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Review Article

Polycystic Ovarian Syndrome and Recent Management: A Comprehensive Review

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ABSTRACT

A common endocrine condition that affects women of reproductive age, polycystic ovarian syndrome (PCOS) is typified by polycystic ovaries, hyperandrogenism, and irregular menstrual periods. Reducing symptoms, increasing fertility, and lowering the risk of related metabolic diseases such type 2 diabetes and cardiovascular disease are the goals of PCOS treatment. Nutraceuticals, pharmaceuticals, and lifestyle changes are all included in treatment plans. By enhancing insulin sensitivity and hormonal balance, lifestyle modifications such as weight control, exercise, and dietary modifications serve as the cornerstone of treatment. Hormonal imbalances are addressed and menstrual regularity is restored by pharmacological treatments such insulin-sensitizing drugs like metformin, oral contraceptives, and anti-androgens. Nutraceuticals like omega-3 fatty acids and inositol, Antioxidants have demonstrated potential in enhancing ovarian function and insulin resistance. By integrating natural and conventional medicines, this integrated approach provides a holistic approach to managing PCOS, encouraging long-term health advantages and symptom relief. To maximize these treatments and create uniform protocols for their application, more study is required.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age. It is characterized by hormonal imbalances, irregular menstrual cycles, and the

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presence of small cysts on the ovaries.^[1] Women with PCOS often have elevated levels of androgens, commonly known as "male hormones," though these are naturally present in both sexes. This hormonal imbalance can lead to symptoms such as excess facial or body hair (hirsutism), acne, and male-pattern baldness.^[2-4]

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Many women with PCOS develop numerous small, fluid-filled sacs (cysts) in their ovaries. However, not all women with PCOS will have cysts, and the presence of cysts is not required for a diagnosis. These cysts result from follicles that fail to release eggs properly during the menstrual cycle. ^[5] A significant number of women with PCOS have insulin resistance, which means their bodies do not use insulin effectively. As a result, the body produces more insulin to compensate. Excess insulin can increase androgen production, worsening PCOS symptoms. Over time, insulin resistance can lead to type 2 diabetes. ^[6]

Phenotypes Of PCOS:

Polycystic Ovary Syndrome (PCOS) presents with a range of clinical manifestations, often described as **phenotypes**.^[7] These phenotypes are variations in how the symptoms and characteristics of PCOS present in different individuals. The recognition of distinct phenotypes helps healthcare providers tailor treatments based on the specific combination of symptoms a woman experience.^[8]

> Phenotype A:

Classic PCOS (Hyperandrogenism + Ovulatory Dysfunction + Polycystic Ovaries)

Hyperandrogenism: Elevated levels of male hormones (androgens), which can lead to symptoms such as excess hair growth (hirsutism), acne, and male-pattern baldness.

Ovulatory Dysfunction: Irregular or absent ovulation, leading to irregular menstrual cycles and fertility issues.

Polycystic Ovaries: The presence of multiple small cysts on the ovaries detected by ultrasound.

> Phenotype B:

Hyperandrogenism + Ovulatory Dysfunction (No Polycystic Ovaries)

Hyperandrogenism: Symptoms such as hirsutism, acne, and hair loss.

Ovulatory Dysfunction: Irregular menstrual cycles, but normal-appearing ovaries on ultrasound.

> Phenotype C:

Hyperandrogenism +Polycystic Ovaries (No Ovulatory Dysfunction)

Hyperandrogenism: High androgen levels causing symptoms like hirsutism and acne.

Polycystic Ovaries: Detected by ultrasound.

Normal/near-normal menstrual cycles and ovulation, meaning fertility may be less affected.

> Phenotype D:

Ovulatory Dysfunction + Polycystic Ovaries (No Hyperandrogenism).

Ovulatory Dysfunction: Irregular periods due to abnormal ovulation.

Polycystic Ovaries: Present on ultrasound.

