VOLUME 11 ISSUE 2 2025

ISSN 2454 – 3055

INTERNATIONAL JOURNAL OF ZOOLOGICAL INVESTIGATIONS

Forum for Biological and Environmental Sciences

Published by Saran Publications, India

International Journal of Zoological Investigations Vol. 11, No. 2, 361-366 (2025)

International Journal of Zoological Investigations

Contents available at Journals Home Page: www.ijzi.net

Editor-in-Chief: Prof. Ajai Kumar Srivastav

Published by: Saran Publications, Gorakhpur, India

ISSN: 2454-3055

Poly Cystic Ovarian Disorder: Etiology, Current Management, and Future Therapeutics

Sai Sharanya P., Praveena Devi CH. B.*, Anjali M., Akhila V. and Aarthi K.

Joginpally B. R. Pharmacy College, Bhaskar Nagar, Yenkapally (V), Moinabad (M), R. R. Dist, Hyderabad 500075, India

**Corresponding Author*

Received: 11th March, 2024; **Accepted:** 22nd June, 2025; **Published online:** 4th September, 2025

https://doi.org/10.33745/ijzi.2025.v11i02.033

Abstract: Polycystic Ovarian Disorder (PCOD), also known as Polycystic Ovary Syndrome (PCOS), is a prevalent endocrine disorder affecting women of reproductive age, with significant implications for fertility, metabolic health, and quality of life. The etiology of PCOD is multifactorial, involving genetic, hormonal, and environmental factors. The hallmark features of PCOD include irregular menstrual cycles, hyperandrogenism, and polycystic ovaries, which often result in infertility, hirsutism, acne, and metabolic disturbances such as insulin resistance. Current management strategies primarily focus on symptom control and may include lifestyle modifications, pharmacological interventions, and, in some cases, surgical procedures. Common treatments include hormonal contraceptives, insulin-sensitizing agents like metformin, anti-androgens, and ovulation induction therapies. While these approaches are effective in managing symptoms, there is no cure for PCOD. Emerging therapies are exploring molecular mechanisms, such as targeting insulin resistance, hormonal imbalances, and inflammation. Potential future therapeutics include novel pharmacological agents, gene therapy, and stem cell-based treatments. Continued research into the underlying pathophysiology of PCOD is essential for developing more personalized and effective treatments, offering hope for improved long-term outcomes for women affected by this condition.

Keywords: PCOS, Infertility, Thyroid, Symptoms, Treatment

Citation: Sai Sharanya P., Praveena Devi CH. B.*, Anjali M., Akhila V. and Aarthi K.: Poly Cystic Ovarian disorder: Etiology, current management, and future therapeutics. Intern. J. Zool. Invest. 11(2): 361-366, 2025.

https://doi.org/10.33745/ijzi.2025.v11i02.033

Introduction

Polycystic ovarian disorder (PCOD) or Polycystic Ovary Syndrome (PCOS), is an affecting case where women of reproductive age are more likely to be affected. It is considered to be a chronic disorder and is not curable. It may generally occur in the period of adolescence. PCOD has a high range effect to cause hormonal imbalance which mostly leads to irregularity of periods. In the condition of these random periods, the majority of the women lack ovulation which results in

difficulty during the pregnancy period.

PCOS also leads to miscarriage and infertility. The cause of PCOS remains unknown but there could be a chance of family history (genetic) or type 2 diabetics which are at high risk. When women's ovaries (producing organs/releasing eggs) create excess hormones, individuals who are suffering from PCOS produce high levels of androgen. In PCOS conditions, the cyst can be visible on women's ovaries on ultrasound. Small follicle cysts appear due to lack of ovulation.

Chronic diseases characterized by hyperandrogenism anovulation. 6-20% depending on diagnostic criteria. Women of childbearing age are affected. Symptoms of PCOS occurs in early adolescence. Both normal women's Adolescent development and her PCOS characteristics are as follows:

Most available clinical data communicate findings and outcomes in adult women. Whereas the Rotterdam criteria are accepted for adult women, different diagnostic standards for polycystic ovarian disorders in adolescent girls have been delineated. Diagnostic features for adolescent girls are menstrual irregularity, clinical hyperandrogenism, and hyperandrogenemia.

It is not necessary for the diagnosis of PCOS in an adolescent girl. Fat adolescents with clinical symptoms before final diagnosis of PCOS is signs of androgen excess and oligomenorrhea/ amenorrhea. The characteristics of PCOS are considered to be at risk of PCOS.

