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Unveiling the Connection between Gut Microbiome and Polycystic Ovary Syndrome (PCOS)

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Abstract: Polycystic ovary syndrome (PCOS) is a multifactorial endocrine metabolic disorder affecting up to one in ten women of reproductive age, with implications on fertility, metabolic health, and quality of life. Recent evidence has shown that gut microbiota dysbiosis plays a role in the PCOS pathophysiology. Based on the 25 articles extracted from PubMed, Ovid Medline, and Scopus (2020–2025), this review reveals that PCOS is consistently associated with reduced gut microbial α-diversity, distinct β-diversity clustering, and compositional shifts marked by depletion of beneficial taxa. These dysbiosis correlate with PCOS phenotypes such as insulin resistance, hyperandrogenism, dyslipidemia, and chronic inflammation via mechanisms involving impaired short-chain fatty acid production, disrupted bile acid metabolism, increased intestinal permeability, and immune-mediated dysregulation of the hypothalamic–pituitary–ovarian axis. Recognising the increasing role of

the gut microbiome in PCOS highlights its systemic pathology and points towards the opportunities for microbiota-targeted therapies that address underlying pathophysiological mechanisms rather than symptomatic care alone.

Keywords: Polycystic ovary syndrome (PCOS); metabolic disorder; gut microbiota; short-chain fatty acid (SCFA); gut microbiota-based therapies; SDG 3 Good health and well-being

1. Introduction

A woman's reproductive and metabolic health are closely connected, with their hormonal balance playing an important role in fertility, energy metabolism, and disease resilience [1, 2]. Any disruptions to this balance can set off a series of effects ranging from menstrual irregularities to risks of diabetes, cardiovascular disease, or psychological distress [3, 4]. Among these conditions, one of the most prevalent and challenging is polycystic ovary syndrome (PCOS), which affects approximately 6-13% of women of reproductive age, and nearly 70% of the cases remain undiagnosed [5].

Polycystic ovarian syndrome is one of the most prevalent hormonal imbalance conditions among women, with estimates suggesting that it affects approximately 1 in every 10 women of reproductive age worldwide [5-8]. This makes PCOS a major public health concern due to its significant implications for overall well-being and fertility outcomes. According to the Rotterdam criteria, PCOS can be diagnosed when patients present with two or more of the following criteria: oligo-anovulation, which often manifests as irregular or absent menstrual cycles; hyperandrogenism leading to symptoms such as acne and hirsutism; and polycystic ovarian morphology, which can be observed on sonography [9-12]. PCOS presents differently across individuals, with symptom severity often changing over the course of a woman's life. The common manifestations include irregular menstrual cycles, subinfertility, infertility, and hirsutism caused by hyperandrogenism. Beyond reproductive consequences, PCOS is strongly linked with insulin resistance, which increases the risk of developing type 2 diabetes mellitus, metabolic syndrome, cardiovascular disease, and obesity [13, 14].

Recent studies have highlighted the potential association of the gut microbiome in the pathophysiology of PCOS, suggesting that alterations in gut microbial composition may contribute to the development and progression of the syndrome [15-19]. A human gut microbiome consists of a vast community of microorganisms, including bacteria, viruses, fungi, protists, and archaea that reside in the gastrointestinal tract [20-23]. The gut microbiome's influence extends beyond gastrointestinal health, with growing evidence

linking it to a wide spectrum of systemic conditions, including metabolic, neurological, hormonal balance, and psychiatric disorders [20]. For instance, an altered microbiota composition has been reported in autism spectrum disorder [24, 25], obsessive-compulsive disorder [26], Alzheimer's disease [27], and major depressive disorder [28-30]. These findings emphasise the bidirectional communication along the gut–brain axis, whereby microbial metabolites, immune modulation, and neuroactive compounds influence host cognition and mood. Moreover, dietary interventions such as garlic supplementation have been shown to modulate gut microbial composition and reduce chronic disease risk, underscoring the role of nutrition in shaping gut ecology [31].

