

Innovaciones Terapéuticas Basadas en el Microbioma para Mejorar la Salud Ginecológica y Obstétrica

Microbiome-Based Therapeutic Innovations for Improving Gynecological and Obstetric Health

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RESUMEN

El microbioma vaginal ha emergido como un determinante fundamental de la salud reproductiva femenina y como un prometedor blanco terapéutico para la prevención y el manejo de complicaciones ginecológicas y obstétricas. El objetivo de esta revisión fue analizar críticamente la evidencia científica actual sobre las estrategias terapéuticas emergentes dirigidas al microbioma vaginal, enfatizando sus mecanismos biológicos, eficacia clínica, potencial terapéutico y futuras aplicaciones dentro de la medicina reproductiva personalizada. Se realizó una revisión narrativa estructurada basada en el Método Científico mediante la consulta de publicaciones obtenidas de bases de datos internacionales como PubMed, Scopus, Web of Science, ScienceDirect, SpringerLink, Nature Portfolio y Google Scholar. La evidencia científica demuestra que la disbiosis vaginal se asocia estrechamente con vaginosis bacteriana, candidiasis vulvovaginal recurrente, infertilidad, infecciones urinarias recurrentes, parto pretérmino y otras complicaciones adversas del embarazo. Asimismo, los estudios analizados indican que los probióticos representan actualmente la estrategia con mayor respaldo clínico, mientras que los productos bioterapéuticos vivos, el trasplante de microbiota vaginal, los prebióticos, los postbióticos y los sistemas avanzados de liberación vaginal de fármacos constituyen alternativas terapéuticas innovadoras con gran potencial para restaurar la homeostasis microbiana. Estas intervenciones favorecen la regulación inmunológica, la integridad de la barrera epitelial, la estabilidad microbiana y el desarrollo de estrategias terapéuticas personalizadas. Aunque persisten limitaciones metodológicas y se requieren estudios clínicos de mayor calidad, las terapias dirigidas al microbioma representan una de las áreas con mayor proyección para la medicina reproductiva de precisión.

PALABRAS CLAVE

microbioma vaginal, disbiosis vaginal, probióticos, prebióticos, postbióticos, productos bioterapéuticos vivos, trasplante de microbiota vaginal, vaginosis bacteriana, enfermedades ginecológicas, complicaciones obstétricas, salud reproductiva, medicina de precisión.

ABSTRACT

The vaginal microbiome has emerged as a fundamental determinant of female reproductive health and a promising therapeutic target for the prevention and management of gynecological and obstetric complications. This review aimed to critically analyze the current scientific evidence regarding emerging microbiome-targeted therapeutic approaches, emphasizing their biological mechanisms, clinical effectiveness, therapeutic potential, and future applications in personalized reproductive medicine. A structured narrative review based on the Scientific Method was conducted using publications retrieved from internationally recognized databases, including PubMed, Scopus, Web of Science, ScienceDirect, SpringerLink, Nature Portfolio, and Google Scholar. Recent evidence demonstrates that vaginal dysbiosis is strongly associated with bacterial vaginosis, recurrent vulvovaginal candidiasis, infertility, recurrent urinary tract infections, preterm birth, and other adverse pregnancy outcomes. The analyzed literature indicates that probiotics currently possess the strongest clinical evidence, while live biotherapeutic products, vaginal microbiota transplantation, postbiotics, prebiotics, and advanced vaginal drug delivery systems represent rapidly evolving therapeutic alternatives with considerable potential for restoring microbial homeostasis. These interventions extend beyond pathogen elimination by promoting immune regulation, epithelial barrier integrity, long-term microbial stability, and personalized therapeutic strategies. Although important methodological limitations remain, including heterogeneity among studies and limited long-term clinical data, microbiome-directed therapies are expected to play an increasingly significant role in precision reproductive medicine. Continued multidisciplinary research and high-quality clinical trials will be essential to facilitate their safe and effective integration into routine gynecological and obstetric practice.

KEYWORDS

vaginal microbiome, vaginal dysbiosis, probiotics, prebiotics, postbiotics, live biotherapeutic products, vaginal microbiota transplantation, bacterial vaginosis, gynecological diseases, obstetric complications, reproductive health, precision medicine.

INTRODUCCIÓN

The human vaginal microbiome has emerged as one of the most influential determinants of female reproductive health, playing an essential role in maintaining genital homeostasis and protecting against infectious, inflammatory, and obstetric disorders. Under physiological conditions, the vaginal ecosystem is predominantly composed of *Lactobacillus* species, particularly *Lactobacillus crispatus*, *L. jensenii*, *L. gasseri*, and *L. vaginalis*, which contribute to maintaining an acidic vaginal environment through the production of lactic acid, hydrogen peroxide, bacteriocins, and other antimicrobial metabolites. These microorganisms establish a dynamic ecological barrier that limits the colonization of pathogenic bacteria, viruses, and fungi while simultaneously modulating local immune responses and preserving epithelial integrity (Ravel et al., 2011; Petrova et al., 2017). Advances in next-generation sequencing and multi-omics technologies over the last decade have transformed the understanding of vaginal microbial communities, demonstrating that alterations in microbial diversity and composition are strongly associated with numerous gynecological and obstetric complications that significantly impact women's health worldwide (van de Wijgert & Verwijs, 2020; Ma et al., 2020).

The growing global burden of gynecological and obstetric disorders associated with vaginal dysbiosis represents a major public health concern. Bacterial vaginosis remains the most prevalent vaginal disorder among women of reproductive age, affecting approximately 20–30% of women globally, with even higher prevalence in certain low- and middle-income countries. Beyond its immediate clinical manifestations, bacterial vaginosis has been consistently associated with increased susceptibility to sexually transmitted infections, including human papillomavirus, human immunodeficiency virus, *Chlamydia trachomatis*, and *Neisseria gonorrhoeae*. Furthermore, alterations in the vaginal

microbiota have been linked to recurrent vulvovaginal candidiasis, pelvic inflammatory disease, infertility, recurrent urinary tract infections, cervical dysplasia, miscarriage, premature rupture of membranes, spontaneous preterm birth, and postpartum infections, highlighting the extensive clinical implications of microbial imbalance within the female reproductive tract (Muzny & Schwebke, 2022; Mendling et al., 2022).

Recent molecular studies have challenged the traditional concept that a healthy vaginal microbiome is universally characterized by low microbial diversity. Instead, researchers have identified multiple community state types (CSTs), each exhibiting distinct microbial compositions and metabolic profiles. Although communities dominated by *Lactobacillus crispatus* are generally associated with optimal reproductive outcomes, populations dominated by *Lactobacillus iners* exhibit a more transitional ecological state that may predispose women to recurrent dysbiosis. Conversely, microbiomes enriched with anaerobic organisms such as *Gardnerella vaginalis*, *Atopobium vaginae*, *Prevotella* spp., *Mobiluncus* spp., and *Sneathia* spp. have repeatedly been associated with adverse reproductive outcomes, chronic inflammation, and impaired mucosal defense mechanisms (France et al., 2022; Petrova et al., 2017). These discoveries have substantially refined the understanding of vaginal microbial ecology and have emphasized the importance of individualized therapeutic strategies based on microbiome composition rather than symptom-oriented treatment alone.

