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Vaginal Microbiome in Health and Disease: Dysbiosis and Microbiome-Based Therapies

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Abstract

Background: The vaginal microbiome represents a specialized microbial ecosystem essential for maintaining female reproductive health. Lactobacillus-dominated communities play a key role in preserving vaginal acidity, preventing pathogen colonization, and supporting mucosal immune balance. Disruption of this equilibrium leads to vaginal dysbiosis associated with multiple gynecological and reproductive disorders.

Aims: This review aims to synthesize recent evidence on vaginal microbiome composition, determinants of microbial stability, dysbiosis-associated conditions, diagnostic advances, and emerging microbiome-based therapeutic strategies.

Study Design: Narrative literature review.

Methods: A literature search was conducted using peer-reviewed publications from 2020–2025 retrieved from international databases including PubMed, Scopus, and Web of Science. Studies addressing vaginal microbiome composition, dysbiosis mechanisms, diagnostic approaches, and microbiome-directed therapies were included. Evidence from clinical trials, cohort studies, and reviews was analyzed through narrative synthesis.

Results: Recent molecular and metagenomic studies demonstrate that Lactobacillus-dominated vaginal ecosystems are strongly associated with microbial stability and protection against infections such as bacterial vaginosis,

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aerobic vaginitis, vulvovaginal candidiasis, Human papilomavirus (HPV) infection, and Human Immunodeficiency Virus (HIV) acquisition. Advances in sequencing technologies and microbiome-targeted therapies, including probiotics and vaginal microbiota transplantation, provide promising opportunities for long-term restoration of vaginal ecosystem balance.

Conclusion: Understanding vaginal microbiome dynamics supports a shift from pathogen-centered management toward ecosystem-based therapeutic strategies. Microbiome-informed diagnostics and interventions may improve prevention, recurrence control, and reproductive health outcomes.

Keywords: microbiome, vaginal dysbiosis, bacterial vaginosis, Lactobacilus, reproductive health.

INTRODUCTION

The vaginal microbiome is a unique microbial ecosystem in the human body. Unlike the diverse gastrointestinal tract, healthy reproductive-age women have a vaginal microbiota with low diversity dominated by *Lactobacillus* species (1,2). This configuration is an evolutionary adaptation that protects the female reproductive tract from infections and supports reproductive success.

Lactobacillus species promote vaginal health through various mechanisms. Key among these is lactic acid production, keeping vaginal pH below 4.5 and preventing pathogen colonization (1,3). Additional protective functions include hydrogen peroxide production, bacteriocin and biosurfactant secretion, competitive exclusion of pathogens, and disruption of pathogen biofilms (3,4). *Lactobacilli* also modulate immunity by shaping local innate responses, maintaining epithelial barrier integrity, and reducing excessive inflammation (5).

Despite its stability, the vaginal microbiome is dynamic and responsive to physiological and environmental factors. Hormonal changes during the menstrual cycle, pregnancy, and menopause significantly alter microbial composition through variations in glycogen, epithelial turnover, and immune function (6). Additionally, sexual behavior, hygiene, antibiotic exposure, genetics, ancestry, and immune status are crucial in shaping vaginal microbiota (7–9). These factors contribute to inter-individual variability and temporal changes in the vaginal microbiome.

Disruption of regulatory processes can lead to vaginal dysbiosis, marked by loss of Lactobacillus dominance, increased microbial diversity, higher vaginal pH, and inflammatory changes that compromise the epithelial barrier. Vaginal dysbiosis is not a single pathological entity but a continuum of microbial and host disturbances. These dysbiotic states are linked to bacterial vaginosis (BV), aerobic vaginitis (AV), vulvovaginal candidiasis (VVC), sexually transmitted infections (STIs), infertility, adverse pregnancy outcomes, and increased risks of viral infections like HPV and HIV (10).

METHODOLOGY

This narrative review was conducted to summarize recent advances in the understanding of vaginal microbiome composition, mechanisms of dysbiosis, diagnostic developments, and microbiome-directed therapeutic approaches relevant to women's reproductive health.

A structured literature search was performed using major international scientific databases, including PubMed, Scopus, and Web of Science. The search focused on publications from 2020 to 2025, in order to capture the most recent developments in microbiome research, while selected earlier foundational studies were included when considered essential for conceptual background.