Any disruption to the normal microbial balance, such as reduced diversity, an increase in abundance of harmful microbiota, or a decrease in abundance of beneficial microbiota, is broadly defined as dysbiosis [32]. This state of imbalance does not typically occur in isolation but is shaped by a range of host-related and environmental factors. For instance, ageing is associated with a natural decline in microbial diversity, while dietary choices such as high-fat, high-sugar, or low-fibre intake can selectively enrich unfavourable microbial populations in the gut. Likewise, the widespread use of medications, including antibiotics and even hormonal therapies, has been shown to alter microbial flora structure and function [33-37]. Collectively, these disturbances can disrupt host–microbe interactions and foster physiological changes that contribute to metabolic dysfunction, chronic inflammation, and altered hormonal regulation.

In the context of women's health, the diversity of gut microbiota plays a role in hormonal balance, including estrogen, androgen, and insulin metabolism [38]. Any marked reduction in diversity or an abnormal increase in specific microbial populations can create significant endocrine imbalances, worsening disease symptoms. Given the influence of gut microbiota on the host, dysbiosis is increasingly recognised as a critical factor in estrogen-driven gynaecological conditions, including uterine fibroids (UF), reproductive cancers, and polycystic ovary syndrome (PCOS) [22]. Hence, researchers have suggested gut microbiota-based therapies aimed at restoring gut microflora in PCOS patients. Interventions such as probiotics, prebiotics, and dietary modifications have shown potential to directly improve gut microbiome composition and, in turn, contribute to the management of PCOS [39-41].

Therefore, this review aims to examine the relationship between the gut microbiome and PCOS, with particular attention to alterations in microbial diversity, the involvement of specific taxa, and their contribution to PCOS manifestation. In addition, the review evaluates

evidence on gut microbiota–based therapeutic strategies, including probiotics, prebiotics, and FMT, as potential approaches for managing PCOS.

2. Methods

A literature search covering the years 2020 and 2025 was conducted in Scopus, PubMed, and Ovid Medline. Search keywords included "Polycystic ovary syndrome" OR "PCOS" AND "Gut microbiota" OR "Gut microbiome" AND "dysbiosis" AND "Microbiota based intervention" OR "Microbiome-based therapies". Eligible articles included primary studies that investigated differences in gut microbiome composition between women with PCOS and healthy controls. Exclusion criteria comprised non-English publications, animal studies without clinical relevance, theoretical papers, and ongoing or incomplete studies.

3. Results

A total of 434 studies were retrieved: 165 from PubMed, 163 from MEDLINE, and 106 from Scopus. After importing the records into Covidence for screening, 204 duplicates were removed, leaving 230 studies for abstract screening. Of these, 42 were assessed in full-text review, and 25 met the eligibility criteria for final data extraction (Figure 1).

