www.ijarp.com ISSN 2456-9992 Page: 01-09

International Journal Advanced Research Publications

Review Article

Volume: 02
Issue: 04

POLY CYSTIC OVARIAN SYNDROME, AN UPDATED REVIEW

Zahid Manzoor*[1], Firoz Ahmed[2], Tanya Sharma[3], Dhananjay Mistry[4], Noorul Huda[5], Kamalesh Mistry[6]

[1]Research Scholar, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

[2]Assistant Professor, Department of Pharmacy, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

[3]Assistant Professor, Department of Pharmacy, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

[4]Lecturer, Department of Pharmacy, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

[5]Assistant Professor, Department of Pharmacy, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

[6]Associate Professor, Dept. Of pharmaceutical Analysis, Nityananda college of pharmacy Balasore Odisha India - 756060

Article Received: 10 March 2026, Article Revised: 30 March 2026, Published on: 20 April 2026

***Corresponding Author: Zahid Manzoor**

Research Scholar, Faculty of Pharmaceutical Science, Mewar University, Gangrar, Chittorgarh 312901, Rajasthan, India.

DOI: https://doi-doi.org/101555/ijarp.2047

ABSTRACT:

Polycystic ovary syndrome (PCOS) is a multifactorial disorder traditionally recognized for its endocrine and metabolic disturbances. However, accumulating evidence indicates that chronic low-grade inflammation and immune dysregulation play a central role in its pathophysiology. This narrative review explores the immunological mechanisms underlying PCOS and their repercussions for reproductive outcomes. Women with PCOS exhibit increased circulating levels of inflammatory cytokines-including interleukin (IL)-6, IL-1β, IL-18, and tumor necrosis factor-alpha (TNF-α)-alongside macrophage and lymphocyte infiltration within ovarian and endometrial tissues. These alterations promote oxidative stress, granulosa cell apoptosis, impaired steroidogenesis, and diminished endometrial receptivity. The adaptive immune response is similarly altered, characterized by imbalances between Th1/Th2 and Th17/regulatory T lymphocyte subsets and the presence of autoantibodies,

including antinuclear, antithyroid, and antiphospholipid antibodies. These immune abnormalities have been associated with implantation failure and recurrent pregnancy loss. Furthermore, autoimmune diseases, including Hashimoto's thyroiditis and type 1 diabetes mellitus occur more frequently among women with PCOS, reinforcing the concept of an underlying systemic immunometabolic imbalance. Unlike prior reviews, this work offers a novel integrative framework that connects systemic inflammation with localized immune dysregulation in reproductive tissues, providing a more comprehensive understanding of PCOS pathophysiology from an immunological standpoint.

KEYWORDS: Immune System Diseases; Immunology; Polycystic ovary syndrome; Pregnancy Outcome, Brain volumetry; Hippocampus; Luteinizing hormone; Magnetic resonance imaging; Polycystic ovary syndrome.

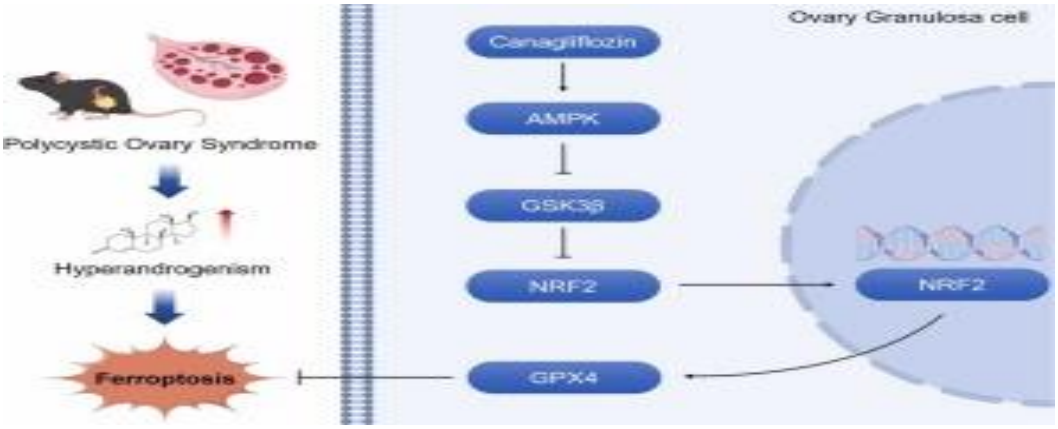
INTRODUCTION:

Polycystic ovary syndrome (PCOS) is one of the most common endocrine and metabolic disorders among women of reproductive age, with a global prevalence of approximately 9.2%. It is primarily characterized by hyperandrogenemia, chronic anovulation, and polycystic ovarian morphology. PCOS not only affects reproductive health but is also closely associated with various metabolic disturbances, such as insulin resistance, type 2 diabetes, cardiovascular diseases, and metabolic syndrome.

Recent studies have shown that oxidative stress plays a significant role in the pathogenesis of PCOS, leading to mitochondrial dysfunction and metabolic abnormalities in ovarian granulosa cells of patients with PCOS. Hence, PCOS involves a systemic oxidative imbalance. The reduction of oxidative stress presents a strategic approach to improving key manifestations of PCOS, including hormonal aberrations, adverse lipid profiles, obesity, and insulin resistance.

Ferroptosis is an iron-dependent form of cell death associated with oxidative stress. As a primary mediator of intracellular oxidative stress, reactive oxygen species (ROS) can trigger ferroptosis when excessive production leads to iron-dependent lipid peroxidation of the cell membrane. Lipid peroxidation is a hallmark process of ferroptosis and is centrally regulated by glutathione peroxidase 4 (GPX4). GPX4 protects the cell membrane from oxidative damage by utilizing glutathione (GSH) to reduce toxic lipid hydroperoxides into non-toxic

lipid alcohols[9]. Studies have indicated that hyperandrogenism-induced ferroptosis in granulosa cells plays a significant role in the pathogenesis of PCOS.



Together, this study was designed to test the hypothesis that PCOS heritability and pathogenesis are governed by a coordinated gut-epigenome axis and that intergenerational disease transmission is interruptible by targeted maternal nutritional interventions. Through the integration of maternal diet, microbiota ecology, and epigenetic inheritance, this study aims to elucidate core mechanisms underlying PCOS heritability and to explore whether safe, non-pharmacological nutritional interventions may modify disease pathways across subsequent generations.

Perspective:

PCOS research is at an inflection point: biological understanding has advanced rapidly, yet clinical translation remains slow and fragmented. We argue that the persistent gap between mechanistic insight and therapeutic innovation reflects structural limitations in how PCOS is defined, studied, and managed. Integrating precision medicine, multi-omics stratification, and AI-enabled analytics may offer one of the most promising routes to disease-modifying therapies. By synthesizing emerging scientific advances and identifying actionable opportunities, this Perspective aims to catalyze a shift toward more targeted, biologically grounded, and patient-centered approaches to PCOS care. presents the conceptual framework proposed in this Perspective, integrating precision medicine, multi-omics analytics, emerging therapeutic strategies, and clinical implementation pathways.

Progress and persistent gaps in PCOS research:

Large-scale genomic and multi-omics studies have identified pathways involved in androgen excess, insulin resistance, and ovarian dysfunction. These insights have revealed biologically

distinct PCOS subtypes, including metabolic-dominant and neuroendocrine-dominant phenotypes . Despite this progress, translation into disease-modifying therapies remains limited. Most available treatments target symptoms -such as menstrual irregularity, infertility, or metabolic risk - rather than underlying mechanisms. Persistent challenges include the absence of validated biomarkers, lack of consensus diagnostic criteria, and limited integration of patient-reported outcomes. These gaps contribute to delayed diagnosis, fragmented care, and persistent unmet needs.

MATERIALS AND METHODS:

1 Study Design and Reporting Standards

This systematic review and meta-analysis were conducted in accordance with the Cochrane Collaboration recommendations and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement and its protocol extension (PRISMA-P) . Although the present work primarily focuses on randomized interventional studies, selected methodological principles from the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines were considered where applicable, particularly with regard to transparency of reporting and handling of heterogeneity

2.Quality Assessment

Methodological quality was assessed using the Effective Public Health Practice Project (EPHPP) tool , a validated instrument applicable to both randomized and non-randomized intervention studies . The tool evaluates six domains (selection bias, study design, confounding, blinding, data collection methods, and withdrawals/drop-outs), each rated as strong, moderate, or weak. Overall study quality was classified as strong (no weak domains), moderate (one weak domain), or weak (two or more weak domains). Quality assessment was incorporated into the interpretation of findings, particularly in relation to potential performance and detection bias for hormonal outcomes.