Management of both patients at risk of PCOS and confirmed PCOS diagnosis includes education, healthy lifestyle, and therapeutic interventions to address the symptoms specifically. Interventions may include a planned transition to the adult caregiver. Full knowledge of the pathogenesis of PCOS allows this early identification with high developmental trends of PCOS. Timely implementation of individualized treatment intervention improves the overall management of PCOS during adolescence, prevention of associated co-morbidities, and improves quality of life.

Epidemiology

PCOS is the most common endocrine pathology in reproductive-aged females globally, affecting between 5% to 15% of women, depending on the diagnosis standard. The Rotterdam criteria include a broader range of prevalence rates than the National Institutes of Health. Based on 2012 NIH workshop report, it is estimated that about 5 of them are affected by PCOS. There are millions of women of childbearing age in the United States.

The cost of diagnosing and treating PCOS is approximately $4 billion annually (not including fees). Serious comorbidities are associated with PCOS. These are -- Infertility, metabolic syndrome, Obesity, glucose intolerance, DM-2, cardiovascular risk, depression, OSA, endometrium cancer, NAFLD/NASH. The higher prevalence is associated with first-degree relatives of PCOS, pre-pubertal obesity, and congenital virilizing disorders, above average or low birth weight.

Pathophysiology

The pathophysiology of PCOS involves a major defect in the hypothalamic-pituitary axis, secretion and action of insulin, and ovarian function. The cause of PCOS is unknown, but PCOS is thought to be associated with insulin resistance and obesity. The relationship with the action of insulin is expected; insulin helps regulate ovarian function, and the ovaries respond to excess insulin. Production of androgens can cause anovulation. Cessation of follicular maturation is a sign that something is wrong with ovaries. Clinical signs of PCOS include elevated luteinizing hormone (LH) levels and increased gonadotropin release. Hormone levels (GnRH) are reduced while follicle-stimulating hormone (FSH) levels are reduced or decreased.

Increased GnRH stimulates the membranous cells of the ovary producing more androgens. The follicular arrest can be corrected by increasing endogenous FSH or by providing exogenous FSH. Some studies suggest that PCOS is the primary defect in girls who are entering adolescence and their families have this disorder. Approximately

25% of people with PCOS have elevated prolactin levels. Therapeutic interventions aim to reduce insulin levels and ovarian androgen production. This ultimately leads to the modification of sex hormone-binding globulin (SHBG). This increases in SHBG values. These values can be used to treat the symptoms of PCOS effectively. A PCOS patient's Cal cells produce higher amounts of testosterone, progesterone, and 17-Hydroxy-progesterone than in normal patients. These cells are altered in PCOS patients Its cytochrome P450 (CYP) 11A, 3-HSD2, and CYP17 gene levels are increased in obesity. Although a common comorbidity of PCOS, it is not necessary for diagnosis.

Diagnostic Tools for Polycystic Ovary Syndrome

Non-pharmacological Approaches

Since the cause of PCOS is not known, treatment is focused on the symptoms. Few treatments work for all aspects of PCOS, and the patient's desire for fertility may keep them from seeking treatment even when they have symptoms. The goals of treatment should be to correct anovulation, stop the effects of androgens on the target tissues, and reduce insulin resistance. Weight loss for obese people with PCOS is helpful in many ways. It helps to reduce androgen, LH, and insulin levels. Additionally, it helps to control ovulation, which improves the chances of pregnancy. The procedure, known as laparoscopic ovarian drilling, is an outpatient surgical procedure in which several perforations are made in the ovaries and stroma. It is believed to destroy androgen-producing tissues, resulting in a decrease in androgen levels. This procedure has been found to work as effectively as medical interventions, and it does not increase the risk of multiple pregnancies (Legro, 1998).

Pharmacological Approaches

Anovulation

Clomiphene

Clomiphene is a drug that is used to induce ovulation in people with PCOS, but the exact way it works is not fully understood. The first dose is usually 50 mg per day for 5 days. If the first cycle does not produce a pregnancy, the 50 mg per day is repeated for the next cycles. If the second cycle does not result in a pregnancy, the dose can be raised to 100 mg per day for a minimum of 30 days following the first cycle. After three courses of treatment, further treatment may not be recommended, but it is possible to try to conceive up to six times before further treatment is considered. Clomiphene leads to successful pregnancies in about 30% of cases; however, in about 20% of cases, the pregnancy leads to spontaneous abortion or stillbirth. Adverse reactions to Clomid may include Ovarian enlargement, Ovarian hyperstimulation (OHSS), Multiple Pregnancies, Hot Flashes, Gastric (GI) Distention, Bloating Pain (Huyghe *et al*., 2023).

