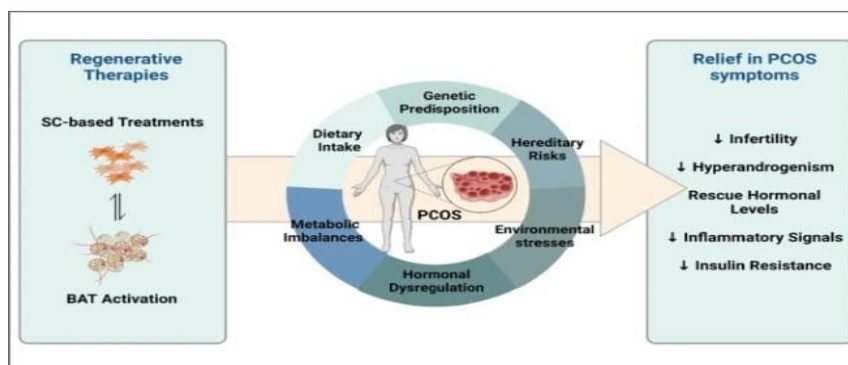


Fig. No. 3 : PCOS.

INSULIN SENSITIZERS

METFORMIN

- Metformin helps manage PCOS by improving insulin sensitivity, which can regulate menstrual cycle, lower androgen levels, and support fertility, especially in those with insulin resistance.
- Overweight/obesity: it's often used with lifestyle changes, sometimes with clomiphene, to aid ovulation, reduce miscarriage risk, and lower IVF complications, though gastrointestinal side effects are common.

MECHANISM OF ACTION

- Reduces hepatic gluconeogenesis.
- Increases peripheral glucose uptake.
- Improve insulin sensitivity in muscle and adipose tissue
- Improves hypothalamic-pituitary-ovarian axis function.

BENEFITS

- Induction improves menstrual regulatory and ovulation
- Reduces insulin resistance and hyperinsulinemia.
- Decrease androgen levels.
- Lowers risk of type 2 diabetes and metabolic syndrome.
- Enhance fertility outcomes when combined with ovulation agents.

ADVERSE EFFECTS

- Gastrointestinal upset (nausea, diarrhea, abdominal discomfort).

- Vitamin B12 deficiency with long-term use.
- Rare risk of lactic acidosis.

HORMONAL THERAPY

Hormonal therapy is primarily used to manage menstrual irregularities and hyperandrogenic symptoms in women not seeking pregnancy.

COMBINED ORAL CONTRACEPTIVES (COCs)

- First-line pharmacological therapy for cycle regulation.
- Suppress ovarian androgen production by inhibiting LH secretion.
- Increase sex hormone-binding globulin (SHBG), reducing free testosterone.
- Hirsutism and improve acne.
- Recent recommendations favor low-dose estrogenic formulations to minimize cardiometabolic

PROGESTINS

- Used to induce regular withdrawal bleeding.
- Protect against endometrial hyperplasia caused by chronic anovulation.
- It can be administered cyclically or continuously.

ANTI-ANDROGENS

- PCOS is a hormonal disorder in women characterized by excess androgen (male hormone) production.
- Androgens normally exist in small amounts in females, but overproduction leads to hormonal imbalance.
- Excess androgens cause acne, excessive hair growth (hirsutism), and menstrual irregularities.

- Hormonal imbalance affects estrogenic and progesterone levels, disrupting the menstrual cycle.
- Due to improper hormone secretion, ovulation does not occur regularly, leading to infertility.
- Insulin resistance is a major contributing factor in PCOS.
- Increased insulin levels stimulate ovaries to produce more androgens.
- PCOS is commonly associated with obesity and sedentary lifestyle.
- Lifestyle factors such as poor diet and lack of physical activity worsen symptoms.
- PCOS has a genetic predisposition; risk increases if a family member is affected.
- PCOS may also be linked with weakened immune system and metabolic disturbances

OVULATION INDUCTION AGENTS

Ovulation induction is a fertility treatment that uses hormonal medication to stimulate the release of one or more eggs in a cycle, enabling a woman to ovulate. For women with PCOS, who often experience irregular or absent ovulation, ovulation induction is a highly effective first step toward achieving pregnancy.

