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Recent advances in gut microbiota alterations in polycystic ovary syndrome; an updated review

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Abstract

The gut microbiome, a complex ecosystem of trillions of microorganisms, has a critical role in metabolic regulation, immune function, and hormonal balance, systems all implicated in polycystic ovary syndrome (PCOS). Evidence suggests that women with PCOS exhibit distinct gut microbial profiles, including reduced microbial diversity, decreased abundance of beneficial bacteria, and increased levels of pro-inflammatory and endotoxin-producing species. These shifts are associated with insulin resistance, obesity, low-grade inflammation, and androgen excess—hallmarks of PCOS. Furthermore, gut microbiota influences bile acid metabolism, short-chain fatty acid production, and gut barrier integrity, thereby modulating systemic inflammation and endocrine function. Interventions such as probiotics, prebiotics, dietary modifications, and fecal microbiota transplantation show promise in ameliorating PCOS symptoms through microbiota modulation. Despite these advances, challenges remain, including heterogeneity in study designs, small sample sizes, and the need for longitudinal data.

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Introduction

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders affecting women of reproductive age, characterized by hyperandrogenism, chronic anovulation, and polycystic ovarian morphology (1). The Rotterdam criteria, established in 2003, define PCOS by the existence of at least 2 of the following; clinical or biochemical hyperandrogenism, oligo- or anovulation, and polycystic ovarian morphology on ultrasound (2). Despite its high prevalence, the precise pathogenesis of PCOS remains elusive, involving a complex interplay of genetic, environmental, and lifestyle factors (3). Traditionally, research has focused on hormonal imbalances, particularly insulin resistance and hyperandrogenism (4). However, growing evidence suggests that the gut microbiota as a dynamic community of bacteria, viruses, fungi, and archaea residing in the gastrointestinal tract, may play a critical role in PCOS development and progression (5). The human gut microbiota consists of approximately 10^{14} microorganisms, primarily bacteria from the phyla Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, and Verrucomicrobia (6). This microbial community is essential for digestion, vitamin synthesis (e.g., B vitamins, vitamin K), detoxification, and protection against pathogens (7). The gut microbiome also communicates with distant organs via the gut-liver, gut-brain, and gut-ovary axes, influencing systemic health (8-10). Microbial balance is influenced by host genetics, diet, antibiotic use, stress,

Key point

Polycystic ovary syndrome (PCOS) is an endocrine-metabolic illness characterized by hyperandrogenism, ovulatory dysfunction, and metabolic abnormalities affecting reproductive-age women globally. The gut microbiota has emerged as an important factor potentially influencing PCOS pathophysiology through its impact on metabolism, hormonal regulation, and inflammation.

and environmental exposures (11). Dysbiosis, which is across with the disruption of microbial homeostasis is accompanying by various diseases, comprising obesity, type 2 diabetes, inflammatory bowel disease, and autoimmune conditions (12). In reproductive health, dysbiosis has been linked to endometriosis, infertility, and recurrent pregnancy loss (9). The gut microbiota which modulates host physiology through several mechanisms. I) Short-chain fatty acids (SCFAs) like acetate, propionate, and butyrate are constructed by bacterial fermentation of dietary fibers, regulate energy homeostasis, insulin sensitivity, and immune responses (13). II) Gut microbes transform primary bile acids into secondary forms, influencing lipid metabolism and FXR/TGR5 signaling (14). III) Beneficial bacteria enhance tight junction proteins, preventing translocation of endotoxins like lipopolysaccharide (LPS), a key driver of inflammation (15) and IV) The microbiota shapes both innate and adaptive immunity, affecting cytokine production and immune cell differentiation (16). Given these roles, it is plausible that gut microbiota dysbiosis contributes to the metabolic and endocrine disturbances observed in PCOS (16). This mini-review aims to provide an analysis of recent findings on gut microbiota alterations in PCOS, investigating the mechanisms by which the microbiome influences PCOS pathophysiology, its interactions with host metabolism and immunity, and the therapeutic potential of microbiota-targeted interventions.

