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Vaginal microbiome towards personalized medicine in women's health: a narrative review

Microbioma vaginal hacia una medicina personalizada en salud femenina: una revisión narrativa

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RESUMEN

Introducción: El microbioma vaginal es un ecosistema dinámico dominado por *Lactobacillus* spp., cuya disrupción se asocia con infecciones, complicaciones obstétricas y posible progresión neoplásica. **Objetivo:** Describir la composición, funciones y alteraciones del microbioma vaginal, y argumentar la necesidad de integrar su análisis en la práctica ginecológica hacia una medicina personalizada. **Métodos:** Revisión narrativa basada en búsqueda en PubMed, SciELO, Scopus y Web of Science (2021-2026). Se priorizaron metaanálisis, ensayos clínicos y revisiones sistemáticas. Se seleccionaron 43 fuentes, de las que se citan 23 por su relevancia y nivel de evidencia. **Resultados:** El microbioma vaginal sano presenta baja diversidad con predominio de *L. crispatus*, *L. iners*, *L. gasseri* o *L. jensenii*. La disbiosis, definida por pérdida de lactobacilos y aumento de anaerobios (*Gardnerella*, *Prevotella*, *Atopobium*), incrementa el riesgo de vaginosis bacteriana, parto pretérmino, infección por VPH y progresión a neoplasia cervical. Los probióticos específicos y la transferencia de microbiota vaginal emergen como estrategias moduladoras prometedoras. **Conclusiones:** La incorporación del análisis del microbioma vaginal en la práctica clínica (escalable mediante secuenciación de siguiente generación) permitiría intervenciones personalizadas en prevención y tratamiento. Se requieren estudios locales en poblaciones cubanas y latinoamericanas.

ABSTRACT

Introduction: The vaginal microbiome is a dynamic ecosystem dominated by *Lactobacillus* spp., whose disruption is associated with infections, obstetric complications and possible neoplastic progression. **Objective:** Describe the composition, functions and alterations of the vaginal microbiome, and argue the need to integrate its analysis into gynecological practice towards personalized medicine. **Methods:** Narrative review based on search in PubMed, SciELO, Scopus and Web of Science (2021-2026). Meta-analyses, clinical trials and systematic reviews were prioritized. 43 sources were selected, of which 23 are cited for their relevance and level of evidence. **Results:** The healthy vaginal microbiome presents low diversity with a predominance of *L. crispatus*, *L. iners*, *L. gasseri* or *L. jensenii*. Dysbiosis, defined by loss of lactobacilli and increase of anaerobes (*Gardnerella*, *Prevotella*, *Atopobium*), increases the risk of bacterial vaginosis, preterm birth, HPV infection and progression to cervical neoplasia. Specific probiotics and vaginal microbiota transfer emerge as promising modulatory strategies. **Conclusions:** Incorporating vaginal microbiome analysis into clinical practice (scalable through next-generation sequencing) would allow personalized interventions in prevention and treatment. Local studies are required in Cuban and Latin American populations.

INTRODUCTION

The concept of the human microbiome has revolutionized the understanding of physiology and pathology in the last two decades ⁽¹⁾. Specifically, the vaginal microbiome has emerged as a complex and dynamic ecosystem, traditionally dominated by species of the genus *Lactobacillus*, whose protective role transcends the mere physical barrier to include sophisticated immunological and metabolic mechanisms ^(2,3). The transition from the notion of "vaginal flora" to the paradigm of the "vaginal microbiome" implies recognizing not only the taxonomic composition but also the functional interactions, metabolism, and temporal stability of this microbial community ⁽⁴⁾.

In Cuba, gynecological infections are a frequent reason for consultation, and obstetric complications related to microbial dysbiosis represent a significant burden on the National Health System ⁽⁵⁾. The World Health Organization has emphasized the importance of understanding the biological factors that determine sexual and reproductive health ⁽⁶⁾.

Despite advances in the study of the vaginal microbiome, limitations remain in its comprehensive understanding and in translating this knowledge into routine clinical practice. Questions persist: What is the composition of the vaginal microbiome under normal conditions? What functions does it perform? And how do its alterations influence the development of diseases such as preterm birth and cervical cancer?

Given the breadth of the topic and the need to synthesize evidence from different levels (mechanisms, clinical associations, interventions), a narrative review is the appropriate approach to offer a comprehensive and contextualized view, without aiming for quantitative exhaustiveness.