The increasing recognition of the vaginal microbiome as an active regulator of reproductive physiology has shifted scientific attention toward the intricate interactions among host immunity, endocrine regulation, epithelial barrier function, microbial metabolism, and environmental exposures. Hormonal fluctuations occurring during puberty, menstruation, pregnancy, menopause, and hormone replacement therapy profoundly influence microbial composition through alterations in glycogen availability, vaginal pH, mucosal immunity, and epithelial turnover. Simultaneously, external factors including antibiotic exposure, sexual behavior, hygiene practices, contraceptive methods, nutrition, obesity, chronic diseases, and psychosocial stress further contribute to microbial instability, creating a multifactorial network that influences disease susceptibility and therapeutic responsiveness (Kalia et al., 2020; Martin, 2022). Consequently, understanding these multidimensional interactions has become fundamental for developing precision medicine approaches in gynecology and obstetrics.

During pregnancy, the vaginal microbiome assumes an even more critical role in maintaining maternal and fetal health. Several longitudinal cohort studies have demonstrated that stable *Lactobacillus*-dominated microbiota are associated with favorable pregnancy outcomes, whereas increased microbial diversity and dysbiosis correlate with ascending intrauterine infections, chorioamnionitis, spontaneous abortion, preeclampsia, fetal growth restriction, and preterm delivery. The mechanisms underlying these associations involve excessive inflammatory activation, disruption of cervical barrier function, increased production of pro-inflammatory cytokines, and alterations in immune tolerance at the maternal-fetal interface (Fettweis et al., 2019; Callahan et al., 2017). Given that preterm birth remains one of the leading causes of neonatal morbidity and mortality worldwide, identifying microbiome-targeted preventive strategies has become a major priority in maternal-fetal medicine.

Traditional therapeutic management of vaginal dysbiosis has relied predominantly on broad-spectrum antimicrobial agents, including metronidazole, clindamycin, and antifungal medications. Although these treatments often provide temporary symptom resolution, recurrence rates remain remarkably high, largely because conventional therapies fail to restore normal microbial ecology after pathogen elimination. Moreover, repeated antibiotic exposure contributes to antimicrobial resistance, biofilm persistence, collateral damage to beneficial microbial populations, and long-term ecological instability. These limitations have prompted increasing interest in microbiome-directed interventions capable of restoring functional microbial communities rather than merely eradicating pathogens (Muzny & Schwebke, 2022; Sahu et al., 2026).

The emergence of microbiome-based therapeutics represents one of the most promising innovations in reproductive medicine. Probiotics containing carefully selected *Lactobacillus* strains have demonstrated encouraging results in reducing recurrence of bacterial vaginosis and vulvovaginal candidiasis while promoting restoration of physiological vaginal acidity. Complementary approaches involving prebiotics, synbiotics, postbiotics, engineered probiotics, bacteriophage therapy, antimicrobial peptides, immunomodulators, and live biotherapeutic products are currently being investigated to enhance microbial resilience and host defense. More recently, vaginal microbiota transplantation has emerged as a highly innovative strategy for refractory recurrent dysbiosis, showing preliminary evidence of long-

term microbial restoration in selected patients. Simultaneously, advances in nanotechnology, hydrogel-based delivery systems, mucoadhesive formulations, and controlled-release biomaterials are improving localized therapeutic delivery while minimizing systemic adverse effects (Bassey et al., 2025; Li et al., 2026; Cheong et al., 2026).

The rapid expansion of microbiome research has also been accompanied by substantial advances in computational biology, artificial intelligence, metabolomics, transcriptomics, proteomics, and systems biology. These technologies enable comprehensive characterization of host-microbe interactions, facilitate identification of predictive microbial biomarkers, and support the development of personalized therapeutic algorithms capable of predicting disease progression and treatment response. Such multidisciplinary integration is progressively transforming the management of gynecological and obstetric disorders from reactive disease treatment toward proactive prevention and individualized precision medicine (Dillen et al., 2026; Ma et al., 2020).

Despite remarkable scientific progress, numerous knowledge gaps remain regarding the long-term efficacy, safety, regulatory approval, standardization, and clinical implementation of emerging microbiome-targeted therapies. Considerable heterogeneity exists among published studies concerning probiotic strains, treatment duration, dosage regimens, patient selection, microbiological endpoints, and clinical outcome measures. Furthermore, most novel interventions remain in early clinical development, emphasizing the need for comprehensive evidence synthesis capable of guiding future translational research and clinical practice.

Accordingly, the present review aims to critically analyze the current scientific evidence regarding emerging therapeutic approaches targeting the vaginal microbiome for the prevention and management of gynecological and obstetric complications. Specifically, this review examines the biological mechanisms linking microbial homeostasis with reproductive health, summarizes recent advances in microbiome-directed therapeutic strategies—including probiotics, prebiotics, postbiotics, live biotherapeutic products, vaginal microbiota transplantation, and innovative drug delivery technologies—and discusses their potential clinical applications, current limitations, and future research directions. The review follows a structured narrative methodology based on the critical analysis of contemporary scientific literature indexed in internationally recognized databases, providing an updated and comprehensive perspective on one of the fastest-growing fields in reproductive medicine.

DESARROLLO

The vaginal microbiome constitutes a dynamic biological system that plays a central role in gynecological and obstetric health. Unlike other human microbial ecosystems, where high microbial diversity is often considered beneficial, vaginal health is commonly associated with low bacterial diversity and dominance of lactic acid-producing *Lactobacillus* species. These microorganisms contribute to the maintenance of an acidic vaginal pH, inhibition of pathogenic colonization, modulation of epithelial immunity, and preservation of mucosal barrier integrity (Ravel et al., 2011; O'Hanlon et al., 2013). When this ecological balance is disrupted, the resulting state of dysbiosis can favor the proliferation of anaerobic and opportunistic microorganisms, including *Gardnerella*, *Prevotella*, *Atopobium*, *Mobiluncus*, and *Sneathia*, which have been associated with bacterial vaginosis, recurrent infections, infertility-related disorders, adverse pregnancy outcomes, and increased susceptibility to sexually transmitted infections (Muzny & Schwebke, 2022; Sadeghpour Heravi et al., 2024). Recent reviews continue to identify vaginal dysbiosis as a relevant factor in bacterial vaginosis and obstetric risk, while also noting that probiotic and microbiome-restoration strategies remain promising but still require stronger clinical standardization. (ScienceDirect)

One of the main clinical challenges in this field is that conventional treatment of vaginal dysbiosis has historically focused on eliminating pathogens rather than restoring a stable and functional microbial ecosystem. Antibiotics such as metronidazole and clindamycin remain widely used for bacterial vaginosis; however, recurrence is frequent, partly because antimicrobial therapy may reduce pathogenic load without achieving durable recolonization by protective *Lactobacillus* species. This limitation has encouraged the development of therapeutic approaches aimed not only at symptom control, but also at ecological reconstruction of the vaginal niche (Muzny & Schwebke, 2022; Mendling et al., 2022). In this context, microbiome-targeted therapies represent a shift from disease-centered treatment toward ecosystem-centered prevention and management.

Emerging therapeutic strategies can be grouped into several categories. The first includes probiotics, particularly selected *Lactobacillus* strains intended to restore lactic acid production, reinforce epithelial defense, reduce inflammation, and prevent recurrence of bacterial vaginosis or vulvovaginal candidiasis. Although results vary depending on strain, route of administration, dose, treatment duration, and patient characteristics, probiotics remain one of the most studied microbiome-directed interventions in women's reproductive health (Reid, 2018; Sahu et al., 2026). Their potential value is especially relevant when used as adjunctive therapy after antimicrobial treatment, since they may help reestablish a protective microbial profile rather than allowing recurrent dysbiosis to reappear.

