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VAGINAL MICROBIOME ALTERATIONS IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders in the population of reproductive-age women. Although there is considerable research on gut dysbiosis in PCOS, alterations in the vaginal microbiome are comparatively understudied, despite their possible reproductive implications. The main aim of this review was to summarize current evidence regarding vaginal microbiome composition in women with PCOS and evaluate its associations with relevant clinical parameters. A literature search was performed using PubMed for studies published between January 2015 and November 2025. Eight studies met the inclusion criteria, each examining vaginal microbiome composition in women with PCOS. The most important findings included reduced Lactobacillus dominance, increased alpha-diversity, and enrichment of anaerobic taxa, such as Gardnerella vaginalis, Prevotella, and Ureaplasma species. Current evidence indicates that vaginal dysbiosis is more common among women with PCOS than in healthy controls, though it is not universal. Causal relationships in this field remain unclear, and data on interventions are insufficient. Randomized controlled trials evaluating interventions that target the microbiome and their impact on reproductive outcomes are an important research priority.

KEYWORDS

PCOS, Vaginal Microbiome, Vaginal Dysbiosis, Lactobacillus, Reproductive Tract Microbiota

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1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders affecting 8-13% of women of reproductive age. It is primarily characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology (Sirmans & Pate, 2013; Bozdag et al., 2016). PCOS has now become the leading cause of anovulatory infertility, and it is frequently associated with metabolic complications, including insulin resistance, type 2 diabetes, and cardiovascular diseases (Churchill et al., 2015). Traditional management of PCOS concentrates on lifestyle changes, hormonal contraceptives, insulin-sensitizing drugs, and fertility treatments. However, many women continue to suffer from ongoing symptoms and unsatisfactory therapeutic responses (Sadeghi et al., 2022). Recent research indicates that the microbiome also plays a role in the pathophysiology of PCOS, with most studies focusing on changes in the gut microbiota. The gut microbiome in PCOS differs from that of healthy controls in several ways: bacterial diversity is reduced, the number of beneficial species is depleted, and the number of pro-inflammatory taxa is increased (Lindheim et al., 2017; Insenser et al., 2018). These changes may also contribute to some metabolic disturbances such as chronic low-grade inflammation, impaired intestinal barrier integrity, and altered bile acid metabolism (Corrie et al., 2023). The vaginal microbiome is a distinct microbial niche that directly impacts reproductive health (Chopra et al., 2022). In healthy premenopausal women, the vaginal microflora is usually characterized by low diversity, with predominance of *Lactobacillus* species (*L. crispatus*, *L. gasseri*, *L. iners*, *L. jensenii*), which maintain acidic pH (3.5-4.5) through lactic acid production (Ravel et al., 2011). This dominance of *Lactobacillus* species provides protection against bacterial vaginosis (BV), reduces susceptibility to sexually transmitted infections (Greenbaum et al., 2019), and has been associated with favorable fertility and pregnancy outcomes (Ma et al., 2012). In contrast, vaginal bacterial dysbiosis is characterized by high bacterial diversity with low *Lactobacillus* counts and a significant proportion of anaerobic species, such as *Gardnerella*, *Prevotella*, *Atopobium*, and others.

It has been observed that the vaginal microbiome exhibits dynamic fluctuations during the menstrual cycle - *Lactobacillus* abundance correlates positively with estradiol levels and decreases during menses (Gajer et al., 2012). Since PCOS is associated with overall hormonal dysregulation, including hyperandrogenism, altered estrogen-to-progesterone ratio, insulin resistance, and systemic inflammation, changes in vaginal

microbiome composition may also contribute to the condition (Elkafas et al., 2022; Wang et al., 2025). The reproductive tract microbiome plays an important role in gynecological health and disease, and dysbiosis is associated with several reproductive disorders (Wang et al., 2025). However, compared to gut microbiome research, vaginal microbiome alterations in PCOS remain substantially less characterized.

2. Methodology

We conducted a literature search in PubMed, focusing on studies published between January 2015 and November 2025. We used the following keyword operators in various combinations: "PCOS", "Polycystic Ovary Syndrome", "vaginal microbiome", "vaginal microbiota", "lower genital tract", "microbiome", "microbiota", "microorganisms", and "Lactobacillus". The reference lists of the included studies were analysed manually to identify additional relevant publications. After analysis, eight studies met our inclusion criteria, all of which addressed the composition of the vaginal microbiome in women with PCOS.

Studies were eligible for inclusion if they:

1. involved human participants and reported vaginal microbiome composition in women with PCOS using molecular profiling techniques (e.g., 16S rRNA gene sequencing, metagenomics, or targeted PCR);
2. used an observational (cross-sectional, case–control, or cohort) or interventional study design; and
3. were published in English.