No evidence of elevated androgens, meaning they typically do not experience symptoms like hirsutism, acne, or male-pattern baldness.

Etiology Of PCOS:

While the fact that the real cause of PCOS is unknown, it is known to be a complex disorder with a genetic component. Compared to an estimated 4-6% prevalence in the general population, 20–40% of first-degree female relatives of women with PCOS go on to develop



PCOS themselves^[9]. Even if PCOS was never identified, many women with the condition have female relatives who also Similar to type 2 diabetes, PCOS is most likely caused by a variety of genes, each of which contributes very slightly to the etiology. Candidate genes have been identified by recent genome-wide association studies. Environmental and epigenetic variables, such as poor food and inactivity, are likely to enhance any underlying genetic danger.^[10]

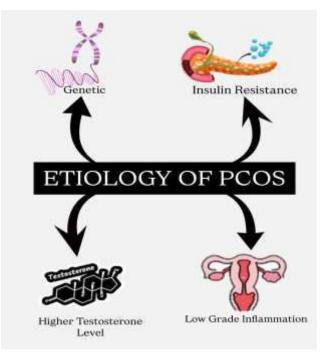


Figure 1: This Figure Illustrate The Various Factors Contributing To The Etiology Of Pcos.

- Genetic factors: Although PCOS is a hereditary disorder, its inheritance pattern is unclear. But it's more likely in women who have a close relative with PCOS; 20–40% of women with PCOS are thought to have a mother or sister who has the disease.
- Greater concentrations of androgens or male hormones: when ovaries are unable to release eggs due to high testosterone levels, which results in irregular menstruation cycles. Small, sacs packed with fluid may also form on ovaries as a result of irregular ovulation. For women and people, high testosterone also results in acne and excessive hair growth.
- **Insulin resistance:** The ovaries produce and release androgens, which are androgen

hormones, in response to an increase in insulin levels. Male hormone excesses suppress ovulation and increase other PCOS symptoms. Insulin promotes the body's use of glucose, or sugar, as energy. When body doesn't process insulin correctly if have insulin resistance, which increases blood glucose levels. Insulin resistance can cause diabetes, however not all people with it have high blood glucose levels or diabetes. Obesity or being overweight might also cause insulin resistance.

• Low-grade inflammation: Chronic lowgrade inflammation is a common symptom of PCOS patients. Blood tests that evaluate white blood cell and C-reactive protein (CRP) levels can be performed by your healthcare provider



to determine the degree of inflammation in your body.

PCOS Symptoms:

PCOS is a collection of symptoms rather than a medical condition. Differences between people may exist with these symptoms. ^{[1][5][8]}

- Skipped, Irregular, Infrequent, Or Extremely Prolonged Menstrual Cycle
- Hair fall
- Excessive body and facial hair (hirsutism)
- Oily Skin
- Skin Darkness
- Skin Lumps
- Weight Gain (Pcos Belly)
- Cysts On The Ovaries.
- Mood Change

Pathophysiology:

It is still unclear what caused the vicious circle of illnesses that make up PCOS pathophysiology. The pathophysiology of PCOS is diverse and complex, which is the primary reason for the challenges in comprehending it.^[19-21] The pathogenesis of PCOS has been linked to hyperandrogenism, ovulatory dysfunction, gonadotropin-releasing irregular hormone (GnRH) pulsation and the ensuing abnormal gonadotropin production, and insulin resistance; these variables interact and exacerbate one another.^[22-23]PCOM is caused by the hypersecretion of androgens in cases of ovarian dysfunction, which is linked to abnormal fibrular dysfunction.^[23-25]By ovulatory growth and changing the follicular microenvironment and/or GnRH pulsation, high amounts of anti-Müllerian hormone (AMH), which are released by pre/small

antral follicles that accumulate in PCOS ovaries, worsen ovarian failure.^[26]

Hyperandrogenism:

Hyperandrogenemia, which shows up clinically as hirsutism, acne, and alopecia, is the biochemical hallmark of PCOS. 75–90% of cases have high levels of androgens, which can manifest as hirsutism, acne, and alopecia. Seventy to ninety percent of PCOS patients with oligomenorrhea also have high levels of androgens, and their concentrations tend to increase with the severity of the phenotypic.^[31]

Hyperinsulinemia:

The primary hormone controlling both lipogenesis and glucose homeostasis is insulin. Insulin mediates the activity of several tissues of the HPO axis and acts as a mitogenic hormone in addition to influencing the metabolism of proteins, lipids, and carbohydrate. [34] In steroidogenic organs like the ovary and the adrenal cortex, insulin amplifies the appropriate trophic hormones to promote steroidogenesis. [40-41] Hyperinsulinemia is the main factor for excessive androgen production because insulin increases GnRH indirectly and directly mimics the effect of LH.^[35] Insulin reduces sex hormone binding globulin (SHBG), a vital circulatory protein that controls testosterone levels. Consequently, increased levels of free androgens, which induce PCOS symptoms like hirsutism, alopecia, and acne, would result from decreasing SHBG levels .Several investigations have demonstrated that reducing insulin resistance will eventually lead to a decrease in androgens and an improvement in the illness state. [35-39]



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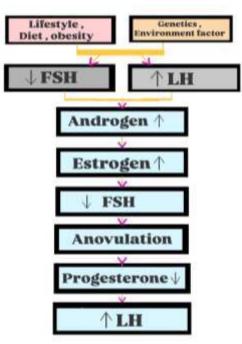


Figure 2: This Figure Is An Key Pathway Involving In The Pathophysiology Of Pcos

DIAGNOSIS:

Those test must be perfrom in order to diagnose polycystic ovarian syndrome.^[13-14]

1.Hormonal Blood Test: LH/FSH ratio: In PCOS, the LH/FSH ratio is often >2:1 (for example, an elevated LH level with a normal FSH level).

Normal LH levels (per cycle phase):

Follicular phase: 2–12 mIU/mL Ovulatory phase: 14–95 mIU/mL Luteal phase: 1–10 mIU/mL

Normal FSH levels (per cycle phase):

Follicular phase: 3-10 mIU/mL

Ovulatory phase: 6–21 mIU/mL Luteal phase: 1–7 mIU/Ml

Testosterone (Total)

Normal range for women: 6–86 ng/dL (depending on the lab and phase of the menstrual cycle). Elevated levels are typically greater than 86 ng/dL in PCOS and can contribute to symptoms like hirsutism (excessive hair growth), acne, and scalp thinning.

Free Testosterone

- **Normal range for women**: 0.3–1.9 ng/dL.
- free testosterone levels are typically elevated.

Thyroid Stimulating Hormone (TSH)

Normal range for TSH: 0.4–4.0 mIU/L (varies by lab). Hypothyroidism can mimic PCOS symptoms (like menstrual irregularities), so ruling out thyroid disorders is important.

2. Ultrasound Imaging (Pelvic Ultrasound)

Ovarian morphology:

Polycystic ovaries: Defined as the presence of 12 or more follicles (2–9 mm in diameter) in each ovary or an ovarian volume >10 mL.



- Ovaries in women with PCOS often appear enlarged with multiple cysts (but not all women with polycystic ovaries will have PCOS).
- Endometrial thickness: In some cases, the endometrial lining may appear thicker due to anovulation, another feature often seen in PCOS.

3. Oral Glucose Tolerance Test (OGTT)

This test is used to assess insulin resistance, which is commonly associated with PCOS.

- Fasting blood glucose (Normal range): 70–99 mg/dL.
- 2-hour post-load glucose (Normal range): <140 mg/dL.</p>
- Insulin levels: Elevated insulin (often above 25–30 µU/mL) may indicate insulin resistance, which is common in PCOS.