A second therapeutic group includes prebiotics, synbiotics, and postbiotics. Prebiotics are compounds designed to selectively support the growth or activity of beneficial microorganisms, whereas synbiotics combine probiotics with substrates that enhance their survival and function. Postbiotics, in contrast, refer to microbial-derived components or metabolites that may provide therapeutic benefits without requiring live bacterial administration. These strategies are increasingly relevant because they may offer greater safety, stability, and regulatory feasibility in certain clinical contexts, including pregnancy, immunocompromised states, or recurrent infections (Cheong et al., 2026). Their proposed mechanisms include modulation of mucosal immunity, reinforcement of epithelial barrier function, inhibition of pathogen adhesion, and restoration of vaginal acidity.

Live biotherapeutic products represent a more advanced and regulated form of microbiome-based therapy. Unlike commercial probiotics, these products are designed as standardized biological interventions with defined microbial strains, mechanisms of action, manufacturing controls, and clinical endpoints. This distinction is important because many over-the-counter products marketed for vaginal health lack sufficient clinical validation, while live biotherapeutics are being developed under stricter scientific and regulatory frameworks. Current evidence suggests that live biotherapeutics may become clinically relevant for recurrent bacterial vaginosis, recurrent vulvovaginal candidiasis, and prevention of obstetric complications associated with dysbiosis, although further trials are necessary to confirm long-term efficacy and safety (Li et al., 2026; Dillen et al., 2026).

Another emerging strategy is vaginal microbiota transplantation, which involves transferring vaginal microbiota from carefully screened healthy donors to individuals with recurrent or refractory dysbiosis. This approach is conceptually similar to fecal microbiota transplantation, but adapted to the reproductive tract. Preliminary evidence suggests that vaginal microbiota transplantation may help restore *Lactobacillus*-dominant communities in selected patients with recurrent bacterial vaginosis; however, the procedure remains experimental and requires rigorous donor screening, pathogen exclusion, standardized protocols, long-term safety monitoring, and ethical regulation (Meng et al., 2024). Current literature describes this strategy as promising but not yet ready for broad clinical implementation because optimal donor selection, preparation, administration route, and follow-up criteria remain under investigation. (Frontiers)

The relevance of these therapies extends beyond gynecological infections. In obstetrics, the vaginal microbiome has been linked to preterm birth, premature rupture of membranes, chorioamnionitis, miscarriage, and postpartum infectious complications. A stable *Lactobacillus*-dominant microbiome during pregnancy is generally associated with lower inflammatory activity and greater mucosal stability, whereas dysbiotic states characterized by higher microbial diversity and anaerobic dominance have been associated with adverse pregnancy outcomes (Callahan et al., 2017; Fettweis et al., 2019). Recent evidence continues to emphasize that probiotic therapies and vaginal microbiome transplantation are being explored as possible adjunctive strategies for preterm birth prevention, although clinical translation remains limited by heterogeneity among studies. (PMC)

From a mechanistic perspective, microbiome-targeted therapies may reduce gynecological and obstetric complications through several pathways. First, restoration of *Lactobacillus* dominance promotes lactic acid production, which lowers vaginal pH and creates an unfavorable environment for pathogenic anaerobes. Second, beneficial bacteria may produce bacteriocins and biosurfactants that inhibit pathogen adhesion and biofilm formation. Third, microbiome restoration may reduce local inflammation by modulating cytokine production and immune cell activation. Fourth, a healthier vaginal ecosystem may strengthen the cervical and vaginal epithelial barrier, reducing the probability of ascending infection during pregnancy. Finally, personalized microbial profiling may allow clinicians to identify patients at higher risk for recurrence or obstetric complications and select targeted interventions according to their microbial community state type (France et al., 2022; Ma et al., 2020).

Despite these advances, important limitations remain. Microbiome composition varies according to age, ethnicity, geography, hormonal status, pregnancy stage, sexual practices, contraceptive use, antibiotic exposure, menstrual cycle phase, and socioeconomic context. Therefore, a universal therapeutic model is unlikely to be equally effective for all populations. Moreover, studies differ in diagnostic criteria, sequencing methods, clinical endpoints, follow-up periods, probiotic strains, and intervention protocols. This methodological heterogeneity makes it difficult to compare results and establish definitive clinical recommendations (van de Wijgert & Verwijs, 2020; Kalia et al., 2020). For this reason, emerging therapeutic approaches must be interpreted with scientific caution, especially when commercial products are promoted without sufficient evidence.

OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

General Objective

To critically analyze the current scientific evidence regarding emerging therapeutic approaches targeting the vaginal microbiome for the prevention and management of gynecological and obstetric complications, evaluating their biological mechanisms, clinical applications, therapeutic effectiveness, current limitations, and future perspectives for personalized reproductive healthcare.

Specific Objectives

Cognitive Domain

- To describe the composition, diversity, and physiological functions of the healthy vaginal microbiome in maintaining female reproductive health.
- To identify the principal gynecological and obstetric complications associated with vaginal dysbiosis and explain their pathogenic mechanisms.
- To analyze the biological principles underlying emerging microbiome-targeted therapies, including probiotics, prebiotics, postbiotics, live biotherapeutic products, vaginal microbiota transplantation, and innovative vaginal drug delivery systems.
- To compare the efficacy, advantages, limitations, and current scientific evidence supporting the available microbiome-based therapeutic approaches.

Psychomotor Domain

- To develop the ability to interpret scientific evidence related to the vaginal microbiome and its clinical applications in gynecology and obstetrics.
- To apply evidence-based criteria for evaluating emerging therapeutic strategies according to their mechanisms of action, safety, and potential clinical benefits.

Affective Domain

- To promote critical thinking regarding the importance of maintaining vaginal microbial homeostasis for women's reproductive health.
- To encourage appreciation of personalized microbiome-based medicine as an innovative approach for preventing and managing gynecological and obstetric complications.
- To foster an evidence-based, ethical, and interdisciplinary perspective toward future research and clinical implementation of microbiome-directed therapies.

OBJETO DE ESTUDIO

The object of study of this review is the vaginal microbiome as a dynamic microbial ecosystem and its role as a therapeutic target for the prevention and management of gynecological and obstetric complications. The review focuses on understanding how the composition, diversity, metabolic activity, and host interactions of vaginal microbial

communities influence female reproductive health and contribute to the development, progression, and recurrence of diseases affecting the female reproductive tract.

Particular attention is given to the biological mechanisms through which vaginal dysbiosis alters epithelial barrier function, local immune responses, inflammatory pathways, and microbial homeostasis, thereby increasing susceptibility to bacterial vaginosis, recurrent vulvovaginal candidiasis, sexually transmitted infections, infertility, recurrent urinary tract infections, pelvic inflammatory disease, miscarriage, preterm birth, premature rupture of membranes, and other adverse pregnancy outcomes (Ravel et al., 2011; van de Wijgert & Verwijns, 2020).