3.Survey

The participants were requested to complete a questionnaire designed by the authors, based on some previous comparable studies . The questionnaire was created using the Google Docs platform, and a hyperlink was disseminated to the participants for their access. The questionnaire included 22 questions related to information about the demographic variables like their age, height, weight, ethnicity, marital status, and current BMI (Body mass index) if available. The responses are collected and stored in a Microsoft Excel sheet.

4. Menstrual characteristics evaluation

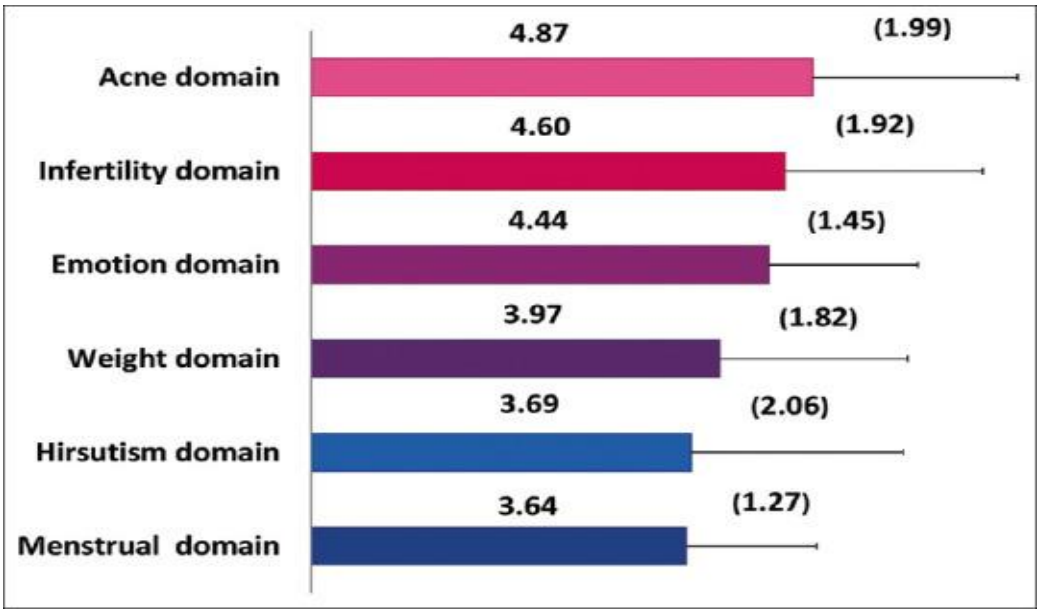
Participants were asked questions concerning their menstrual patterns like, age at menarche, cycle length in days, flow duration in days, and menstrual regularity. Questions related to "Typical bleeding length" were with answers ranging from "1 to 7 d" and " symptoms felt during periods". Cycle length was examined by asking, "What was the average number of days from the start of one period to the start of another?" and the answers ranged from "28 to 40 d". The type of menstrual blood flow was examined by responding to answers ranging from "mild to heavy".

5. Evaluation of mental issues during periods

Questions were asked of the respondents describing their mental state during their periods. The questions answered were whether they had feelings of depression, anxiety, sleep problems or poor sleep quality, eating disorders, poor body image, or social phobia during their periods.

RESULTS:

The average total score of HRQOL of the study participants was 125.41 ± 29.1 The scores ranged from 43 to 199. depicts the weighted mean scores, which were lowest for the domain of menstrual problems, followed by hirsutism and weight issues. These three main problems affect the HRQOL most among PCOS girls.



DISCUSSION:

Ever since the role of IR in the pathogenesis of PCOS has been established, a positive effect of insulin-sensitizing drugs in the treatment of PCOS has been demonstrated. In accordance with this, our study is the first one to report for the potential of swertiamarin, a bio active herbal insulin sensitizers for amelioration of IR and reestablishment of steroidogenesis in hLGC's isolated from follicular fluid of PCOS-IR and PCOS-NIR patients using metformin as a positive control.