4. Lipid Profile (Cholesterol and Triglycerides)

Women with PCOS are at an increased risk for cardiovascular diseases due to insulin resistance and metabolic abnormalities.

- > Total Cholesterol: <200 mg/dL (optimal)
- Low-Density Lipoprotein (LDL): <100 mg/dL (optimal)
- ➤ High-Density Lipoprotein (HDL): ≥50 mg/dL (optimal for women)
- **Triglycerides**: <150 mg/dL (normal)

COMPLICATION:

Although PCOS can have severe effects on health, many women with the condition lead happy,

healthy lives when given the right care and support. ^[15] Minimizing problems requires a customized treatment plan and routine check-ups. If left untreated, polycystic ovarian syndrome (PCOS) can result in a number of issues. Below is a summary of some typical issues related to PCOS. ^[16-17]

- Menstrual Cycle Disorders
- Endometrial Wellness
- Higher Chance of Miscarriage
- Resistance to Insulin
- Difficulties in Losing Weight.
- Dyslipidemia
- Fatty Liver
- Higher Risk of Cardiovascular Disease
- Blood pressure
- Potential of atherosclerosis
- Depression and Anxiety
- Stress
- Sleep Disorders

Treatment and Management Of PCOS:

1: Lifestyle Modifications: ^[23-30]

- Well-Balanced Diet: Stress on Whole Foods: Include an abundance of fruits, vegetables, whole grains, lean meats, and good fats in your diet.
- Foods with a low Glycemic Index (GI): Foods with a low GI can aid in blood sugar stabilization. Legumes, whole grains, and nonstarchy veggies are a few examples. Limit Processed Foods and Sugars: Cutting back on sugar and processed carbs can improve insulin sensitivity and aid with weight control.
- Regular Exercise: Cardio and Strength Training Combined: Aim for two to three times a week of strength training exercises in addition to at least 150 minutes of moderateintensity aerobic activity per week.Embrace Movement in Your Everyday Life: Look for



opportunities to move throughout the day, such as increasing your walking or using the stairs.

- Goal for Losing Weight: Define Reasonable Objectives: Reducing body weight by 5–10% can greatly improve symptoms and metabolic health. Pay Attention to Long-Term Changes: Make little, steady adjustments instead of abrupt, more difficult-to-maintain diets.
- Stress Reduction: Mindfulness and Relaxation Techniques: Stress can worsen the symptoms of PCOS, so it's crucial to learn how to manage it. Techniques like yoga, meditation, or deep breathing exercises can assist.
- Healthcare Providers with Medical Support Consult: Consulting with a physician or a certified nutritionist knowledgeable in PCOS might offer specialized guidance and assistance
- Medication: To assist with insulin sensitivity and weight management, doctors may occasionally prescribe drugs like Metformin.
- > Insulin Sensitizing Agent: Metformin: Insulin sensitizing agents Insulin-sensitizing medications are being utilized more frequently to treat PCOS patients' insulin resistance in the short term. Metformin lowers fasting plasma insulin and encourages weight loss, according to controlled trials. Other studies demonstrate that the medication lowers progesterone production with recovery of ovulation, regardless of weight loss. [31-35] Metformin usage In order to improve hirsutism and restore menstrual periods, this medication is currently being explored for first-line treatment in women with PCOS. [34-36] Metformin is a biguanide that increases the sensitivity of peripheral tissue to insulin, decreases hepatic gluconeogenesis, and increases the muscle's absorption and use of glucose. Metformin insulin lowers plasma levels. which significantly reduces hyperandrogenism in PCOS. Pregnancies have been documented in PCOS patients on metformin, with no associated risks. [38-42]

2: Pharmacological Treatment:

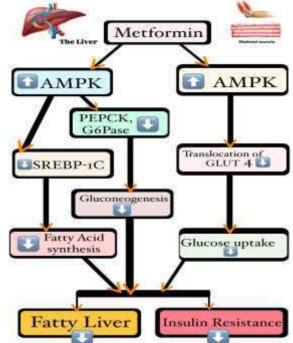


Figure 3: This Figure Represent The Mechanism Of Metformin Action In Pcos.