Studies were excluded if they:

1. focused exclusively on the gut microbiome without analysis of vaginal samples;
2. involved animal models;
3. were case reports, conference abstracts, or narrative reviews; or
4. did not primarily investigate PCOS or included women with PCOS only as a small subgroup.

We screened titles, abstracts, and full-text articles. Data extracted included study design, sample size, microbial profiling methods, taxonomic findings, diversity measures, and associations with hormonal, metabolic, and reproductive outcomes. Multiple reviewers independently extracted the data to ensure accuracy and reliability.

We have compiled selected studies in Table 1 and described their characteristics - design, sample size, sequencing method, and key findings. Sample sizes ranged from 33 to 713 PCOS participants (Table 1).

Table 1. Characteristics of Included Studies on Vaginal Microbiome in PCOS.

Study	Design	Sample Size (PCOS/Controls)	Sequencing Method	Key Findings
Hong et al., 2020*	Case-control	39/40 (PCOS/controls)	16S rRNA V3-V4	Increased α-diversity; decreased *Lactobacillus*; increased anaerobic taxa
Tu et al., 2020	Case-control	47/50 (PCOS/controls)	16S rRNA V3-V4	Increased α-diversity; decreased *Lactobacillus*; increased *Prevotella, Gardnerella, Mycoplasma*
Hong et al., 2021*	Cross-sectional	89 PCOS	16S rRNA V3-V4	Vaginal microbiome associated with testosterone levels; increased *L. crispatus*
Lu et al., 2021	Cross-sectional	42/24 (PCOS/controls)	16S rRNA V4	Decreased α-diversity in *Lactobacillus*-dominant PCOS; increased *Actinomyces* and *Enterococcus*
Hong et al., 2023*	Longitudinal cohort	50 PCOS	16S rRNA	Oral contraceptives increased *Lactobacillus* dominance over 6 months
Jin et al., 2023	Cross-sectional	713/733 (PCOS/controls)	16S rRNA	Higher diversity; decreased *Lactobacillus*; increased *Gardnerella* and *Ureaplasma*
Espinosa et al., 2024	Cross-sectional	33 PCOS	None (targeted PCR + microscopy)	Vaginal dysbiosis associated with pro-inflammatory status in PCOS
Lee et al., 2025	Prospective case-control	52/37 (PCOS/controls)	Ion Torrent sequencing	Reproductive tract microbiome varied across menstrual phases; no difference in α-diversity between groups

** Hong et al. 2020, 2021, and 2023 represent the same research group with related but distinct cohorts.*

3. Results

3.1 Study Cohort Clarifications

Three included studies were carried outby the same research group (Hong et al., 2020, 2021, 2023) and represented three related but distinct investigations. Although these studies share researchers and institution, they appear to cover different cohorts of participants, based on the recruitment periods and sample sizes provided. However, the potential overlap of participants cannot be completely excluded.

3.2 Vaginal Microbiome Composition in Women with PCOS

Several studies of the vaginal microbiome have demonstrated that *Lactobacillus* remains the dominant genus in most PCOS women. However, its relative abundance was often lower than that in healthy controls (Tu et al., 2020; Hong et al., 2021; Lu et al., 2021; Jin et al., 2023). In addition, PCOS cohorts consistently showed greater inter-individual heterogeneity, with some patients exhibiting *Lactobacillus*-deficient microbial communities (Hong et al., 2020; Tu et al., 2020).

The mentioned literature identified enrichment of specific non-*Lactobacillus* taxa in PCOS women, including *Gardnerella*, *Prevotella*, *Mycoplasma*, *Ureaplasma*, *Atopobium*, *Actinomyces, Enterococcus, Sneathia*, and *Megasphaera* (Tu et al., 2020; Hong et al., 2021; Lu et al., 2021). These microorganisms are associated with bacterial vaginosis and vaginal dysbiosis in PCOS. Moreover, one case-control study of newly diagnosed PCOS patients showed significant enrichment of *Mycoplasma* and *Prevotella* in PCOS cases, with strong ability to distinguish them from controls (Hong et al., 2020).

3.3 Microbial Diversity Patterns

Findings regarding vaginal microbial diversity were inconsistent across studies. Some investigations reported that α-diversity (within-sample microbial diversity measuring species richness and evenness) was significantly higher among PCOS patients than in controls (Hong et al., 2020; Lu et al., 2021; Jin et al., 2023). This stands in contrast to the healthy vaginal microbiome, which is usually determined by low diversity and *Lactobacillus* dominance. In comparison, several studies observed no significant differences in α- or β-diversity (microbiological diversity between samples measuring differences in composition between samples or communities) when PCOS status was considered on its own, particularly once menstrual cycle phase and features of the vaginal microenvironment were taken into account (Espinosa et al., 2024; Lee et al., 2025).