Insulin resistance in PCOS has been associated with increase in granulosa cell death . The recovery of hLGC viability after incubation with swertiamarin in our study may be interpreted as indicative of reduced susceptibility of the PCOS-IR cells to undergo apoptosis as is observed with metformin in earlier studies . However, swertiamarin did not show any effect on cell viability in hLGC from PCOS-NIR indicating the process of granulosa cell death in PCOS-NIR to be other than IR.

It is well known that ISD's can modulate insulin signalling that can recruit its downstream docking proteins to activate several other signalling pathways in different cell types . Swertiamarin is well known for its anti-diabetic and anti-hyperlipidemic effects in various animal models, different cell lines and clinical trials with humans. Our results for the first time show a direct interaction of swertiamarin with key components of the classical insulin-signaling pathway thereby highlighting their ability to sensitize IR condition in hLGC's from PCOS-IR. Moreover swertiamarin with a dose of 66 µM seemed to be a potent insulin sensitizing drug for reversing insulin sensitivity in PCOS-IR as compared to metformin 1 mM. Surprisingly metformin increased the basal expression of key signalling proteins in the insulin signalling pathway which might result in increased insulin sensitivity and decreased insulin levels to less than normal even in PCOS-NIR group in the long term.

DIAGNOSTIC ASSESSMENT:

On detailed evaluation of subjective and objective parameters patient was diagnosed as primary infertility associated with PCOS. From Ayurvedic perspective this condition could be considered as *Vandhyatva* associated with *Nashtartava* where *Avarana* (enclosure) of *Artavavavaha srotas* (channel transporting Artava) *Kapha Medoduṣhti* and *Srotorodha* became the causative factors. Detailed analysis of her signs and symptoms showed the increase of *Vata Kapha* and reduction of *Pitta* . Considering all those factors treatment principles of *Vandhya, Nashtartava* and *Medohara were* followed in this case.

THERAPEUTIC INTERVENTION:

Therapeutic approach	Medicines with dose	Specific advises
Deepana (carminative) *Pachana* (Digestive) *Anulomana* *Lekhana* (scraping) *Rajapravartaka* (Induces menstruation)	1) *Chiruvilvadi kwatha* [8] −15 ml with 45 ml luke warm water and *Vaisvanara curna* [8] −5 gm early morning empty stomach. 2) *Nirgundyadi kwatha* [8]-15 ml luke warm water and Tablet *Triphala gugulu* [9] 2 Nos. evening before food. 3) Tab.*Annabhedi sinduram* [10] 2 Nos with fresh lime juice as *Sahapana* at 2 pm.	Less oily less spicy pure vegetarian diet. Absolute restriction for deep fried food articles. Regular exercise for a period of 30 min Regular walking for a period of 45 min.

ENDOMETRIAL HYPERPLASIA

The association between PCOS and endometrial carcinoma (EC) was initially described more than 60 years ago . A systematic review showed that the risk of EC was three times higher in women with PCOS compared to women without the disease , and also noted in a meta-analysis demonstrating that women with PCOS had a 3 fold increased odds of developing EC (OR 2.90, 95% CI 1.52–5.48) . Further, EC is usually preceded by endometrial hyperplasia , and a case–control study showed that women with PCOS and endometrial hyperplasia have a four times greater risk of developing EC than non-PCOS women .

Increased risk of endometrial cancer in PCOS is usually explained by chronic anovulation and therefore prolonged exposure to unopposed estrogen, and lack of progesterone activity. Progestins have been widely used to treat endometrial hyperplasia in women, however, approximately 30% of women with endometrial hyperplasia fail to respond to progesterone treatment and undergo progression to atypical hyperplasia and further transformation to EC . Additionally, excess androgen levels in PCOS results in increased bioavailability of unopposed estrogens due to the peripheral conversion of endogenous androgens into estrogen . Finally, obesity and hyperinsulinemia/insulin resistance are the two other metabolic disorders involved in PCOS that are linked to endometrial hyperplasia and endometrial cancer. Obesity relates to high estradiol levels from aromatization of androgens in adipose tissue to estrone and conversion to estradiol , while insulin promotes cell proliferation .