> Troglitazone: Troglitazone Recently, thiazolidinediones, another class of insulinsensitizing drugs, have been made accessible for the treatment of insulin-resistant conditions. Troglitazone is one of these; it acts on muscle and adipose tissue to improve insulin sensitivity and inhibits hepatic gluconeogenesis to reduce insulin resistance and ameliorate hyperinsulinemia. ^[50] The medication lowers insulin-mediated ovarian androgen excess and improves menstrual periods in women.400 mg used once a day raises SHBG levels while lowering plasma and free testosterone levels. Liver dysfunction is one of the side effects, hence liver function must be evaluated.^[51]

Oral Contraceptives:

Cyproterone acetate (CPA):

Cyproterone acetate (CPA) is an effective antiandrogen and progestagn. It decreases 5-alpha reductase activity, inhibits androgen steroidogenesis, and prevents dihydrotestosterone (DHT) from attaching to its receptor. For endometrial shedding and hyperandrogenism management, CPA has been used cyclically in conjunction with ethinyl estradiol (EE). Light headedness, depression, weight gain, decreased libido, and fluid retention are a few typical adverse effects ^[54] Research indicates that women with PCOS who present with acne and hirsutism can benefit from combination medication, which is both safe and effective. ^[53]

Spironolactone:

The management of hyperandrogenism with spironolactone has been very well-established. Oral contraceptives plus spironolactone are more effective when taken together than when taken alone. By avoiding pregnancies, it also avoids any potential teratogenic involvement with the development of the male fetus. Despite the lack of any documented cases of terotogenicity, there is a general consensus that pregnancy should be avoided for at least 4 months. Normally, the medication lowers insulin resistance and does not result in weight gain. Since it is a diuretic, it might cause salt depletion, therefore serum potassium levels and renal function should be monitored. Spironolactone may result in mood swings, exhaustion, decreased lipid level, headaches, menstrual irregularities.^[55]

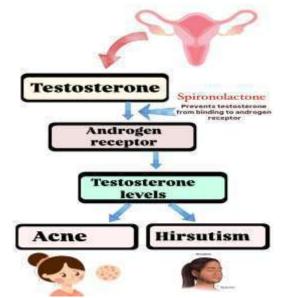


Figure 4: This Figure Represent The Mechanism Of Spironolactone In Pcos.



> Infertility:

Clomiphene citrate:

Many anovulatory women with PCOS can induce ovulation and pregnancy with even modest levels of FSH introduced into the circulation, either directly by FSH injections or indirectly through pulsatile GnRH or clomiphene citrate. For a long time, the first line of treatment for people with irregular or missing ovulation has been clomiphene citrate. Starting on day 2–5 of spontaneous or induced bleeding, it is administered at a dose of 50–250 mg per day for 5 days. The lowest dose is started at and is increased by 50 mg/day per cycle until an ovulatory cycle is reached. ^[56-59]

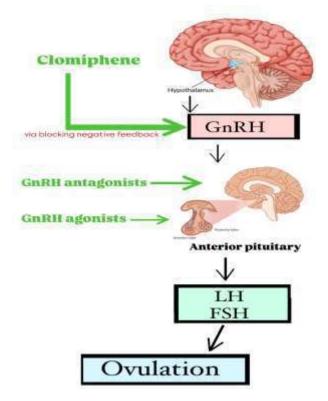


Figure 5: This Figure Represent The Mechanism Of Clomiphene Citrate In Pcos.