Search terms included combinations of the following keywords: *vaginal microbiome, vaginal dysbiosis, bacterial vaginosis, Candida*

infections, probiotics, vaginal microbiota transplantation, and *microbiome sequencing*.

Eligible sources included peer-reviewed clinical studies, cohort studies, randomized controlled trials, and recent review articles addressing microbiome composition, diagnostic methodologies, host–microbiome interactions, and microbiome-based therapeutic strategies. Publications not directly related to vaginal microbiome clinical relevance, as well as non–peer-reviewed sources, were excluded.

A total of 70 relevant publications meeting the inclusion criteria were selected after title and abstract screening and were analyzed using a narrative synthesis approach. This method allowed integration of findings from heterogeneous study designs and facilitated interpretation of emerging microbiome-based concepts not suitable for systematic meta-analysis.

RESULTS

Composition and Classification of the Vaginal Microbiome - Advancements in high-throughput sequencing have enabled detailed characterization of vaginal microbial communities into community state types (CSTs). The VALENCIA system provides a standardized framework for categorizing vaginal microbiota by dominant taxa and community structure (5).

In healthy individuals, *vaginal microbiomes mainly consist of Lactobacillus crispatus, Lactobacillus gasseri, Lactobacillus iners,* or *Lactobacillus jensenii* (5,11). These CSTs correlate with lower vaginal pH, reduced microbial diversity, and greater resistance to pathogens. Conversely, CST IV features dysbiotic communities with less *Lactobacillus and more anaerobic taxa like Gardnerella, Atopobium, Prevotella,* and *Mobiluncus* (12).

Table 1. Vaginal community state types and clinical associations

CST	Dominant taxa	Key features	Clinical implications
I	*L. crispatus*	High lactic acid, stable	Optimal vaginal health
II	*L. gasseri*	Moderate stability	Generally healthy
III	*L. iners*	Transitional, adaptable	Health or dysbiosis
IV	*L. jensenii*	Protective, less prevalent	Healthy state
V	Mixed anaerobes	High diversity, inflammation	Bacterial vaginosis

Bacterial Vaginosis - BV is the most common form of vaginal dysbiosis worldwide. It features a loss of *Lactobacillus*, an overgrowth of anaerobic bacteria, increased vaginal pH, and polymicrobial biofilms on the vaginal epithelium (13-15). Molecular and microscopic studies identify *Gardnerella* species as key organisms in these biofilms, initiating structure and facilitating colonization by other anaerobes (16,17).

Investigations at the species and strain level show considerable variability in the *Gardnerella* genus, including differences in virulence factors,

sialidase activity, cytotoxicity, immune modulation, and biofilm formation (18,19). These traits enhance antimicrobial resistance and explain the high recurrence rates after standard antibiotic treatments (20).

Clinically, BV is linked to pelvic inflammatory disease, infertility, increased risk of STIs, higher HIV acquisition risk, and adverse pregnancy outcomes like preterm birth (21-24). These links are mainly due to prolonged inflammatory responses, compromised epithelial barrier, and dysregulated local immunity.

Aerobic vaginitis - AV is an inflammatory disorder of the vaginal epithelium, marked by epithelial damage, leukocyte infiltration, and aerobic bacteria, mainly *Escherichia coli, Streptococcus spp, and Staphylococcus spp*. Unlike BV, which has minimal inflammation, AV features significant inflammation and cytotoxicity, indicating a different pathogenic mechanism. (25,26).

Clinically, AV correlates with adverse pregnancy outcomes, such as preterm labor, premature rupture of membranes, and intrauterine infection. The rising antimicrobial resistance among pathogens complicates management and highlights the need for precise diagnosis and targeted therapies (27).

Vulvovaginal Candidiasis and the Vaginal Mycobiome - VVC is mainly caused by *Candida albicans*, but non-albicans species are rising (3,26,28,29). Recurrent VVC is linked to immune tolerance issues, fungal biofilms, and bacterial dysbiosis (8,30).

Evidence highlights the interplay between the vaginal mycobiome and bacteria as key to inflammation and pathogen persistence. Mixed bacterial–fungal biofilms increase virulence and reduce antifungal susceptibility, explaining chronicity and recurrence in VVC (31-35).