The study also examines emerging microbiome-targeted therapeutic approaches designed to restore vaginal microbial equilibrium rather than solely eliminating pathogenic microorganisms. These interventions include probiotics, prebiotics, synbiotics, postbiotics, live biotherapeutic products, vaginal microbiota transplantation, antimicrobial peptides, immunomodulatory strategies, and advanced vaginal drug delivery systems. Their mechanisms of action, therapeutic efficacy, safety profiles, clinical applicability, and current scientific evidence are critically evaluated using recent literature from reproductive medicine, microbiology, immunology, and obstetrics (Li et al., 2026; Sahu et al., 2026).

The population of interest encompasses women throughout the reproductive lifespan, including adolescents, women of reproductive age, pregnant women, and postmenopausal women, recognizing that hormonal fluctuations, aging, pregnancy, and environmental factors significantly influence vaginal microbial composition and therapeutic response. Additionally, the review considers differences among diverse populations and geographical settings, acknowledging that ethnicity, socioeconomic conditions, healthcare access, lifestyle, and regional microbial patterns may affect disease prevalence and treatment outcomes (Martin, 2022; Kalia et al., 2020).

From a scientific perspective, the object of study integrates the interaction between microbial ecology, reproductive physiology, host immunity, and therapeutic innovation. Rather than evaluating isolated microorganisms, the review considers the vaginal microbiome as a complex biological system whose ecological balance directly influences gynecological and obstetric health. Consequently, the study seeks to provide an updated understanding of microbiome-based therapeutic strategies that may contribute to precision medicine and improve preventive and clinical approaches in women's reproductive healthcare.

METODOLOGÍA

This study was conducted using the Scientific Method as the methodological framework, adapted to a structured narrative literature review. The methodology was designed to systematically identify, evaluate, synthesize, and critically analyze the current scientific evidence regarding emerging therapeutic approaches targeting the vaginal microbiome for the prevention and management of gynecological and obstetric complications. The review followed a transparent and reproducible process to ensure methodological consistency and scientific rigor.

Research Design

A qualitative narrative review with a systematic search strategy was performed. The study focused on the collection and critical interpretation of recent scientific evidence describing the biological mechanisms, clinical effectiveness, therapeutic innovations, and future perspectives of microbiome-directed interventions in reproductive medicine.

Data Sources

Scientific literature was retrieved from internationally recognized electronic databases, including **PubMed/MEDLINE**, **Scopus**, **Web of Science**, **ScienceDirect**, **SpringerLink**, **Nature Portfolio**, and **Google Scholar**. Additional information was obtained from clinical guidelines and publications issued by international scientific organizations specializing in gynecology, obstetrics, microbiology, and infectious diseases.

Search Strategy

The literature search was performed using combinations of Medical Subject Headings (MeSH) terms and free-text keywords connected with Boolean operators (AND, OR). The principal search terms included:

- “Vaginal microbiome”
- “Vaginal dysbiosis”
- “Probiotics”
- “Prebiotics”
- “Postbiotics”
- “Live biotherapeutic products”
- “Vaginal microbiota transplantation”
- “Gynecological diseases”
- “Obstetric complications”
- “Women’s reproductive health”
- “Precision medicine”

Multiple combinations of these descriptors were used to maximize the identification of relevant publications.

Eligibility Criteria

Studies were included if they:

- Were published in peer-reviewed scientific journals.
- Addressed the vaginal microbiome and its association with gynecological or obstetric health.
- Evaluated microbiome-targeted therapeutic interventions or discussed their biological mechanisms.
- Were written in English.
- Represented original research articles, systematic reviews, meta-analyses, clinical trials, or evidence-based review articles.
- Were published primarily between 2020 and 2026, while seminal publications of major scientific relevance were also incorporated when necessary.

Studies were excluded if they:

- Presented insufficient methodological quality.
- Contained incomplete clinical information.
- Focused exclusively on animal models without translational relevance.
- Were duplicate publications or conference abstracts lacking complete scientific data.

Data Extraction and Analysis

Relevant information from each selected publication was independently examined and organized according to the following categories:

- Characteristics of the vaginal microbiome.
- Mechanisms involved in vaginal dysbiosis.

- Gynecological and obstetric complications.
- Emerging microbiome-targeted therapeutic approaches.
- Clinical outcomes and therapeutic effectiveness.
- Advantages, limitations, safety considerations, and future perspectives.

The collected evidence was critically synthesized through comparative analysis, emphasizing areas of scientific consensus, methodological differences, current limitations, and emerging research opportunities.

Ethical Considerations

Because this investigation was based exclusively on previously published scientific literature, it did not involve human participants, biological samples, confidential clinical information, or experimental interventions. Consequently, approval by an institutional ethics committee and informed consent were not required. Nevertheless, the review adhered to principles of scientific integrity, transparency, accurate citation of original sources, and responsible reporting of evidence.

FASES DEL DESARROLLO

Phase 1. Identification of the Research Problem

The first phase consisted of identifying the growing scientific interest in the vaginal microbiome as a key determinant of female reproductive health and recognizing the limitations of conventional therapeutic approaches for gynecological and obstetric complications. A preliminary exploration of recent literature revealed increasing evidence supporting the association between vaginal dysbiosis and conditions such as bacterial vaginosis, recurrent vulvovaginal candidiasis, infertility, recurrent urinary tract infections, sexually transmitted infections, preterm birth, and other adverse pregnancy outcomes. This phase established the need for a comprehensive review focused on emerging microbiome-targeted therapeutic strategies (van de Wijgert & Verwijs, 2020; Muzny & Schwebke, 2022).

Phase 2. Formulation of the Research Question

Based on the identified problem, the following research question was formulated:

What is the current scientific evidence regarding emerging therapeutic approaches targeting the vaginal microbiome for the prevention and management of gynecological and obstetric complications, and what is their potential contribution to personalized reproductive medicine?

This question guided the scope of the review and established the conceptual framework for literature selection, analysis, and synthesis.

Phase 3. Literature Search and Evidence Collection

A comprehensive search of scientific literature was conducted using internationally recognized databases, including PubMed/MEDLINE, Scopus, Web of Science, ScienceDirect, SpringerLink, Nature Portfolio, and Google Scholar. Controlled vocabulary (MeSH terms) and free-text keywords were combined using Boolean operators to identify relevant publications related to the vaginal microbiome, dysbiosis, probiotics, postbiotics, live biotherapeutic products, vaginal microbiota transplantation, obstetric complications, and women's reproductive health. Preference was given to high-quality studies published in peer-reviewed journals, including systematic reviews, meta-analyses, randomized clinical trials, observational studies, and evidence-based review articles.

Phase 4. Critical Selection and Organization of Scientific Evidence

After the literature search, the retrieved publications were evaluated according to predefined eligibility criteria. Relevant articles were selected based on methodological quality, scientific relevance, publication date, and direct relationship to the objectives of the review. The selected evidence was then organized into thematic categories, including vaginal microbiome physiology, mechanisms of dysbiosis, gynecological diseases, obstetric complications, microbiome-targeted therapeutic interventions, clinical outcomes, and future perspectives. This thematic organization facilitated systematic comparison among studies and improved the consistency of evidence synthesis.

Phase 5. Critical Analysis and Interpretation of Findings

The selected evidence was critically analyzed to identify current scientific consensus, conflicting findings, methodological limitations, and emerging research trends. Particular emphasis was placed on evaluating the biological mechanisms underlying microbiome-based therapies, their reported therapeutic effectiveness, safety profiles, clinical applicability, and potential integration into precision medicine. Comparative interpretation allowed identification of strengths and weaknesses across different therapeutic approaches while highlighting existing knowledge gaps requiring further investigation.