PCOS affects the normal functioning and work of the ovaries and it is one of the most common causes of infertility in women. Many women with PCOS struggle with irregular or delayed periods, which means that they don't ovulate regularly as the body should or at all. This can make it difficult for the couple to get pregnant without any medical or fertility care intervention. Ovulation induction in PCOS helps stimulate ovulation through medication such as:

- **Clomiphene citrate (clomid)**
- **Letrozole (femora)**

CLOMIPHENE

Clomiphene citrate comes under schedule H in India (as per drugs & cosmetics act, 1940 & rules 1945). It is a prescription-only medicine.

- Clomiphene citrate (CC) remains a cornerstone of fertility treatment, particularly for ovulation induction in Polycystic Ovary Syndrome (PCOS), but its role has evolved in recent years to include significant off-label use for male hypogonadism and in advanced, modified IVF protocols. While it is a cost-effective first-line treatment, recent focus has been on managing its anti-estrogenic side effects on the endometrium, its comparative efficacy against aromatase inhibitors, and its application in "mini-IVF".
- "Mini-IVF" and IVF Adjuvant: In IVF, CC is used in "minimal stimulation" (mini-IVF) cycles, which are lower-cost alternatives to conventional stimulation. Recent studies show that continuous, rather than just 5-day, administration of CC can suppress premature LH surges, offering a cost-effective, "antagonist-

free" protocol that is particularly useful for poor responders or in low-cost IVF clinics.

- **Male Hypogonadism and Infertility:** Clomiphene citrate has gained widespread attention as a "first-line" off-label, non-testosterone therapy for men with low testosterone (secondary hypogonadism) who wish to preserve fertility. Unlike testosterone replacement therapy (TRT), which suppresses sperm production, CC stimulates the hypothalamus-pituitary-gonadal (HPG) axis, increasing natural testosterone production while often improving semen parameters.

LETROZOLE

Letrozole comes under the schedule H in India (as per drugs & cosmetics act, 1940 & 1945). It is a prescription only for medicine.

- In recent years, Letrozole has solidified its position as a leading, often first-line, medication for infertility treatment, particularly in women with Polycystic Ovary Syndrome (PCOS), surpassing older treatments like Clomiphene Citrate (Clomid) in effectiveness. Originally developed to treat hormone-sensitive breast cancer, its off-label application in reproductive medicine has been heavily studied and validated, focusing on inducing ovulation by lowering estrogen and increasing follicle-stimulating hormone (FSH).
- **Lower Multiple Pregnancy Risk:** Letrozole typically promotes the development of a single dominant follicle (mono-ovulation), significantly reducing the risk of multiple pregnancies (twins/triplets) compared to other, more potent fertility treatments.
- **Unexplained Infertility:** Studies have shown Letrozole to be highly effective for women with unexplained infertility, often showing better pregnancy rates than Clomiphene.

COMBINED LIFESTYLE AND PHARMACOLOGICAL APPROACH

In recent years (2023–2025), the management of Polycystic Ovary Syndrome (PCOS) has shifted toward a pharmacological agent to address metabolic, reproductive, and psychological symptoms. International guidelines now emphasize that lifestyle modification (diet, exercise, and behavior) is the first line, "non-negotiable" therapy for all PCOS patients, particularly to address underlying insulin resistance and chronic inflammation. Combining lifestyle modifications with pharmacological treatments for Polycystic Ovary Syndrome (PCOS) creates a synergistic effect that tackles the root causes: insulin resistance, hyperandrogenism, and chronic inflammation—more effectively than either approach alone. This holistic approach is essential for managing metabolic, reproductive, and psychological symptoms.

Lifestyle Modifications (First-Line Approach)

- **Dietary Strategies:** There is no single superior diet, but Mediterranean and low-glycemic index (GI)

diets are highly recommended to improve insulin sensitivity and reduce inflammation.

- **Strategic Eating:** Studies from 2023–2025 highlight the "breakfast priority" strategy, where eating the largest meal in the morning improves glucose, insulin, and testosterone levels.
- **Exercise Intensity:** While any physical activity is beneficial, 150–300 minutes per week of a combination of aerobic and resistance training is recommended for better weight management and insulin sensitivity.