Mixed Vaginal Infections - Mixed vaginal infections encompassing BV, VVC, and AV are increasingly acknowledged in clinical practice, presenting considerable diagnostic and therapeutic challenges (36–38). These complex infections are frequently associated with more pronounced clinical manifestations, higher recurrence rates, and increased antimicrobial resistance, reflecting the interaction of multiple microbial and inflammatory mechanisms (39).

Mixed infections should be interpreted as a clinically significant overlap between BV, AV, and VVC rather than as independent pathological entities. Compared with isolated infections, BV is typically polymicrobial and biofilm-associated with minimal inflammatory response, AV is characterized by inflammation-dominant epithelial damage, whereas VVC is primarily fungal-driven and linked to alterations in immune tolerance. Their coexistence further increases diagnostic complexity and recurrence risk, highlighting the importance of microbiome-informed diagnostic strategies for accurate identification and targeted management.

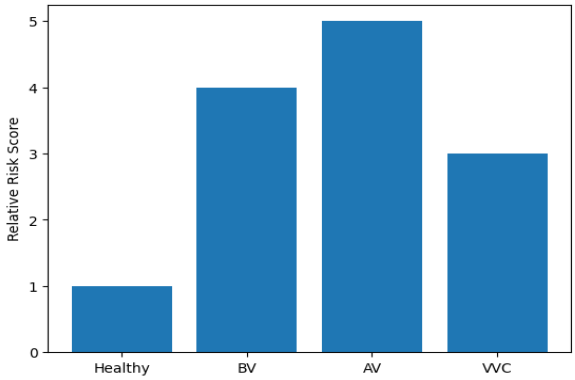


Figure 1. Relative Risk of Vaginal Dysbiosis-Associated Conditions

Figure 1 presents a schematic summary of the major clinical consequences associated with vaginal dysbiosis, including bacterial vaginosis, aerobic vaginitis, vulvovaginal candidiasis, infertility, adverse pregnancy outcomes, and susceptibility to viral infections. The illustration integrates evidence from the reviewed literature (2020–2025) and highlights the interconnected nature of dysbiosis-associated conditions.

Vaginal Microbiome and Viral Infections - A *Lactobacillus*-dominated vaginal microbiome is linked to lower HPV susceptibility and improved viral clearance. In contrast, dysbiotic communities promote viral persistence and cervical neoplasia progression (4,19-21). Similarly, vaginal dysbiosis increases HIV susceptibility by damaging epithelial barriers and activating local immunity, aiding viral transmission (37).

Host and Environmental Determinants - Hormonal changes from menstruation, pregnancy, and menopause, along with genetics, greatly affect the vaginal microbiome (23,40–45). Additionally, behaviors like hygiene, sexual activity, and antibiotic exposure significantly influence microbial stability and recurrent vaginal dysbiosis (46,47).

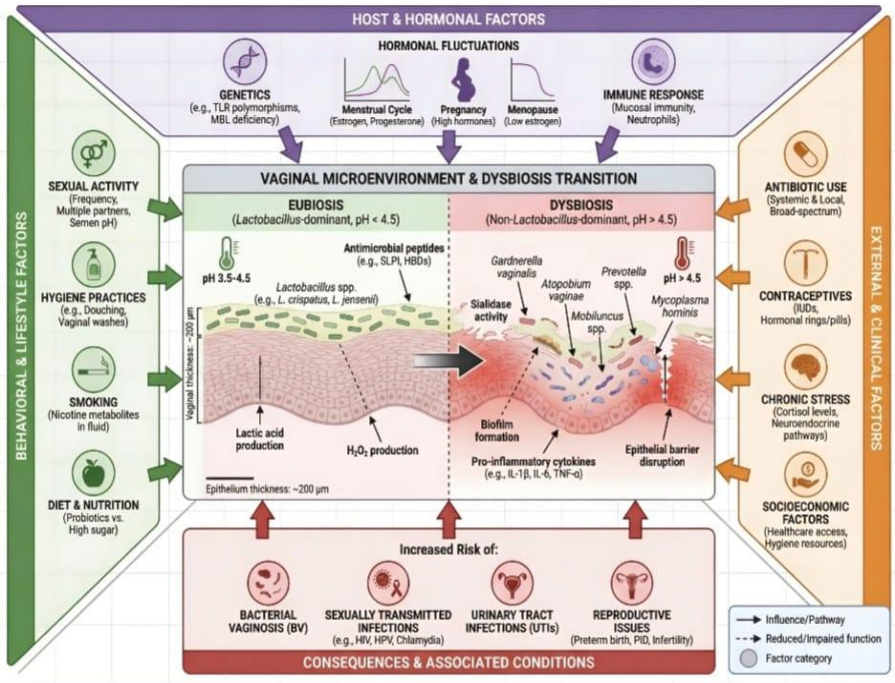


Figure 2. Multi-Factor Influences on Vaginal Dysbiosis: Mechanisms and Consequences