Aromatase Inhibitor:

Letrozole:

Women with polycystic ovarian syndrome (PCOS) are increasingly being treated with letrozole (Femara) to induce ovulation, particularly if they do not react to clomiphene citrate. Letrozole is an aromatase inhibitor that lowers estrogen synthesis in the ovaries by preventing androgens from being converted to estrogens.^[60]Follicle-stimulating hormone (FSH) and luteinizing hormone (LH) secretion rises as a

result of the hypothalamus's enhanced release of gonadotropin-releasing hormone (GnRH) in response to this drop in estrogen levels. Ovulation may result from this procedure, which encourages the development of ovarian follicles.Normal Initial Dosage: The initial dosage is typically 2.5 mg taken five days a day on cycle days three through seven.

Management for Metabolic Disorder:

Atorvastatin:



The atorvastatin pretreated group significantly outperformed the placebo pretreated group in terms of HOMA-IR, the free androgen index (FAI), total testosterone, and SHBG when both groups received metformin for an additional 12 weeks This suggests that atorvastatin enhances the effects of metformin. As a result of atorvastatin's considerable reduction in inflammatory and adipose tissue dysfunction indicators, ASP, IL-6, and monocyte chemoattractant protein-1 (MCP-1) in this study, HOMA-IR and testosterone levels significantly improved.^[665]

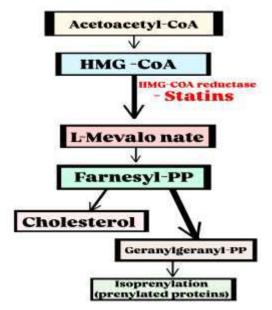


Figure 6: This Figure Represent The Mechanism Of Atorvastatins In Pcos .

Neutraceutics For Treatment:

Oxidative Stress and Antioxidants:

One significant element in the pathophysiology of PCOS is oxidative stress. Therefore, it has been suggested that these patients receive antioxidant treatment. The tiny algae Haematococcuspluvialis produces a natural source of astaxanthin, a potent antioxidant with supplementary anti-inflammatory properties, in its biomass. Astaxanthin is a member of the carotenoids and is neither poisonous nor teratogenic. ^[71] It provides favorable effects in a number of disorders and guards against oxidative damage to DNA and the cell membrane. Ubiquinol Q10 (CoQ-10) is an oxido-reductase co-enzyme that primarily functions as an antioxidant and enhances mitochondrial activity. Patients with

PCOS have been successfully treated with CoQ-10. ^[66]

Minerals:

Zinc and Selenium Glutathione peroxidase that is dependent on selenium has anti-tumor capabilities and is relevant to patients with PCOS]. It has been observed that women with PCOS had reduced selenium levels. Selenium-salt food supplements were linked to better metabolic response in these people and may lower their chance of developing cancer. Many PCOS patients have long-term metabolic imbalances and mitochondrial abnormalities. Zinc supplementation can remedy this particularly when combined with ubiquinol Q10.^[67]

Fatty Acids with Omega-3:



Fatty Acids with Omega-3 Through a variety of pathways, the long-chain polyunsaturated (PUFA) omega-3 fatty acids docosohexaenoic acid (DHA) and eicosapentaenoic acid (EPA) do lessen the consequences of PCOS [30]. These PUFAs that are esterified in phospholipids are abundant in krill oil. Compared to pure fatty acids, esterified DHA and EPA are more readily absorbed through the mouth, and krill oil is more environmentally friendly than fish oil.^[68]

Vitamin D:

Low levels of vitamin D are detected in many women with polycystic ovarian syndrome (PCOS), a disorder that is heavily reliant on this vital vitamin for control. When the body is exposed to sunshine, vitamin D is naturally produced. Depending on your skin type and the climate where you live, aim for 15 to 30 minutes of sun exposure several times a week. Cholecalciferol, or vitamin D3, is frequently advised as a supplement. Although dosages might differ, standard advice falls between 1,000 and 2,000 IU per day, contingent on personal requirements and baseline levels of vitamin D.For many women with PCOS who develop insulin resistance, vitamin D may improve insulin sensitivity. It may have a favorable impact on hormone levels, particularly androgens, and help regulate menstrual cycles.One potential factor in improving ovulatory function, which is advantageous for women who are attempting to become pregnant. Its anti-inflammatory properties could aid in reducing the persistent, low-grade inflammation that PCOS patients frequently experience.^[69]