Search strategy

For this mini-review, we searched PubMed, Web of Science, EBSCO, Scopus, Google Scholar, Directory of Open Access Journals (DOAJ), and Embase, using different keywords like; polycystic ovary syndrome, PCOS, gut microbiota, metabolic dysregulation, endocrine disorders and inflammation

A short look at the gut-ovary axis

The concept of the gut-ovary axis has emerged as a framework for understanding how gut microbiota influences ovarian function and vice versa (17). This bidirectional axis involves neural, endocrine, and immune pathways (18,19). The vagus nerve transmits signals from the gut to the brain and hypothalamus, which regulates gonadotropin-releasing hormone secretion (20). Additionally, gut-derived metabolites (e.g., SCFAs, bile acids) enter circulation and affect ovarian steroidogenesis (21). In addition, systemic inflammation from gut-derived LPS can infiltrate ovarian tissue, disrupting folliculogenesis and promoting cyst formation (22). Additionally, LPS activates Toll-like receptor 4 (TLR4) on immune cells, initiating inflammatory pathways (e.g., NF-κB), which interfere with insulin receptor signaling, thereby inducing and worsening insulin resistance (23). Conversely, sex hormones influence gut microbiota composition; since estrogen and testosterone modulate gut motility, mucus production, and immune responses, thereby shaping the microbial environment (24). For example, androgen excess in PCOS may favor the growth of pro-inflammatory bacteria, creating a vicious cycle (25,26).

Therapeutic modalities targeting gut microbiota in PCOS

Growing evidence supports interventions aimed at restoring gut microbiota balance to improve PCOS symptoms (27). Previous studies regarding probiotics and prebiotics found that supplementation with specific strains (e.g., *Lactobacillus, Bifidobacterium*) and dietary fibers improves insulin sensitivity, hormonal balance, and inflammatory markers in patients with PCOS and animal models (28). Moreover, dietary modifications like increasing intake of fiber and polyphenols beneficially modulate gut microbiota composition and functions, aiding symptom management (29,30). Other investigations detected that exercise and stress management may positively influence gut microbiota, contributing to improved clinical outcomes (31). Finally, experimental application of fecal microbiota transplantation from healthy donors reverses dysbiosis and ameliorates metabolic and reproductive abnormalities in animal models of PCOS, highlighting its therapeutic potential (32).

Focus on the administration of metformin

Metformin, commonly prescribed for insulin resistance in PCOS, exerts beneficial effects not only through its direct actions on glucose metabolism but also by modulating the gut microbiota (33). It notably increases the abundance of *Akkermansia*, a beneficial gut bacterium associated with improved metabolic health (34). This shift in the gut microbiota composition helps reduce endotoxemia, which can drive inflammation and worsen insulin resistance (35). Consequently, these microbiota-mediated changes contribute to metformin's overall therapeutic efficacy in managing PCOS symptoms (36, 37).

Conclusion

Beyond its reproductive implications, such as infertility and irregular menstruation, PCOS is strongly associated with significant metabolic comorbidities like insulin resistance, obesity, type 2 diabetes mellitus, and cardiovascular disease. In recent years, a burgeoning body of research

has increasingly implicated the gut microbiota as a pivotal factor in the etiology and progression of PCOS. In fact, recent advances have firmly established gut microbiota dysbiosis as a key feature of PCOS. Women with PCOS exhibit distinct microbial profiles characterized by reduced diversity, depletion of beneficial taxa, and enrichment of pro-inflammatory species. These alterations contribute to insulin resistance, hyperandrogenism, and chronic inflammation through mechanisms involving gut barrier dysfunction, SCFA deficiency, and disrupted bile acid signaling. The emerging gut-ovary axis provides a novel framework for understanding PCOS pathophysiology and opens new avenues for treatment. Hence, microbiota-targeted therapies, including prebiotics, probiotics, dietary changes, and fecal microbiota transplantation, hold significant promise for improving PCOS outcomes.

Authors' contribution

Conceptualization: Abnoos Mokhtariardekani, Zahra Hamidi Madani, and Farzin Banei.
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Writing–original draft: All authors.
Writing–review and editing: All authors.

Conflicts of interest

The authors declare that they have no competing interests.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors utilized Perplexity.ai to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Ethical issues

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