Figure 2 illustrates the interaction between host hormonal factors, immune status, behavioral determinants, environmental exposures, and microbial interactions influencing vaginal microbiome stability and the development of dysbiosis. The schematic summarizes key mechanisms contributing to ecosystem disruption and associated clinical consequences, based on findings from the reviewed literature.

Diagnostic Advances - Conventional diagnostic methods like Amsel criteria and Nugent scoring are widely used but suffer from subjectivity and low sensitivity (11,16). In contrast, new diagnostic methods using molecular techniques, metagenomic sequencing, and AI offer better accuracy, reproducibility, and discrimination, enabling more precise evaluations (12,38,48).

Microbiome-Directed Therapeutic Strategies - Probiotic formulations with specific *Lactobacillus* strains vary in restoring vaginal eubiosis and reducing recurrent BV, influenced by strain specificity and clinical context (10,49-51). Emerging therapies include microbiome-derived metabolites, postbiotics, and engineered *Lactobacillus* strains to improve vaginal colonization and microbial ecosystem resilience (52-54).

Vaginal microbiota transplantation (VMT) is a promising treatment for refractory vaginal dysbiosis. Early studies show sustained donor microbiome engraftment and positive reproductive outcomes, including successful pregnancies, indicating VMT's potential as a transformative therapeutic strategy (48,55-57).

DISCUSSION

The vaginal microbiome represents a dynamic ecological system that plays a central role in maintaining reproductive tract homeostasis through regulation of epithelial barrier integrity, metabolic activity, and mucosal immune responses. Rather than functioning as a static microbial environment, the vaginal ecosystem reflects continuous interactions between host determinants and microbial communities influencing susceptibility to infection and reproductive outcomes.

Current evidence supports the interpretation of vaginal dysbiosis as a continuum of microbial and immunological alterations rather than a single disease entity. Differences between bacterial vaginosis, aerobic vaginitis, vulvovaginal candidiasis, and mixed infections reflect distinct inflammatory profiles, microbial structures, epithelial responses, and clinical outcomes. This heterogeneity explains variations in symptom severity, recurrence risk, and therapeutic response, highlighting the limitations of uniform diagnostic and treatment strategies.

A major conceptual advance in understanding bacterial vaginosis involves the transition from pathogen-centered models toward biofilm-driven ecological disruption. Polymicrobial biofilms dominated by *Gardnerella* species contribute to antimicrobial tolerance and explain the high rates of post-antibiotic treatment recurrence (13,26,52,58-63). These findings support ecosystem restoration strategies aimed at re-

establishing Lactobacillus dominance rather than targeting individual pathogens alone.

In contrast, aerobic vaginitis represents an inflammation-dominant dysbiosis phenotype characterized by epithelial injury, leukocyte infiltration, and cytotoxic effects mediated by aerobic bacteria such as *Escherichia coli, Streptococcus spp.,* and *Staphylococcus spp*. (24,47,64). The association between AV and adverse pregnancy outcomes further emphasizes the clinical importance of inflammation-mediated microbiome disruption in obstetric risk assessment (24,64). Increasing antimicrobial resistance among AV pathogens reinforces the need for targeted diagnostics and antimicrobial stewardship strategies (65).

Recognition of the vaginal mycobiome has expanded the understanding of vulvovaginal candidiasis beyond fungal overgrowth alone. Recurrent disease appears to involve complex interactions between bacterial dysbiosis, fungal biofilm formation, and host immune tolerance mechanisms (3,8,27,30). Mixed bacterial–fungal biofilms enhance microbial persistence and antifungal resistance, supporting the need for therapeutic approaches targeting microbial interactions rather than isolated pathogens (31,32,35).