Surgical Approach For PCOS:

Polycystic Ovary Syndrome (PCOS) is a hormonal disorder that affects women of reproductive age, characterized by irregular menstrual cycles, excess androgen levels, and polycystic ovaries. While the primary treatment options for PCOS include lifestyle changes, medications, and hormonal therapy, surgery may be considered for certain patients, especially when other treatments fail or for those who wish to conceive. The primary surgical approach for PCOS.^[70]

- **Ovarian Drilling (LOD):** Primary surgical option for inducing ovulation in clomiphene-resistant PCOS.
- **Surgery of the Ovarian Wedge:** (Historically Used) Before LOD was created, this was an older surgical method. To reduce the ovarian's volume and induce ovulation again, a wedge-shaped section of the ovary is removed
- **Bariatric Surgery:** Indirect benefit for women with severe obesity-related PCOS.
- **Endometrial Ablation:** For abnormal uterine bleeding management, not directly for PCOS treatment.

FUTURE PROSPECTS:

Clinically speaking, PCOS is a complicated ailment that can have long-term effects on a person's life. It is also becoming more common in women who are fertile. Personalized therapeutic techniques when implemented on time will increase quality of life, lower comorbidities, and improve overall PCOS management. Women who may become infertile during their reproductive years must be diagnosed and treated early to enhance their prognosis. Important gene polymorphisms may be helpful in the early detection and screening of PCOS subtypes. It will take further research on the pathophysiology and genetics of PCOS to determine effective therapeutic and preventive measures. Further investigation is necessary to determine whether variations in steroid levels in PCOS patients affect



the makeup of gut bacteria and the mechanisms underlying these changes. Supplementing.^[71] The use of gut microbiota as a biomarker for PCOS will be made possible by future thorough and functional study, and the focused, individualized alteration of gut microbiota will further the field's progress. Since current treatments focus more on treating symptoms than the underlying cause of the illness, there isn't a magic bullet. Comprehensive research on the syndrome should be done in order to enhance treatment and postpone the disease's grave long-term effects on patients' health. A number of recently developed treatments for type 2 diabetes may be directly helpful in managing the metabolic components of PCOS; however, further research is required to assess these treatments' safety and clinical usefulness in PCOS-affected women. To demonstrate the potential of novel treatments, including IL-22 therapy, miRNA therapy, and others, in effectively treating PCOS, more research is needed.^[72]

CONCLUSION:

Polycystic Ovarian Syndrome (PCOS) is most common endocrine system condition in women of reproductive age. Numerous risk factors, including as obesity, glucose intolerance, and dyslipidemia, have been studied in connection to PCOS. It is well recognized that a key factor in the pathogenesis of PCOS is insulin resistance. Numerous studies recommend the use of novel or modified medicines to treat PCOS-related obesity and metabolic syndrome. Inositols, statins, letrozole, and vitamin D have been the subjects of recent clinical trials aimed at treating PCOS. Larger clinical investigations are still required, despite the encouraging outcomes of clinical trials using DPP-4 inhibitors, SGLT2 antagonists, and GLP-1 agonists. The experiments' conclusions are not clear. The adoption of lasers and other cosmetic procedures to remove unwanted hair has enhanced

these patients' physical appearance and, consequently, their quality of life. Studies on the use of traditional and folk medicine to treat PCOS, however, are conflicting and require further investigation on their efficacy and safety profiles. The need for thorough and ongoing research into innovative approaches to treating PCOS is urgent since it can lead to the development of more effective treatment plans for PCOS patients, enhance their quality of life, and stop the onset of comorbidities.

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