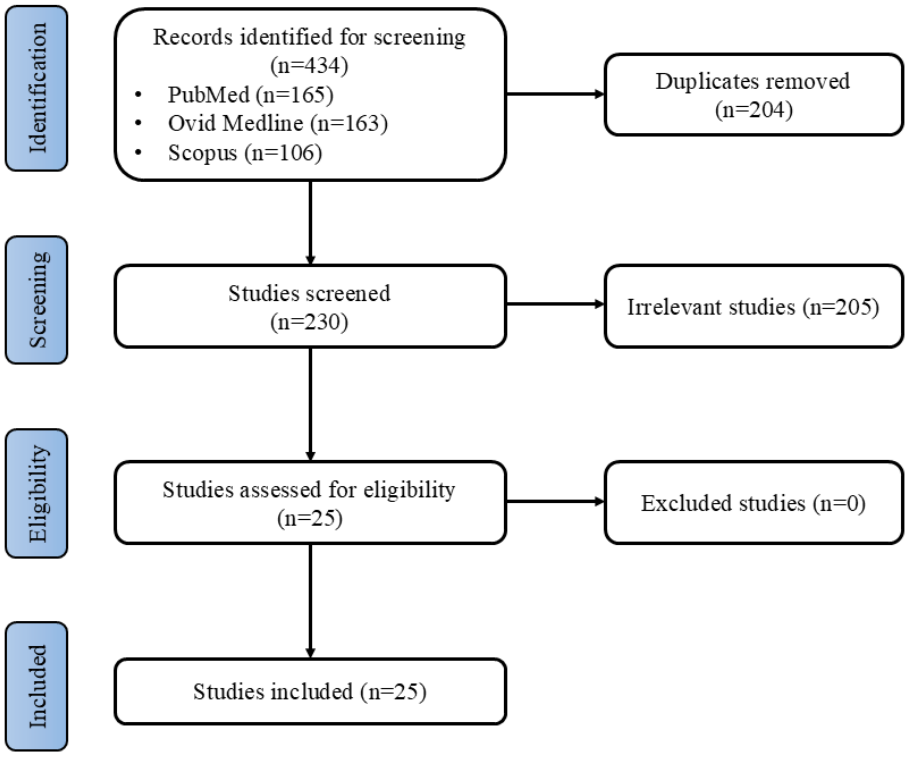

Figure 1. The PRISMA flow diagram depicts the study selection process.

3.1. Study Design

Within the included studies in this review, 14 of them are cross-sectional studies, along with 3 case-control studies, 2 randomised controlled trials (RCTs), 1 prospective case-control cross-sectional study, 1 prospective case-control study, 1 prospective observational study, 1 experimental animal study, 1 experimental research study, and 1 pilot study. The study population ranged from 20 to 303 patients, with most of them having a small sample size. Almost 76% of the studies are based in Asia countries, mainly China (17 studies), followed by India (2 studies), and the remaining articles are based in South America and European countries. Most studies compared the faecal microbiota of PCOS women to non-PCOS women controls, except 1 study, which included 6 male healthy controls. The majority of studies adapted 16S rRNA gene sequencing for faecal microbiota genomic studies, with the exception of 1 using shotgun metagenomic sequencing, 1 using real-time PCR, and 1 using a metagenomic dataset downloaded from the NCBI-SRA database.

3.2. Defining the gut microbiome in PCOS

The gut microbiome composition is easily influenced by external factors and varies across healthy individuals [42]. Despite this deviation, clinicians are still able to define a healthy gut microbiome by not only considering the absence of diagnosed disease, but also considering the ability to function without causing any form of distress [43]. Dysbiosis is defined as a disruption of the microbial species, causing imbalance, and is commonly associated with impaired gut function and inflammation [44]. It could either be a loss of overall diversity or certain beneficial microbes, as well as a sudden increase of pathobionts [44].

In terms of gut microbiome diversity changes in PCOS, alpha diversity measures the overall richness and evenness of an average faecal sample, while beta diversity quantifies the community structure within the sample [45]. The reduction of alpha diversity in PCOS groups compared to healthy controls has been consistently observed across studies [16, 17, 46-54]. Reduced Shannon, Simpson, and Chao1 indices indicate a lower microbial richness in the faecal samples of PCOS patients. PCOS patients who have comorbidities such as obesity and insulin resistance are reported to have a more pronounced reduction of alpha diversity [53]. There are also significant beta diversity differences observed between PCOS and controls, measured using PCoA based on Bray-Curtis and UniFrac distance [47, 49, 50, 53, 55-60].

At the phylum level, the most common taxa in both PCOS and healthy controls consist of *Firmicutes, Bacteroidetes, Proteobacteria,* and *Actinobacteria* [61]. A number of studies have shown a decrease in richness of *Bacteroidetes* in the PCOS group [16, 46, 47, 49, 52, 62, 63]. There is also consistent evidence showing that the *Firmicutes* to *Bacteroidetes* (F:B) ratio has been increased in PCOS groups [61, 62]. However, this finding is not universal, as some