The vaginal microbiome also represents an important determinant of susceptibility to viral infections. Lactobacillus-dominated ecosystems are associated with reduced acquisition and improved clearance of human papillomavirus infections, whereas dysbiotic communities promote viral persistence and epithelial inflammation (4,19-21). Similar mechanisms increase susceptibility to Human Immunodeficiency Virus transmission through epithelial barrier disruption and immune activation (37).

Host-related determinants including hormonal status, genetic background, ancestry, immune regulation, and reproductive stage significantly influence vaginal microbial composition and resilience (6,23,42,66,67). Behavioral and environmental factors such as antibiotic exposure, hygiene practices, and sexual activity further contribute to microbiome variability and recurrence risk following treatment (23,46,47,68).

Advances in molecular diagnostics are reshaping the clinical evaluation of vaginal dysbiosis.

Compared with traditional microscopy-based techniques such as Amsel criteria and Nugent scoring, sequencing-based approaches provide improved sensitivity and allow identification of microbial interactions and biofilm-associated communities (11,12,16,38,48,69). However, cost, accessibility, and lack of standardized implementation remain important barriers to routine clinical adoption.

Microbiome-directed therapeutic strategies represent one of the most promising developments in this field. Probiotic interventions demonstrate strain-specific effects on microbiome restoration, supporting the need for personalized treatment selection (9,10,51). Emerging approaches involving microbial

metabolites, postbiotics, and engineered Lactobacillus strains further expand therapeutic possibilities for ecosystem-level modulation (36,53,54,58,70).

Vaginal microbiota transplantation represents an experimental but promising intervention for refractory dysbiosis. Early studies demonstrate successful donor microbiome engraftment and improved reproductive outcomes, although challenges related to donor selection, long-term safety evaluation, regulatory approval, and ethical considerations remain unresolved (42,48,55-57).

Strengths of this review - This review integrates recent multidisciplinary evidence published between 2020 and 2025 across microbiology, immunology, reproductive medicine, and translational microbiome research. Particular emphasis is placed on ecosystem-level interpretation of dysbiosis and emerging microbiome-directed therapies.

Limitations - As a narrative review, the study does not include quantitative meta-analysis. Additionally, variability in diagnostic methodologies, sequencing platforms, and study populations across included publications limits direct comparability between studies. Another limitation relates to the evolving availability of microbiome diagnostics across clinical settings.

Novelty and clinical relevance - The novelty of this review lies in its integrative interpretation of vaginal dysbiosis as a dynamic ecological continuum linking bacterial, fungal, and viral susceptibility pathways with emerging microbiome-directed therapeutic strategies. By combining sequencing-based insights with reproductive health implications, this review supports ecosystem-oriented management approaches in modern gynecological practice.

CONCLUSIONS

- The vaginal microbiome is vital for female reproductive health, influencing infection susceptibility, inflammation, and reproductive outcomes. *Lactobacillus*-dominated ecosystems, especially *Lactobacillus crispatus*, are linked to microbial stability, epithelial barrier function, and immune homeostasis. In contrast, vaginal dysbiosis indicates various microbial and immunological issues that lead to disease.
- This review emphasizes that vaginal dysbiosis is a continuum including bacterial vaginosis, aerobic vaginitis, vulvovaginal candidiasis, and mixed infections. These disorders vary in microbial composition, inflammation, and clinical presentation, highlighting the need for varied diagnostic and therapeutic approaches. Advances in sequencing and computational biology have reshaped understanding of vaginal ecology, revealing complex host-microbe and microbe–microbe interactions that affect disease persistence.
- Recent diagnostic and microbiome-directed therapies offer chances to achieve long-term restoration of vaginal function rather than just symptom control. Probiotics, postbiotics, engineered strains, and vaginal microbiota transplantation are promising, but more research

is needed for long-term safety, efficacy, and patient selection. Successful microbiome interventions will need to consider host factors, behaviors, and clinical context.

- Future progress will require longitudinal studies to track microbiome changes, multi-omics integration to clarify mechanisms, and translating microbiome science into personalized care.

- By shifting to ecosystem-based management from pathogen-centered treatments, microbiome-informed strategies could transform gynecological practice and improve women's reproductive health outcomes.

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Conflict of Interest Statement: The authors declare that they have no conflict of interest.

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