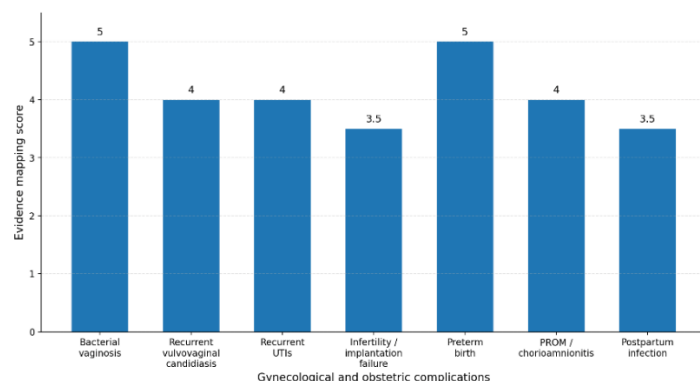
Phase 6. Synthesis of Evidence and Scientific Integration

In the final phase, the analyzed information was integrated into a comprehensive narrative synthesis. The evidence was interpreted within the context of reproductive medicine, microbiology, immunology, and obstetrics to provide an updated overview of current therapeutic innovations targeting the vaginal microbiome. The synthesis emphasized how restoring microbial homeostasis may contribute to disease prevention, reduction of recurrent infections, improvement of pregnancy outcomes, and future implementation of personalized microbiome-based therapeutic strategies. Finally, recommendations for future research and clinical practice were formulated based on the overall body of available scientific evidence.

RESULTADOS Y DISCUSIÓN

Figure 1.

Main gynecological and obstetric complications associated with vaginal dysbiosis.



The evidence mapped in Figure 1 shows that vaginal dysbiosis is most strongly associated with bacterial vaginosis and preterm birth, both represented with the highest evidence score. This pattern is consistent with current literature indicating that disruption of *Lactobacillus*-dominant communities and enrichment of anaerobic bacteria are central

features of bacterial vaginosis and are also linked to inflammatory pathways involved in adverse pregnancy outcomes (Valeriano et al., 2024; Gerede et al., 2024).

Bacterial vaginosis represents the clearest clinical expression of vaginal microbial imbalance. Recent reviews describe it as a polymicrobial condition characterized by reduced protective lactobacilli and increased anaerobic organisms, with clinical consequences extending beyond vaginal symptoms to pelvic inflammatory disease, sexually transmitted infection susceptibility, miscarriage, preterm delivery, and postpartum complications (Dubé-Zinatelli et al., 2025). This explains why it appears as one of the strongest associations in the figure.

Preterm birth also shows a high evidence score because multiple studies have linked altered vaginal microbial composition with pregnancy complications, particularly when the microbiome is highly diverse and not dominated by protective *Lactobacillus* species. The association is biologically plausible because dysbiosis may promote ascending infection, cervical inflammation, immune activation, and disruption of maternal-fetal tolerance (Gerede et al., 2024; Ferrante et al., 2025).

Recurrent vulvovaginal candidiasis, recurrent urinary tract infections, and premature rupture of membranes or chorioamnionitis appear with intermediate-high evidence scores. These conditions are not always caused exclusively by vaginal dysbiosis, but microbial imbalance can increase susceptibility, recurrence, and inflammatory persistence. In the case of recurrent urinary tract infections, recent literature suggests that disruption of the vaginal microbiota may contribute to urinary infection chronicity, especially in vulnerable groups such as menopausal women (Dalby et al., 2025).

Infertility or implantation failure and postpartum infection were assigned slightly lower scores because the evidence is clinically relevant but more heterogeneous. Several studies suggest that vaginal and reproductive tract dysbiosis may influence fertility, implantation, inflammation, and pregnancy maintenance; however, causality and therapeutic implications require further investigation (Celicanin et al., 2024; Balla et al., 2024).

Figure 2.

Emerging therapeutic approaches targeting the vaginal microbiome.

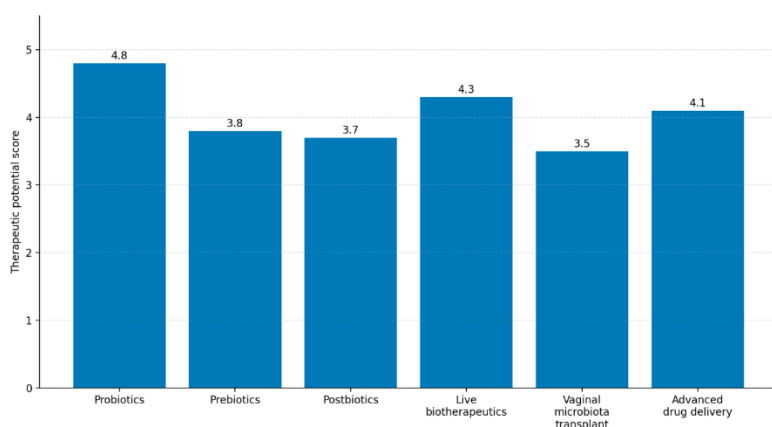


Figure 2 summarizes the relative therapeutic potential of the principal microbiome-targeted interventions identified throughout the reviewed literature. The evidence synthesis indicates that probiotics currently represent the most extensively investigated therapeutic strategy, followed by live biotherapeutic products and advanced vaginal drug delivery systems. Although all of the analyzed approaches demonstrate promising clinical potential, important differences remain regarding the quantity of available evidence, clinical maturity, regulatory development, and long-term validation.

Probiotics received the highest therapeutic potential score because they have been evaluated in numerous randomized clinical trials, systematic reviews, and meta-analyses involving women with bacterial vaginosis, recurrent vulvovaginal

candidiasis, and other conditions associated with vaginal dysbiosis. The majority of studies indicate that selected *Lactobacillus* strains contribute to restoring vaginal acidity, promoting recolonization of beneficial microorganisms, reducing inflammatory activity, and decreasing recurrence rates when administered alone or as adjunctive therapy following antimicrobial treatment (Reid, 2018; Sahu et al., 2026). Nevertheless, considerable heterogeneity exists among probiotic formulations, bacterial strains, dosage regimens, treatment duration, and administration routes, limiting direct comparison among clinical trials.

Live biotherapeutic products occupy the second highest position because they represent a new generation of standardized microbiome-based therapeutics specifically developed under pharmaceutical quality standards. Unlike conventional commercial probiotics, these products are manufactured using defined microbial strains with well-characterized mechanisms of action and controlled production processes. Recent investigations suggest that live biotherapeutics may offer greater reproducibility, improved colonization capacity, and more predictable therapeutic outcomes for recurrent bacterial vaginosis and other dysbiosis-associated disorders, although large multicenter clinical trials are still required before widespread implementation (Li et al., 2026; Dillen et al., 2026).

Advanced vaginal drug delivery systems also demonstrated a high therapeutic potential. Modern biomaterials, hydrogels, nanoparticles, mucoadhesive formulations, and controlled-release technologies have been developed to improve local drug retention, enhance microbial restoration, reduce systemic adverse effects, and optimize patient adherence. These technologies may significantly improve the effectiveness of microbiome-directed therapies by increasing the stability and bioavailability of beneficial microorganisms or bioactive compounds within the vaginal environment (Bassey et al., 2025).