Pharmacological action

- **Metformin:** Remains a staple for managing insulin resistance and improving ovulation, often used alongside lifestyle changes to increase success rates.
- **Inositol's (Myo-inositol/D-chiro-inositol):** Inositol (specifically in a 40:1 ratio) is increasingly used to improve ovulation and reduce androgen levels, often considered a "safer" or more natural alternative to pharmacological drugs.

Letrozole vs. Clomiphene: For ovulation induction, letrozole is now preferred over clomiphene citrate Synergistic

Combining lifestyle modifications with pharmacological treatments for Polycystic Ovary Syndrome (PCOS) creates a synergistic effect that tackles the root causes—insulin resistance, hyperandrogenism, and chronic inflammation—more effectively than either approach alone. This holistic approach is essential for managing metabolic, reproductive, and psychological symptoms.

- **ENHANCED OUTCOMES:** Combining lifestyle modification (LSM) with metformin is more effective than either alone in reducing insulin resistances (IR), BMI, and improving menstrual cycles.
- **LONG-TERM MANAGEMENT:** While pharmacological treatments manage symptoms, lifestyle modification are essential for long-term weight maintenance and reducing the risk of comorbidities like type 2 diabetes.

CHALLENGES IN MANagements

- psychological components, making standardized management difficult. The heterogeneous nature of PCOS presents a major challenge, as clinical manifestations vary widely and include reproductive, metabolic, and
- Unclear etiology and complex pathophysiology limit the development of disease-modifying therapies; current management strategies primarily target symptoms rather than the underlying cause.
- Lack of universally accepted diagnostic criteria and phenotypic overlap with other endocrine disorders often result in delayed or inconsistent diagnosis, adversely affecting early intervention.
- Management is further complicated by the high

prevalence of insulin resistance, obesity, and metabolic syndrome, which require long-term lifestyle modification that is often difficult to sustain

FUTURE PERSPECTIVES

- Polycystic ovary syndrome (PCOS) remains a complex and heterogeneous disorder, with its etiology still poorly understood despite extensive clinical and experimental research.
- Genetic evaluation of PCOS has emerged as a crucial gateway for identifying novel molecular pathways and understanding disease heterogeneity. Identification of specific genomic loci may provide critical insights into disease progression and phenotypic variability.
- Increasing evidence suggests that genetic factors play a primary role in PCOS pathogenesis, influencing metabolic dysfunctions such as insulin resistance and hyperandrogenism.
- Genetic abnormalities associated with PCOS have been observed not only in affected women but also among male and female first-degree relatives, indicating a strong heritable component and supporting the concept of familial clustering.
- relationship between PCOS and metabolic traits in male relatives remains controversial; however, advances in genetic and genomic technologies may help clarify this association.
- Current genetic studies in PCOS demonstrate significant inconsistencies, highlighting the need for larger, well-designed, multi-ethnic studies and re-evaluation of previously published findings.
- Although multiple therapeutic interventions are available, current treatments are largely symptomatic, focusing on managing hyperandrogenism-related and metabolic complications rather than addressing the underlying cause.
- Future research should prioritize detailed mechanistic investigations to trace the origin of PCOS at molecular and genetic levels, facilitating the identification of novel therapeutic targets. Improved understanding of genotype–phenotype correlations may enable the development of personalized treatment strategies and potentially disease-modifying therapies for PCOS.

CONCLUSION

This retrospective study highlights that polycystic ovarian syndrome (PCOS) is a multifactorial disorder strongly associated with modifiable risk factors such as sedentary lifestyle, unhealthy dietary habits, obesity, and metabolic disturbances. The findings emphasize that early identification of risk factors and timely lifestyle modifications—particularly weight management, regular physical activity, and balanced nutrition—play a crucial role in improving clinical outcomes and preventing long-term complications. The pharmacological profile indicates that treatment is primarily symptom-oriented, targeting menstrual irregularities, hyperandrogenism,

insulin resistance, and infertility, often requiring individualized therapy. Furthermore, the high prevalence of associated co-morbidities such as insulin resistance, type 2 diabetes, dyslipidaemia, and cardiovascular risks underlines the need for a multidisciplinary approach and long-term monitoring. Overall, comprehensive management combining lifestyle interventions and appropriate pharmacotherapy is essential to reduce disease burden and improve quality of life in women with PCOS.

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