studies suggest a decrease in the ratio while some report no significant difference [17, 48, 54]. At the family level, there has been a significant increase in *Bifidobacteriaceae* and *Streptococcaceae* in the PCOS group [47, 56, 58, 59, 61]. Their faecal samples also showed a reduction of beneficial microbes in PCOS groups, mainly *Ruminococcaceae* [48, 64]. In addition, an increased abundance of potential inflammation-triggering microbes, such as *Enterococcaceae* and *Peptostreptococcaceae*, is found in faecal samples of PCOS patients [47, 49, 55, 58]. At the genus level, a number of studies reported a decrease in the relative abundance of *Bacteroidetes*, *Faecalibacterium*, and *Lactobacillus* in PCOS women's faecal samples, while there is an increase in the abundance of pathobionts such as *Bifidobacterium, Streptococcus,* and *Klebsiella* [16, 47, 48, 65]. Besides, several studies identify a higher relative abundance of opportunistic bacteria, for example, *Escherichia/Shigella* and *Fusobacterium,* which may potentially cause increased gut permeability and lead to systemic inflammation in PCOS women [48, 58].

Out of the studies that recruited obese PCOS women as participants, other than a greater reduction of alpha diversity compared to lean PCOS, they also displayed an increased relative abundance of *Blautia* and *Romboutsia* [55, 58, 66]. On the other hand, PCOS women with insulin resistance portrayed a distinct gut microbiota shift. Results of faecal metagenomic sequencing and metabolic studies show a positive correlation between the abundance of *Enterococcus, Ruminococcus,* and *Lachnospira* with insulin resistance [55, 63]. In one of the studies that focused on faecal metabolites, a positive correlation of faecal propionic acid levels with insulin resistance was reported [17].

3.3. Key metabolic and endocrine findings

The primary key factors of PCOS metabolic consequences include insulin resistance and impaired glucose metabolism [5]. Insulin resistance is a clinical condition where the cells of the body are not responsive to insulin stimulation, leading to hyperglycemia and ultimately causing a refractory spike of serum insulin levels due to negative feedback [67]. Insulin resistance (IR) was found to be strongly connected to gut dysbiosis in PCOS, especially in obese and insulin-resistant subgroups. Dysregulated F:B ratio is associated with higher fasting insulin levels and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), a surrogate measure for insulin resistance [53, 63]. Reduction of an abundance of *Bacteroidetes*, which is commonly reported in PCOS groups, is also involved in gut permeability, glucose regulation, and weight gain [47, 50, 61, 65, 68].

Another evident endocrine alteration in PCOS is the elevation of serum testosterone levels, which is also known as hyperandrogenism [69]. Symptoms of hyperandrogenism

include irregular menses, excess acne growth, and male pattern hair loss [69]. The current main approach of PCOS treatment is targeted to ameliorate symptoms of hyperandrogenism, as the effect of altered physical appearance can mentally affect the patient as well [70]. Increased testosterone levels are linked to reduced gut microbial diversity. Serum testosterone is found to be positively correlated with reduced alpha diversity and abundance of the *Enterobacteriaceae* family [46, 49, 61]. Elevated dehydroepiandrosterone (DHEA) levels are also correlated with alpha diversity, suggesting a positive correlation with their role in hyperandrogenism [46].

Dyslipidemia, although not considered one of the diagnostic markers, is also a common phenotype observed in PCOS populations [71]. PCOS patients display higher LDL and triglyceride levels, correlating with gut dysbiosis. From the results of PCOS faecal sample gene sequencing, increased *Blautia* and *Romboutsia* are linked to lipid metabolism and weight gain [50, 58]. In addition, some studies suggest that excess production of SCFA is linked to obesity due to excess energy stored in the gut, while others show no correlation [16, 58].

4. Discussion

Polycystic ovary syndrome is a common cause of infertility, and it is usually associated with other chronic comorbidities [72]. One of the major chronic conditions is insulin resistance, where insulin that is produced in the body for blood sugar regulation cannot be utilised effectively [72]. This condition will increase a woman's risk of developing Type 2 diabetes mellitus later in life [72]. In addition, women with PCOS are also at higher risk of developing other metabolic complications such as obesity and dyslipidemia; hormonal imbalance such as hyperandrogenism; cardiovascular events such as myocardial infarction and hypertension; and psychological conditions such as depression and anxiety [73]. Current treatments for PCOS are based on individual phenotypes and focus on alleviating symptoms and achieving fertility rather than reversing the condition [74]. For example, metformin is prescribed to manage insulin resistance; clomiphene citrate or letrozole are used to induce ovulation; while Yasmin and Diane-35 are oral contraceptives which have shown efficacy in acne control [74].