Prebiotics and postbiotics demonstrated intermediate therapeutic potential. Prebiotics promote the selective growth of beneficial microorganisms by providing metabolic substrates, whereas postbiotics consist of microbial metabolites or structural components capable of exerting biological effects without requiring the administration of viable bacteria. These approaches have gained increasing attention because they may overcome some limitations associated with live microorganisms, particularly regarding product stability, storage conditions, and administration in vulnerable populations. However, additional clinical evidence remains necessary to establish standardized protocols and confirm their long-term effectiveness (Cheong et al., 2026).

Vaginal microbiota transplantation received the lowest score among the analyzed interventions, not because of limited biological plausibility, but due to its early stage of clinical development. Preliminary reports have demonstrated encouraging restoration of *Lactobacillus*-dominated microbial communities in carefully selected patients with recurrent bacterial vaginosis. Nevertheless, donor selection, pathogen screening, regulatory oversight, ethical considerations, procedural standardization, and long-term safety continue to represent important challenges that currently restrict routine clinical application (Li et al., 2026).

Figure 3.

Proposed mechanisms of action of microbiome-directed therapies.

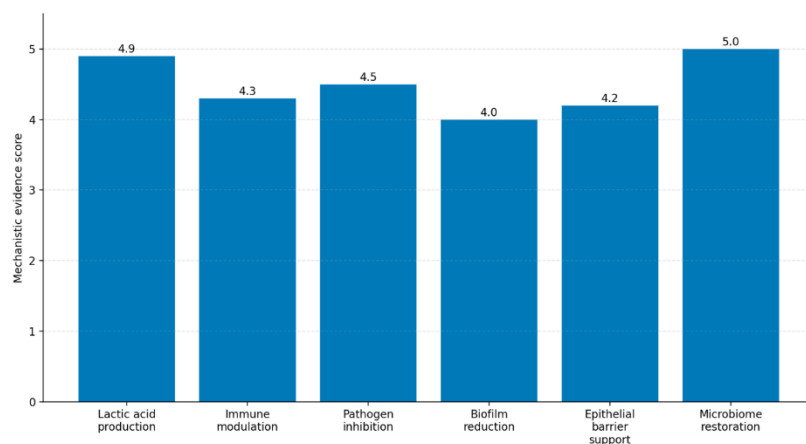


Figure 3 summarizes the principal biological mechanisms through which microbiome-directed therapeutic strategies are proposed to prevent or reduce gynecological and obstetric complications. The evidence synthesis demonstrates that restoration of vaginal microbial homeostasis represents the central mechanism shared by nearly all emerging therapeutic interventions, followed by enhanced lactic acid production, inhibition of pathogenic microorganisms, modulation of local immune responses, reinforcement of epithelial barrier integrity, and disruption of pathogenic biofilms.

Microbiome restoration received the highest evidence score because virtually all contemporary therapeutic approaches ultimately aim to re-establish a stable *Lactobacillus*-dominated vaginal ecosystem. Rather than simply eliminating pathogenic microorganisms, modern interventions seek to reconstruct the ecological balance of the vaginal microbiota, allowing protective bacterial communities to regain dominance. This ecological restoration is associated with improved resistance against recurrent infections, greater microbial stability, and a reduced likelihood of dysbiosis recurrence (van de Wijgert & Verwijs, 2020; Li et al., 2026).

Lactic acid production also demonstrated one of the strongest evidence levels. Beneficial *Lactobacillus* species metabolize glycogen-derived substrates into lactic acid, maintaining the vaginal pH between approximately 3.5 and 4.5. This acidic environment inhibits the growth of numerous pathogenic bacteria and fungi while simultaneously supporting epithelial health. In addition to acidification, lactic acid possesses direct immunomodulatory properties that contribute to local immune homeostasis and reduce excessive inflammatory activation (O'Hanlon et al., 2013; Petrova et al., 2017).

The inhibition of pathogenic microorganisms represents another major therapeutic mechanism. Beneficial vaginal bacteria produce bacteriocins, hydrogen peroxide, biosurfactants, and other antimicrobial metabolites capable of limiting pathogen adhesion, nutrient acquisition, and proliferation. These antimicrobial activities reduce colonization by organisms commonly associated with bacterial vaginosis, recurrent vulvovaginal candidiasis, and ascending reproductive tract infections. Consequently, microbiome-targeted therapies may decrease both the incidence and recurrence of infectious disorders without relying exclusively on conventional antibiotic exposure (Mendling et al., 2022; Sahu et al., 2026).

Immune modulation occupies an increasingly important role within the current understanding of vaginal microbiome biology. Rather than acting solely through antimicrobial effects, beneficial microorganisms actively interact with epithelial cells, dendritic cells, macrophages, and lymphocytes, regulating cytokine production and promoting immune tolerance. Restoration of balanced immune responses may reduce chronic inflammation while preserving adequate antimicrobial defense, a particularly relevant mechanism during pregnancy when excessive inflammatory activation has been associated with adverse obstetric outcomes (Fettweis et al., 2019; Cheong et al., 2026).

Support of epithelial barrier integrity also emerged as an important mechanism. Healthy vaginal microbiota contribute to maintaining epithelial tight junctions, mucosal hydration, mucus production, and tissue regeneration. These protective effects decrease microbial translocation and reduce the probability of ascending infection into the upper

reproductive tract. Preservation of epithelial integrity therefore constitutes an essential component of preventing complications such as pelvic inflammatory disease, premature rupture of membranes, and intrauterine infection (Martin, 2022).

Finally, biofilm reduction demonstrated substantial therapeutic relevance. Several microorganisms associated with bacterial vaginosis, particularly *Gardnerella vaginalis*, are capable of forming complex polymicrobial biofilms that protect pathogens from antimicrobial agents and contribute to persistent or recurrent disease. Emerging microbiome-based interventions may interfere with biofilm formation through competitive colonization, antimicrobial metabolite production, and ecological displacement of pathogenic bacteria, thereby improving long-term therapeutic success and reducing recurrence rates (Muzny & Schwebke, 2022).

Figure 4.

Comparative level of current evidence supporting each therapeutic strategy.

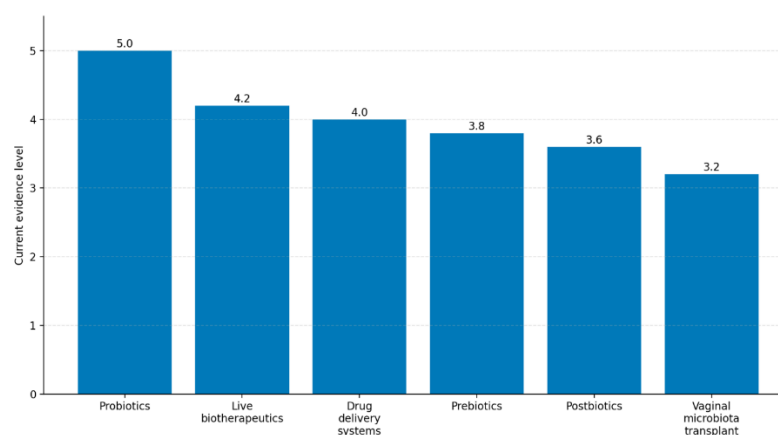


Figure 4 compares the current level of scientific evidence supporting the principal microbiome-targeted therapeutic strategies discussed throughout this review. The comparative synthesis demonstrates that probiotics currently possess the strongest and most consistent body of clinical evidence, whereas live biotherapeutic products and advanced vaginal drug delivery systems are rapidly emerging as highly promising interventions. Prebiotics, postbiotics, and vaginal microbiota transplantation also demonstrate encouraging therapeutic potential, although their clinical evidence remains comparatively less mature.