Antidiabetic agents

Additional medications can be combined with clomiphene to enhance the chances of successful ovulation. Antidiabetic medications can also be utilized to improve fertility, reduce insulin resistance, and lower levels of circulating androgens. There is more available data on the effectiveness of metformin (Glucophage, Bristol-Myers Squibb) compared to thiazolidinediones in the treatment of polycystic ovary syndrome (PCOS). A study involving 320 women compared the use of metformin with a placebo for the treatment of infertility in PCOS. After 3 months of treatment without achieving any pregnancies, participants were allowed to incorporate an appropriate infertility treatment into their regimen, regardless of the assigned group (Ndefo *et al*., 2013).

In comparison to placebo, the live birth rates were 41.9% and 28.8% for the treatment group and placebo group, respectively (P = 0.014). However, a meta-analysis assessing the efficacy of metformin in enhancing reproductive outcomes for women with PCOS did not show any significant improvement in live birth rates with metformin alone or in combination with clomiphene. A combination of clomiphene and metformin may be

considered if individual treatments are unsuccessful, although the evidence. supporting improved outcomes is limited (Lord *et al*., 2003).

Fifty women received pioglitazone 15 mg + metformin 850 mg once daily from the first day of the cycle for 10 days, and 50 women received metformin (500 mg three times daily). Clomiphene citrate (CC) 100 mg from the third day of the cycle for 5 days was added to each group. Treatment was continued for three cycles. Ovulation rate was significantly higher in the pioglitazone + metformin and CC group than the metformin and CC group (69.8% versus 48.8%) (P= 0.002). Significantly higher serum E_2 on day 12 and thicker endometrium were found in the pioglitazone + metformin and CC group in the three follow up cycles. Also, cummulative pregnancy rate was significantly higher in the pioglitazone + metformin and CC group than the metformin and CC group (58% versus 34%) (P= 0.027) (Ghada *et al*., 2014).

Live birth rates were significantly higher in the combination and clomiphene arms compared to the metformin arm. In a separate analysis, women with PCOS and elevated serum testosterone levels were randomly assigned to receive clomiphene alone or clomiphene with extended-release metformin. The prevalence of at least one ovulation after treatment was 75% and 83% for the clomiphene-only and clomiphene/metformin groups, respectively.

The addition of extended-release metformin did not reduce the required dose of clomiphene for ovulation induction. Metformin is generally well tolerated, although it may cause initial GI disturbances such as diarrhea and nausea. In a meta-analysis comparing pioglitazone with metformin in PCOS patients, pioglitazone was more effective in reducing fasting insulin levels, while metformin was more effective in reducing body weight. Gonadotropins, such as HMG and FSH, can be used if clomiphene and/or metformin therapy is unsuccessful in inducing ovulation. One study showed higher pregnancy and live birth rates with FSH compared to clomiphene. Despite the potential effectiveness of gonadotropins, the cost and ease of administration favor clomiphene as a first-line therapy for fertility in PCOS (Hochberg *et al*., 2011).

It was found that FSH resulted in higher pregnancy rates compared to clomiphene (58% vs. 44%, respectively; P = 0.03). Additionally, there were more live births with FSH (52% vs. 39%, respectively; P = 0.04). However, it is important to consider that while gonadotropins may be more effective in inducing ovulation, clomiphene is favored as a first-line therapy for fertility in PCOS due to its lower cost and easier administration. It is worth noting that low-dose FSH was used in this study to minimize the risk of multiple pregnancies and OHSS associated with high doses (Lee and Rausch, 2012).

Oral contraceptives

Women diagnosed with PCOS who are not looking to conceive may opt for oral contraceptives (OCs). The primary mode of action of OCs in managing PCOS is by regulating menstrual cycles. Additionally, these medications help in reducing hirsutism, acne, and androgen levels. Estrogen and progestin combinations are the main types of OCs prescribed for addressing hirsutism and acne linked with PCOS.

While there is limited data available, some newer OCs contain anti-androgenic progestins like Bayer's drospirenone (e.g., Yaz) and dienogest (e.g., Natazia). In theory, these medications are more effective in alleviating androgenic symptoms when compared to older formulations. Women experiencing hirsutism typically observe clinical improvement after around 6 months of OC treatment. The data also suggest that OCs can be combined with antiandrogens for synergy.