There is emerging research evidence suggesting that gut microbiota dysbiosis in PCOS contributes to the imbalance of metabolic and hormonal secretions that might affect the severity of PCOS. Dysbiosis of the gut microbiota can lead to increased permeability of the intestines and cause systemic inflammation, which in turn dysregulates the hypothalamic-pituitary-ovarian (HPO) axis [75]. This will lead to a disruption in gonadotropin secretion,

causing hyperandrogenism and anovulation, which are both diagnostic criteria for PCOS [75]. Moreover, gut microbiota-derived metabolites, such as short-chain fatty acids (SCFAs) and lipopolysaccharides (LPS), alter neurotransmitter production, further impacting appetite regulation, mood, and stress responses in PCOS patients [76].

Findings from this review highlight the growing evidence from genomic analyses of faecal samples demonstrating strong associations between gut dysbiosis and gynaecological conditions such as PCOS. The overall trend of microbial changes in PCOS patients compared to healthy controls, namely a reduction in alpha diversity and reports regarding imbalance of the *Firmicutes* to *Bacteroidetes* (F:B) ratio. However, there are discrepancies between studies in terms of the extent of imbalances in F:B ratios. This could be due to variations in study populations. Further research and meta-analysis are needed to clarify the relationship between PCOS and F:B ratio. Some examples of microbes belonging to the *Firmicutes* phylum include *Lactobacillus, Ruminococcus*, and *Enterococcus*, while *Alistipes*, *Bacteroides*, and *Prevotella* belong to the *Bacteroidetes* phylum [77]. Since these mycobionts are the main taxa found in a healthy gut microbiota and they make up almost 90% of the community, an alteration of their abundance may suggest the presence of gut dysbiosis [78]. A study by Annapure et al. suggests that the imbalance of the F:B ratio could be attributed to the mutation of the leptin gene [77]. A mutation resulting in a lower expression of leptin leads to increased appetite and decreased energy expenditure, subsequently resulting in obesity [79]. Nevertheless, due to the vast diversity of the gut microbiome, F:B ratio cannot be a sole determinant of obesity, but could serve as one of the potential biomarkers for its diagnosis [77, 80].

At the genus level, there is an overall reported increase in abundance of *Bifidobacteriaceae* and *Streptococcaceae* observed in PCOS groups, with a few studies that show the opposite. These families are associated with health-promoting effects, but an excess abundance could possibly be linked to inflammation and metabolic consequences in PCOS. For example, *Bifidobacterium lactis V9* is known to be a regulator of sex hormones, and it is widely used in probiotic products, resulting in a significant decrease in luteinizing hormone/follicle-stimulating hormone (LH/FSH) levels after the intervention [81]. While certain strains like *B. lactis V9* offer therapeutic benefits, the broader impact of elevated *Bifidobacterium* in the gut requires further investigation to ensure safety and efficacy across diverse patient populations.

The overall results also revealed a decrease in beneficial microbes such as *Rumminococcaceae*. The bacterial family is involved in fibre fermentation, SCFA, butyrate

production, and maintaining gut barrier function [82]. Butyrate is a potential moderator of PCOS progression as it is the main energy source for the gastrointestinal cells, such as enterocytes and colonocytes. This SCFA also helps to restore gut hormones like glucagon-like peptide-1 (GLP-1) and peptide YY(PYY), which inhibit histone deacetylase (HDAC), both of which play important roles in insulin regulation [83]. Moreover, its anti-inflammatory properties also effectively inhibit the activation of the nuclear factor kappa-B (NF-κB) inflammatory pathway [83]. Hence, reduced abundance of these beneficial families potentially leads to increased gut permeability, systemic inflammation, and insulin resistance. In addition, an increased abundance of inflammation-triggering microbes, such as *Peptostreptococcaceae* and *Enterococcaceae*, is found in PCOS women. Their tendency to induce cytokines and chemokines production, such as TNF-α, IL-6, and IL-8, may elicit an inflammatory response in human macrophages [84].