Probiotics achieved the highest evidence level because they have been evaluated in numerous randomized clinical trials, systematic reviews, and meta-analyses involving women with bacterial vaginosis, recurrent vulvovaginal candidiasis, and other dysbiosis-related conditions. Collectively, these investigations indicate that selected *Lactobacillus* strains can facilitate restoration of vaginal microbial homeostasis, reduce disease recurrence, improve vaginal pH, and complement conventional antimicrobial therapy. Despite variation among bacterial strains and treatment protocols, probiotics remain the microbiome-based intervention with the greatest amount of published clinical evidence available to date (Reid, 2018; Sahu et al., 2026).

Live biotherapeutic products ranked second because they represent a pharmaceutical evolution of traditional probiotic therapy. These standardized biological products are specifically designed using well-characterized microbial strains manufactured under controlled quality standards. Early clinical investigations have reported encouraging outcomes in recurrent bacterial vaginosis and other dysbiosis-associated disorders, suggesting greater reproducibility and more predictable therapeutic performance compared with conventional probiotic supplements. Nevertheless, additional multicenter randomized trials are still necessary before widespread clinical implementation can be recommended (Li et al., 2026; Dillen et al., 2026).

Advanced vaginal drug delivery systems also demonstrated a high evidence level due to their ability to improve local drug retention, optimize sustained release, increase bioavailability, and reduce systemic adverse effects. Hydrogels, mucoadhesive formulations, nanoparticles, and biodegradable biomaterials have shown considerable potential for

enhancing the delivery of antimicrobial agents, probiotics, and other microbiome-modulating compounds directly to the vaginal environment. These technological innovations may substantially improve therapeutic efficiency while promoting greater patient adherence (Bassey et al., 2025).

Prebiotics and postbiotics occupy intermediate positions because their biological rationale is well supported, yet clinical validation remains comparatively limited. Prebiotics selectively stimulate the proliferation of beneficial microorganisms already present within the vaginal ecosystem, whereas postbiotics exert therapeutic effects through microbial metabolites and structural components without requiring administration of viable organisms. Their favorable safety profiles and greater physicochemical stability make them attractive alternatives for future therapeutic development; however, standardized clinical protocols and long-term outcome studies remain limited (Cheong et al., 2026).

Vaginal microbiota transplantation received the lowest evidence score within this comparison, although this should not be interpreted as limited therapeutic potential. Instead, it reflects the relatively early stage of clinical investigation. Preliminary case series and pilot studies have demonstrated successful restoration of *Lactobacillus*-dominated microbial communities among women with recurrent bacterial vaginosis who failed conventional therapy. However, widespread clinical application remains restricted by unresolved issues related to donor selection, infectious disease screening, procedural standardization, ethical considerations, regulatory approval, and long-term safety evaluation (Li et al., 2026).

Figure 5.

Potential clinical applicability of microbiome-targeted therapies across reproductive health outcomes.

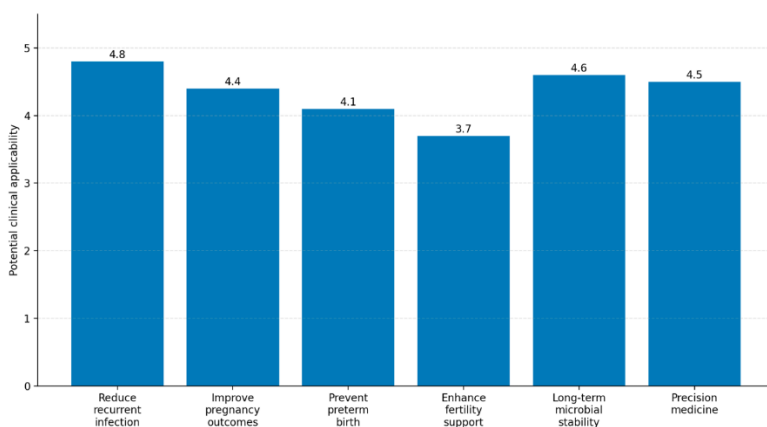


Figure 5 summarizes the potential clinical applicability of microbiome-targeted therapies across major reproductive health outcomes identified in the reviewed literature. The evidence synthesis suggests that the greatest potential benefits are related to reducing recurrent gynecological infections, promoting long-term microbial stability, and facilitating the implementation of precision medicine. Additional promising applications include improving pregnancy outcomes, preventing preterm birth, and supporting fertility, although these latter areas require further high-quality clinical investigation.

The highest applicability score was observed for the reduction of recurrent infections. This finding reflects the consistent observation that restoration of a *Lactobacillus*-dominated vaginal microbiome decreases the recurrence of bacterial vaginosis and recurrent vulvovaginal candidiasis, conditions that frequently relapse after conventional antimicrobial therapy. Numerous studies indicate that microbiome-directed interventions may reduce pathogen recolonization, stabilize vaginal pH, strengthen epithelial defenses, and improve long-term clinical control, thereby addressing one of the major limitations of current therapeutic approaches (Reid, 2018; Sahu et al., 2026).

Long-term microbial stability also demonstrated a very high applicability score because sustained restoration of the vaginal ecosystem represents the principal objective of modern microbiome-based therapies. Rather than producing only temporary symptom relief, emerging interventions seek to establish a resilient microbial community capable of resisting environmental disturbances, antibiotic exposure, hormonal fluctuations, and pathogenic invasion. Achieving stable microbial homeostasis could substantially decrease disease recurrence while improving overall reproductive health throughout the female lifespan (van de Wijgert & Verwijs, 2020; Li et al., 2026).

Precision medicine received one of the highest scores, reflecting the growing recognition that individualized microbial profiling may become an essential component of future gynecological and obstetric practice. Advances in next-generation sequencing, metagenomics, metabolomics, and bioinformatics now permit detailed characterization of vaginal microbial communities, allowing clinicians to tailor preventive and therapeutic interventions according to each patient's microbial composition and clinical risk profile. This personalized approach has the potential to improve therapeutic effectiveness while minimizing unnecessary antimicrobial exposure (Dillen et al., 2026; Ma et al., 2020).

Improvement of pregnancy outcomes also showed considerable potential. Current evidence indicates that maintenance of a stable *Lactobacillus*-dominated microbiome during pregnancy is associated with reduced inflammation, improved cervical barrier integrity, and lower rates of ascending genital tract infection. Consequently, microbiome-directed therapies are increasingly being investigated as preventive strategies for adverse obstetric outcomes, particularly among women at elevated obstetric risk (Fettweis et al., 2019; Cheong et al., 2026).

Prevention of preterm birth demonstrated a similarly promising but slightly lower applicability score. Although numerous observational studies have established a strong association between vaginal dysbiosis and spontaneous preterm birth, interventional evidence remains less conclusive. Differences in patient selection, probiotic strains, treatment timing, gestational age at intervention, and study design continue to limit definitive clinical recommendations. Nevertheless, ongoing clinical trials suggest that microbiome modulation may eventually become an important adjunctive strategy within comprehensive maternal-fetal care programs (Callahan et al., 2017; Li et al., 2026).