Importantly, Lu et al. (2021) found that the microflora of women with PCOS who were *Lactobacillus*-dominant showed lower diversity, whereas those without Lactobacillus dominance showed a significant increase in diversity. Taken together, these findings suggest that vaginal dysbiosis in PCOS does not follow a single microbiological pattern, but instead it's largely shaped by the presence and relative abundance of *Lactobacillus*.

3.4 Menstrual Cycle Phase and Hormonal and Clinical Features

Menstrual cycle phase emerged as a major determinant of vaginal microbiome composition. Lee et al. (2025) showed that microbial diversity and composition varied more substantially across cycle phases than by PCOS status alone. When cycle timing was taken into account, PCOS diagnosis was not associated with pronounced differences in overall vaginal microbiome diversity.

The links between the composition of the vaginal microbiome and the clinical or hormonal characteristics of PCOS were also investigated. In particular, irregular or prolonged cycles were associated with microbial variability and an enrichment of taxa other than *Lactobacillus* (Tu et al., 2020). Furthermore, elevated testosterone levels were associated with a higher relative abundance of *Lactobacillus crispatus* and a lower abundance of *Lactobacillus iners* in one PCOS cohort (Hong et al., 2021). Another study found a negative correlation between follicle-stimulating hormone levels and *Streptococcus* abundance (Lu et al., 2021). Nevertheless, after adjusting for confounding factors, correlations with BMI or obesity were weak or absent (Tu et al., 2020; Hong et al., 2021; Lu et al., 2021). Anti-Müllerian hormone and testosterone levels, along with pregnancy history, intermenstrual bleeding, and the presence of acanthosis nigricans, showed associations with vaginal microbiome composition in multivariate analyses. However, these relationships were modest and appeared to reflect changes in specific microbial taxa rather than consistent alterations in overall microbial community diversity (Hong et al., 2021).

3.5 Vaginal Microenvironment, Inflammation, and Dysbiosis

In addition to differences in microbial composition, several studies have drawn attention to signs of local inflammation in the vaginal environment of women with PCOS. Espinosa et al. (2024) reported that markers of vaginal inflammation, including polymorphonuclear neutrophil infiltration and neutrophil extracellular trap formation, were frequently observed, regardless of microbiota state. Taken together, these observations suggest that PCOS may promote a pro-inflammatory vaginal environment, which does not appear to depend solely on the underlying microbial composition.

3.6 Longitudinal Changes During PCOS Treatment

Longitudinal evidence suggests that the vaginal microbiome in PCOS is dynamic and potentially modifiable. In one study conducted on patients using oral contraceptives, the abundance of *Lactobacillus* increased over six-month period in some patients, although trajectories varied between individuals. Baseline testosterone levels were associated with differences in the course of changes in *Lactobacillus* bacterial counts. These findings point to considerable variability among individuals in the evolution of the vaginal microbiome under hormonal interventions. No consistent association was observed between changes in hormone levels and broader microbiome diversity (Hong et al., 2023).

4. Discussion

The evidence from literature examining the vaginal microbiome in women with PCOS supports the concept that this condition is associated with subtle but significant alterations in the vaginal ecosystem, rather than a single, uniform pattern of dysbiosis. One of the most recurring themes in research is heterogeneity. It was found that the microbiological profiles of people with PCOS vary considerably, and there is no single characteristic microbiological pattern that can define this syndrome (Hong et al., 2020; Tu et al., 2020; Lu et al., 2021; Lee et al., 2025). This heterogeneity most likely reflects the biological diversity of PCOS itself, which encompasses multiple phenotypes with different hormonal, metabolic, and reproductive characteristics.

One of the key conclusions from the reviewed studies is that *Lactobacillus* dominance is often maintained in women with PCOS. However, a larger proportion of them show reduced stability of *Lactobacillus*-dominated communities or increased representation of taxa commonly found in dysbiosis, including *Gardnerella*, *Prevotella*, and *Mycoplasma* (Hong et al., 2020; Tu et al., 2020; Lu et al., 2021). What is important is that these changes often occur without clinical signs of infection. It suggests that PCOS may be associated with subclinical shifts in microbial ecology rather than overt pathological states (Hong et al., 2021; Espinosa et al., 2024). This distinction is clinically relevant, as it suggests that standard diagnostic criteria for vaginitis may underestimate ecological changes occurring in PCOS.