The predominant gut microbiome dysbiosis observed in PCOS women at the family level is decreased abundance of *Lactobacillus*. One of the many beneficial effects of *Lactobacillus* is its ability to regulate fat metabolism [85]. It is proven that this microbe can reduce cholesterol levels by co-precipitation of bile acid, leading to reduced levels of plasma lipoprotein and raised triglyceride levels [85]. Another commonly observed gut dysbiosis in PCOS women is the growth of opportunistic pathobionts such as *Escherichia, Shigella,* and *Bacteroides.* Some studies also reported an increased relative abundance of *Staphylococcus* and *Clostridium perfringens*. While some strains of these microorganisms are generally harmless, an overgrowth of such bacteria poses a risk of impairing tight junction protein expression, leading to a breach of gut wall integrity. Increased gut permeability will cause toxin translocation into the systemic circulation, triggering a systemic inflammatory response, further burdening the chronic inflammation of the gynaecological system in PCOS patients [16].

A biomarker is a biological trait that can be measured and evaluated as an indicator for disease [86]. An ideal biomarker should be readily accessible, easy to identify, minimally invasive, and low-cost for the interpretation of results [86]. Current biomarkers available for PCOS include a few categories, namely hormonal, metabolic, inflammatory, genetic, and microbial [86]. The initial four approaches require the clinical procedure of collecting blood samples to measure respective parameters. On the contrary, microbial markers only require the collection of faecal samples, which could be done remotely at the patients' residences. According to a cross-sectional study done in 2024, reduced *Bacteroidaceae* in faecal samples increased the likelihood of PCOS by 4.4-fold [47]. Besides, faecal enzymes such as β-glucuronidase and β-glucoside served as promising biomarkers for early detection and

monitoring in PCOS women with metabolic disturbances [87]. These enzymes are secreted mainly by *Bacteroidetes*, such as *Escherichia coli* and *C. perfringens* [88].

Alterations in the gut microbiota community show great correlation with PCOS, suggesting the potential effectiveness of symptom alleviation through gut microbiota-based therapies. Gut microbiome-based therapeutics are treatment approaches that aim to restore the microbiome community and functionality of a healthy gut [89]. Common methods include faecal microbiota transplant (FMT), prebiotics, probiotics, and lifestyle modifications that can improve the balance of the gut ecosystem [26, 89-93]. Probiotics are live microorganisms that, when taken in adequate amounts, confer measurable health benefits to the host [94]. Probiotics are increasingly recognised for their ability to influence host physiology through the modulation of key microbial metabolites such as SCFAs, which have anti-inflammatory properties [94-97]. This modulation represents a particularly promising avenue for intervention, with evidence from gastrointestinal oncology showing that probiotic supplementation can enhance SCFA production, restore mucosal barrier function, and reduce inflammation, as observed in patients receiving 5-fluorouracil chemotherapy [98].

Experimental animal studies of FMT from PCOS patients to mice models induced increased disruption of serum androgen levels, fat metabolism and glucose regulation, triggering an obese-like phenotype [57]. Interestingly, butyric acid administered intraperitoneally in these PCOS obese mice displayed improved ovarian function and reduced local inflammatory factors expression [58]. These results suggest that the gut microbiota plays a pivotal role in the pathogenesis of PCOS (Figure 2). However, there are limited sources published regarding FMT from healthy donors to letrozole-induced PCOS mice. Given the current research gaps, further studies are required to evaluate the potential therapeutic efficacy of FMT from healthy donors to PCOS patients, which could also help establish the causality between gut dysbiosis and PCOS. In terms of the potential of prebiotics in the management of PCOS, the two RCTs that include prebiotics treatment as intervention exhibited inconsistent outcomes, possibly due to dissimilar classes of prebiotics. Future research on probiotics, prebiotics, and postbiotics in the treatment of PCOS could focus on the efficacy of specific bacterial strains in modulating the gut microbiota to influence key metabolic and hormonal pathways.