CONCLUSION:

To the best of our knowledge, this is the first study which investigated and compared the association between BW and body composition in PCOS patients with matched healthy

women. However, the generalization of these findings requires replication of data in wider populations with different ethnic backgrounds.

An extended amount of knowledge has been learned about PCOS since it was initially described by Stein and Leventhal . Yet, we are still lacking knowledge about many of its aspects, including its etiology, progression throughout life, spectrum of symptoms, and various morbidities. The pathogenesis of PCOS remains obscure, with unregulated steroidogenesis, insulin resistance, oxidative stress, and genetic factors contributing, possibly from prenatal life, to the disease. Supplementary studies are needed to bridge between the various susceptibility factors that might contribute to PCOS.

The current diagnostic guidelines are still vague and might not detect patients with less severe non-classic phenotypes. The guidelines in adolescents lack specificity, as they might fail to differentiate between normal development and pathogenesis. Since proper diagnosis is a crucial step to initiate treatment and prevent future morbidities, further clinical research should seek not only to update and unify guidelines but also to provide an appropriate rationale for diagnostic tools that can detect all PCOS phenotypes.

REFERENCES:

1. Jacobsen VM, Li S, Wang A, Zhu D, Liu M, Thomassen M, et al. Epigenetic association analysis of clinical sub-phenotypes in patients with polycystic ovary syndrome (PCOS). Gynecol Endocrinol. (2019) 35(8):691–4. 10.1080/09513590.2019.1576617
2. Nandi A, Chen Z, Patel R, Poretsky L. Polycystic ovary syndrome. Endocrinol Metab Clin N Am. (2014) 43(1):123–47. 10.1016/j.ecl.2013.10.003
3. Grigoryan OR, Zhemaite NS, Volevodz NN, Andreeva EN, Melnichenko GA, Dedov II. Otdalennye posledstviia sindroma polikistoznykh iaichnikov [Long-term consequences of polycystic ovary syndrome]. Ter Arkh. (2017) 89(10):75–9. Russian. 10.17116/terarkh2017891075-79
4. Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. Nat Rev Endocrinol. 2018;14:270–84.
5. Sills ES, Perloe M, Palermo GD. Correction of hyperinsulinemia in oligoovulatory women with clomiphene-resistant polycystic ovary syndrome: a review of therapeutic rationale and reproductive outcomes. Eur J Obstet Gynecol Reprod Biol. 2000;91:135–41.

6. Dennett CC, Simon J. The role of polycystic ovary syndrome in reproductive and metabolic health: overview and approaches for treatment. Diabetes Spectr. 2015;28:116–20.
7. Singh S, Pal N, Shubham S, Sarma DK, Verma V, Marotta F, Kumar M. Polycystic ovary syndrome: etiology, current management, and future therapeutics. J Clin Med. 2023;12:1454
8. Raaf GB, Mohammed AA, Jawad MA. The comparison of the effect of recombinant FSH in antagonist protocol on serum and follicular fluid Kisspeptin between PCOS and non-PCOS infertile women during ICSI. Int J Drug Deliv Technol. 2022;12:33–38.
9. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril. 2004;81:19–25.
10. Dapas, M. et al. Distinct subtypes of polycystic ovary syndrome with novel genetic associations: an unsupervised, phenotypic clustering analysis. *PLoS Med.*17, e1003132 (2020).
11. Teede, H. J. et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Clin. Endocrinol.*89, 251–268 (2018).
12. Parker, J. Understanding the pathogenesis of polycystic ovary syndrome: transgenerational evolutionary adaptation to lifestyle and the environment. *J. Australas. Coll. Nutr. Environ. Med.*39 (4), 18–26 (2020).
13. Hardiman P, Pillay OS, Atiomo W. Polycystic ovary syndrome and endometrial carcinoma. Lancet. 2003;361(9371):1810–2.
14. Liu J, Wu Q, Hao Y, Jiao M, Wang X, Jiang S, Han L. Measuring the global disease burden of polycystic ovary syndrome in 194 countries: Global Burden of Disease Study 2017. Hum Reprod. 2021;36(4):1108–19.
15. Ganie MA, Vasudevan V, Wani IA, Baba MS, Arif T, Rashid A. Epidemiology, pathogenesis, genetics & management of polycystic ovary syndrome in India. Indian J Med Res. 2019;150(4):333.