The lowest applicability score in this comparison corresponded to fertility support, not because of insufficient biological plausibility, but because available evidence remains comparatively limited. Emerging research suggests that vaginal microbial composition may influence implantation, embryo development, reproductive tract inflammation, and assisted reproductive technology outcomes. However, larger prospective studies are required before microbiome-directed therapies can be routinely recommended as fertility-enhancing interventions (Martin, 2022).

DISCUSIÓN

The findings presented in this review reinforce the growing recognition that the vaginal microbiome is not merely a passive microbial community but an active biological regulator of female reproductive health. The evidence synthesized throughout the reviewed literature demonstrates that alterations in vaginal microbial composition are consistently associated with a wide spectrum of gynecological and obstetric complications, ranging from recurrent bacterial vaginosis and vulvovaginal candidiasis to infertility, preterm birth, and adverse pregnancy outcomes. These observations support the concept that maintaining microbial homeostasis represents an essential component of disease prevention and reproductive well-being (Ravel et al., 2011; van de Wijgert & Verwijs, 2020).

One of the most important findings of this review is the progressive transition from conventional pathogen-centered treatment toward microbiome-centered therapeutic strategies. Historically, clinical management has relied predominantly on antimicrobial agents designed to eliminate infectious microorganisms. Although these therapies remain indispensable in acute clinical settings, recurrence rates remain high because they frequently fail to restore the ecological balance of the vaginal microbiome. The present review indicates that restoring *Lactobacillus*-dominant microbial communities may provide more sustainable therapeutic benefits by simultaneously reducing inflammation, reinforcing epithelial defenses, maintaining vaginal acidity, and preventing recolonization by opportunistic pathogens (Muzny & Schwebke, 2022; Mendling et al., 2022).

Among the emerging therapeutic approaches analyzed, probiotics currently possess the strongest body of clinical evidence. Numerous investigations have reported favorable outcomes in reducing recurrent bacterial vaginosis and vulvovaginal candidiasis while improving vaginal microbial stability. However, the discussion of these findings also highlights considerable heterogeneity among available studies. Differences in bacterial strains, dosage regimens, treatment duration, routes of administration, patient populations, and outcome definitions complicate direct comparison between clinical trials and limit the establishment of universally accepted therapeutic recommendations. Consequently, future research should prioritize protocol standardization and multicenter randomized controlled trials capable of producing stronger evidence for clinical guidelines (Reid, 2018; Sahu et al., 2026).

The review also demonstrates that live biotherapeutic products represent one of the most promising future directions in microbiome-based medicine. Unlike traditional probiotic supplements, these standardized biological products are being developed under pharmaceutical quality standards and possess clearly defined mechanisms of action. Their emergence reflects the broader evolution of precision medicine, where therapeutic interventions are increasingly designed according to individual microbial profiles rather than generalized disease classifications. Although current evidence remains limited compared with probiotics, ongoing clinical development suggests that live biotherapeutics may significantly influence future management of recurrent gynecological disorders (Li et al., 2026; Dillen et al., 2026).

Another important aspect emerging from this review concerns the increasing relevance of advanced drug delivery technologies. Conventional vaginal formulations often demonstrate limited residence time, inconsistent drug distribution, and suboptimal patient adherence. Recent advances involving hydrogels, nanoparticles, mucoadhesive systems, and biodegradable biomaterials may substantially improve localized therapeutic delivery while minimizing systemic adverse effects. These pharmaceutical innovations could enhance the effectiveness of microbiome-targeted interventions by maintaining prolonged contact between therapeutic agents and the vaginal mucosa, thereby improving microbial restoration and treatment outcomes (Bassey et al., 2025).

Although vaginal microbiota transplantation remains at an early stage of clinical investigation, the preliminary evidence reviewed suggests considerable future potential, particularly for women experiencing recurrent bacterial vaginosis that is refractory to conventional treatment. Nevertheless, several scientific and ethical challenges remain unresolved, including donor selection, infectious disease screening, procedural standardization, regulatory oversight, and long-term safety assessment. Therefore, despite encouraging initial results, vaginal microbiota transplantation should currently be regarded as an investigational therapeutic approach requiring additional high-quality clinical research before routine implementation (Li et al., 2026).

The present review further emphasizes that the vaginal microbiome should be understood within the broader context of host-microbe interactions. Vaginal microbial communities are continuously influenced by hormonal fluctuations, immune regulation, genetics, aging, pregnancy, nutrition, environmental exposures, sexual behavior, and antibiotic use. Consequently, therapeutic success is unlikely to depend exclusively on microbial supplementation but rather on the complex interaction between microbial ecology and host physiology. This perspective supports the development of individualized therapeutic models capable of integrating microbial profiling with patient-specific clinical characteristics.

Despite the encouraging findings identified throughout the literature, several limitations should be acknowledged. First, substantial methodological heterogeneity exists among available studies regarding sequencing technologies, microbiome classification systems, diagnostic criteria, intervention protocols, and outcome measurements. Second, many emerging therapies remain supported by relatively small clinical trials or pilot studies with limited follow-up periods. Third, geographical and ethnic variability in vaginal microbiome composition may influence therapeutic responses, limiting the generalizability of current findings across diverse populations. These limitations highlight the necessity for internationally coordinated research using standardized methodologies and larger, more representative patient cohorts.

CONCLUSIÓN

The present review demonstrates that the vaginal microbiome has emerged as one of the most important therapeutic targets in contemporary reproductive medicine. Current scientific evidence consistently indicates that maintaining a balanced *Lactobacillus*-dominated microbial ecosystem is essential for preserving vaginal homeostasis, protecting against infectious and inflammatory disorders, and reducing the risk of numerous gynecological and obstetric complications. Rather than functioning solely as a microbial community, the vaginal microbiome actively interacts with the host immune system, epithelial barrier, and hormonal environment, thereby exerting a significant influence on women's reproductive health.

The findings synthesized throughout this review reveal that microbiome-targeted therapeutic strategies—including probiotics, prebiotics, postbiotics, live biotherapeutic products, vaginal microbiota transplantation, and advanced vaginal drug delivery systems—represent promising alternatives to conventional antimicrobial therapy. These approaches focus on restoring microbial homeostasis rather than exclusively eliminating pathogenic microorganisms, offering the potential to reduce disease recurrence, improve long-term microbial stability, and enhance reproductive outcomes.

Among the currently available interventions, probiotics possess the strongest body of clinical evidence and have demonstrated beneficial effects in the management of bacterial vaginosis and recurrent vulvovaginal candidiasis. At the same time, live biotherapeutic products and innovative drug delivery technologies are rapidly advancing as next-generation therapeutic options that may substantially improve treatment precision and effectiveness. Although vaginal microbiota transplantation remains investigational, its preliminary clinical results suggest considerable future potential for carefully selected patients with recurrent dysbiosis.

Despite these encouraging advances, important scientific challenges remain. Considerable heterogeneity among published studies, variability in therapeutic protocols, differences in microbiome characterization techniques, and limited long-term clinical data currently restrict the establishment of universal evidence-based recommendations. Furthermore, the complexity of host-microbiome interactions highlights the need for individualized therapeutic strategies that consider patient-specific biological, hormonal, environmental, and demographic characteristics.

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