Fungal and viral dysbiosis are not the main focus of this research; nevertheless, there is some evidence that shows a predominant increased abundance of *Candida* and *Quimbyviridae* in the faecal samples of PCOS women compared to healthy controls [51, 60]. While most published articles focused on bacterial dysbiosis, the role of fungal and viral dysbiosis in PCOS pathophysiology remains understudied, urging future research for a more

comprehensive understanding. By broadening the focus beyond bacterial dysbiosis, researchers may uncover new mechanisms and treatment targets for PCOS.

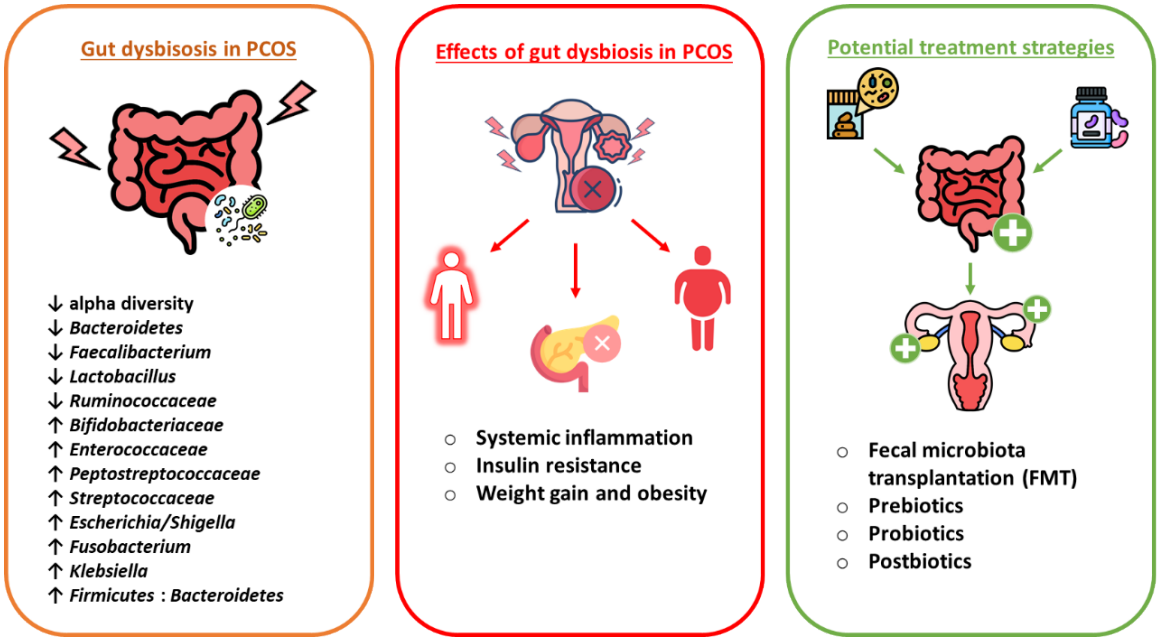

Figure 1. The effects of gut dysbiosis in PCOS and potential microbiome-based treatment strategies.

5. Conclusions

This literature review highlights the intricate relationship between gut microbiota dysbiosis and PCOS, emphasising how dysbiosis can lead to metabolic and hormonal changes observed in women with PCOS. Research consistently shows a reduction in the diversity of gut bacteria, reduced abundance of beneficial microbes, as well as an overgrowth of pathogenic bacteria. These major shifts are significantly correlated with systemic consequences such as insulin resistance, hyperandrogenism, and chronic inflammation, all of which are hallmarks of PCOS. Beyond the gut microbiota community, dysbiosis in PCOS further affects key metabolic pathways such as SCFA production, bile acids secretion, fat metabolism, gut wall integrity, and immune regulation. The growing evidence suggests a gut-brain axis involvement in the pathogenesis of PCOS. This further complicates the proposed relationship, reinforcing the idea that PCOS is not solely a gynaecological condition but a disorder that is intertwined with gut health. Research on efforts to restore a healthy gut microbiome through gut microbiota-based therapies is limited, encouraging future studies to consider developing targeted microbiome-based therapeutics in order to achieve effective and holistic treatments for PCOS patients.

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