Particularly important for interpreting the results is the observation that the phase of the menstrual cycle has a stronger influence on the composition of the vaginal microbiome than the diagnosis of PCOS itself. Hormonal cyclicity influences the regulation of epithelial maturation, glycogen availability, and lactic acid production, all of which are major factors determining the dominance of *Lactobacillus* (Lee et al., 2025). Chronic anovulation and abnormal hormonal variations in PCOS may therefore contribute to reduced microbiome stability over time, even if cross-sectional samples appear similar to those collected from healthy control subjects. Therefore, in future studies, the methodology should be carefully designed, especially with regard to cycle phase control and sampling over time.

Associations between microbiota composition and clinical or hormonal features of PCOS appear modest but plausible. Several studies have described relationships between hormonal markers and specific taxa. Hong et al. (2021) found a connection between testosterone levels and shifts between *Lactobacillus crispatus* and *Lactobacillus iners* in PCOS patients. Another study by Lu et al. (2021) examined the correlation between follicle-stimulating hormone levels and the abundance of *Streptococcus*. These findings are relevant because different species vary in their functional properties, resilience, and interactions with the host immune system. Therefore, even subtle changes at the species level can affect vaginal stability or susceptibility to dysbiosis, without necessarily altering overall microbial dominance.

There is also emerging evidence that the vaginal environment in PCOS may be accompanied by local activation of the immune system. Espinosa et al. (2024) reported frequent polymorphonuclear neutrophil infiltrates and the formation of extracellular neutrophil traps in vaginal samples from women with PCOS, even in the absence of evident infection. However, because inflammatory markers were not consistently assessed alongside detailed microbial community profiles, it remains unclear whether inflammation precedes microbial changes, results from them, or reflects broader host-related factors. Nevertheless, these findings support the

concept that both the microbiological and immunological characteristics of the vaginal environment may be altered in PCOS.

Longitudinal findings further emphasize that the vaginal microbiome in PCOS is dynamic rather than fixed. Individual differences in response to hormonal interventions, such as oral contraceptive use, suggest that microbial communities are shaped by a combination of baseline hormone levels, host factors, and possibly environmental influences. No consistent associations between hormonal changes and overall diversity indices were observed. This supports the view that broad measures of diversity may be too general to capture clinically relevant change. Possibly, species-level or functional analyses may provide more information.

Several limitations of the current evidence should be acknowledged. Most studies are cross-sectional, which limits causal inferences. Sample sizes are modest, populations vary in ethnicity and lifestyle, and sequencing and analytical processes vary significantly across studies. Moreover, few studies combine microbiome data with functional, immunological, or metabolomic analyses, limiting our understanding of the biological consequences of the observed microbial shifts.

Taken together, current research findings support the view that vaginal microbiome alterations in PCOS are best understood as part of a complex interaction between endocrine dysregulation, mucosal immunity, and microbial ecology, rather than as a distinct microbiological disorder.

5. Conclusion

Summarizing, current evidence indicates that women with PCOS exhibit certain alterations in the composition of the vaginal microbiome. These changes are mainly characterized by increased interindividual heterogeneity and, in some patients, reduced *Lactobacillus* dominance and an enrichment of non-*Lactobacillus* taxa. Even though *Lactobacillus* remains the dominant genus of bacteria in most PCOS women, the relative abundance of specific species and the stability of *Lactobacillus*-dominated communities appear to be altered compared to healthy women. Importantly, these changes do not define a single specific “PCOS microbiome”, but instead appear to reflect the biological diversity of this syndrome.

Microbiological differences in PCOS are not the same in all patients and are influenced by menstrual cycle irregularity, hormonal environment, and the characteristics of the vaginal microenvironment.

Associations between microbiota composition and clinical or hormonal characteristics are generally taxon-specific and rather subtle. This suggests that microbiological changes reflect complex interactions between the host and the microbiome rather than widespread dysbiosis.

Evidence of local vaginal inflammation in some women with PCOS further suggests that immunological changes may accompany or influence microbiological changes, although current data are insufficient to determine causality or directionality. Longitudinal studies indicate that the vaginal microbiome in PCOS is dynamic and may respond to hormonal modulation, but individual trajectories vary considerably.

Overall, the available data support an association, but not causation, between PCOS and changes in the vaginal microbiome. The heterogeneity observed across studies highlights that microbiological changes in the vagina are likely related to specific PCOS phenotypes rather than the syndrome itself. The goal should be to clarify the clinical relevance of changes in the vaginal microbiome in PCOS and their potential implications for reproductive health. This requires well-designed longitudinal studies with careful control of the menstrual cycle phase and integrated hormonal and immunological assessment.

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