Other Therapies

Medroxyprogesterone acetate

Women with PCOS who are not trying to get pregnant and do not wish to do so can use MPA in a dosing regimen of 5-10 mg/day for 10-14 days each month. MPA can help prevent abnormal

endometrial growth, but it does not suppress the production of ovarian androgen. MPA may also help to improve insulin sensitivity and lipids in PCOS patients. Statins have a place in PCOS treatment due to their ability to lower testosterone levels, LDL-C, triglycerides, and total cholesterol. A study on women with PCOS compared simvastatin with metformin and simvastatin plus metformin showed that total testosterone levels decreased by 17.1-13.6% when simvastatin was used in combination with metformin, but the effect of the combination was not as strong as the simvastatin-metformin combination (15.1%).

Future Perspectives

PCOS is a complicated condition with long-term complications and is becoming increasingly common among women of reproductive ages. The most difficult aspect of this syndrome is the inaccurate diagnosis criteria and the vast complexity of its features. Early treatment with personalized therapy will improve overall PCOS management, decrease comorbidity, and enhance quality of life (QoL). Early detection and treatment of women who may become infertile in their reproductive years may improve prognosis. Key gene polymorphisms may be useful in the early diagnosis and screening of PCOS. Genetic and pathophysiological studies on PCOS will need to be conducted in order to identify effective prevention strategies as well as therapeutic approaches. More research needs to be conducted to determine if intestinal microbial dysbiosis is altered by steroid alteration and the underlying mechanisms. Pebiotics, probiotics and synbiotics appear to improve many biochemical findings and may have positive effects on PCOS patients, but more research is needed. Drugs such as prebiotics, and probiotics may be important in the treatment of PCOS. However, the role of these medications on PCOS is yet to be determined.

Future in-depth and functional studies will enable the use of gut microbiota as a PCOS biomarker, and targeted personalized manipulation of gut microbiota will advance research. There is no miracle cure, because until now treatment has focused on the symptoms, not the disease itself. A comprehensive study of the syndrome requires extensive efforts to improve treatment and delay the serious long-term effects of the disease on the health of patients. Several new treatments for T2DM may be directly beneficial in managing the metabolic aspects of PCOS; however, clinical trials are needed to evaluate its clinical efficacy and safety in women with PCOS. Further studies are needed to demonstrate the potential of new therapeutic agents such as miRNA therapy, IL-22 therapy, and others in the positive management of PCOS.

Conclusion

Polycystic ovarian disease is a complex disease that requires multiple treatments; depending on the reason for which the patient is seeking treatment. Clomifene has shown the best results in the treatment of infertility, while little is known about the pharmacological treatment of androgenic symptoms. Long-term effects of PCOS, including type 2 diabetes and cardiovascular disease, can be treated with antidiabetic drugs and statins.

Ethical Statement

This is a review article hence no Ethical Approval needed.

Author Contributions

Each author has contributed equally to the study's planning, analysis, writing, and editing. All authors have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

References

Ghada A, Maged AM and Dalia AH. (2014). Combined pioglitazone–metformin and clomiphene citrate versus metformin and clomiphene citrate in induction of ovulation in women with clomiphene citrate-resistant polycystic ovary syndrome, Middle East Fertility Soc J. 19: 27-33.

Hochberg Z, Feil R, Constancia M, Fraga M, Junien C, Carel JC, Boileau P, LeBouc Y, Deal CL, Lillycrop K, Scharfmann R, Sheppard A, Skinner M, Szyf M,Waterland RA, Waxman DJ, Whitelaw E, Ong K and Albertsson-Wikland K. (2011) Child health, developmental plasticity, and epigenetic programming. Endocr Rev. 32: 159-224.

Huyghe L, Robin C, Dumont A, Decanter C, Kyheng M, Dewailly D, Catteau-Jonard S and Robin G. (2023) How to choose the optimal starting dose of clomiphene citrate (50 or 100 mg per Day) for a first cycle of ovulation induction in anovulatory PCOS women? J Clin Med. 12(15): 4943.

Lee TT and Rausch ME. (2012) Polycystic ovarian syndrome: Role of imaging in diagnosis. Radiographics 32: 1643–1657.

Legro RS. (1998) Polycystic ovarian syndrome: Current and future treatment paradigms. Am J Obstet Gynecol. 179: S101-S108

Lord JM, Flight IH and Norman RJ. (2003) Metformin in polycystic ovary syndrome: Systematic review and meta-analysis. BMJ. 25: 951-953.

Ndefo UA, Eaton A and Green MR. (2013) Polycystic ovary syndrome: a review of treatment options with a focus on pharmacological approaches. P T. 38(6): 336-355