This work aims to describe the composition, functions, and alterations of the vaginal microbiome and to argue for the need to integrate its analysis into gynecological practice toward personalized medicine.

METHODS

A narrative review of the scientific literature published between January 2021 and April 2026 was conducted. The search strategy was executed in the PubMed, SciELO, Scopus, and Web of Science databases, using the DeCS/MeSH descriptors: "vaginal microbiome," "vaginal microbiota," "dysbiosis," "Lactobacillus," "preterm birth," "HPV," "cervical cancer," "probiotics," "personalized medicine," and "women's health." Terms were combined using the Boolean operators

AND and OR. Articles in English, Spanish, and Portuguese were included.

Inclusion criteria: meta-analyses, systematic reviews, randomized clinical trials, prospective cohort studies, and cross-sectional studies of high methodological quality that addressed the composition, functions, alterations, or modulation of the vaginal microbiome. Classic foundational studies (prior to 2021) were also included when necessary to contextualize concepts.

Exclusion criteria: case series without a control group, expert opinions not supported by data, animal studies, letters to the editor, and conference abstracts.

Two reviewers (YNA and DVE) independently selected titles and abstracts; disagreements were resolved by consensus. Data extraction was organized into thematic categories: community composition and types (CST), functions (barrier, immunomodulatory, metabolic), influencing factors, dysbiosis and its relationship with obstetric complications, sexually transmitted infections, HPV and cervical cancer, and modulation strategies (probiotics, microbiota transfer). The synthesis was critical, prioritizing the evidence according to study design (with meta-analyses and clinical trials being prioritized). Patterns, controversies, and knowledge gaps were identified.

Initially, 312 articles were identified; After applying criteria and removing duplicates, 43 sources were selected for full-text review, of which 23 are cited in this review due to their representativeness and level of evidence (the remainder were used for contextual information but are not directly cited due to space limitations). A PRISMA diagram was not created because this is a narrative review.

RESULTS

1. Definition and characteristics of the vaginal microbiome

The microbiota includes the species, genera, and phyla that inhabit a given environment, while the microbiome encompasses not only these microorganisms but also their interactions, metabolic products, and genetic material ⁽⁴⁾. The vaginal microbiome constitutes an anaerobic microecosystem that fluctuates during the menstrual cycle and throughout life. The vaginal mucosa, composed of non-keratinized stratified squamous epithelium, obtains nutrients by diffusion, creating a relatively anaerobic habitat ⁽²⁾.

2. Composition of the vaginal microbiome

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The main bacteria belong to the genus *Lactobacillus*, which represents more than 70% of the microorganisms in healthy individuals ⁽⁴⁾. Studies based on 16S rRNA sequencing have classified the vaginal microbiome into five community states (CSTs) ⁽³⁾: CST I: dominated by *L. crispatus*, CST II: *L. gasseri*, CST III: *L. iners*, CST V: *L. jensenii*, CST IV: high microbial diversity with few lactobacilli and a predominance of anaerobes (*Gardnerella*, *Prevotella*, *Atopobium*, *Bifidobacterium*, etc.).

CST IV is associated with a higher risk of dysbiosis and pathology. However, this classification does not fully capture metabolic function or temporal stability ⁽³⁾. Furthermore, it has been observed that healthy women of African and Latin descent may have microbiomes with greater diversity and a lower predominance of lactobacilli, without necessarily indicating disease ⁽⁷⁾. This is especially relevant for Latin American and Cuban populations.

Table 1. Characteristics of the main vaginal CSTs

CST	Dominant species	Typical pH	Association with health/illness
I	<i>L. crispatus</i>	3,5–4,0	Strong protective effect (low risk)
II	<i>L. gasseri</i>	4,0–4,5	Intermediate protective effect
III	<i>L. iners</i>	4,0–4,7	Less stable, transition to dysbiosis
IV	Mixed anaerobic	>4,5	High risk of vaginosis, HPV, preterm birth
V	<i>L. jensenii</i>	4,0–4,5	Protective, less frequent

Source: own elaboration based on (3,4,7).

3. Factors that influence the vaginal microbiome

The vaginal microbiome is dynamic and varies according to hormonal factors (menstrual cycle, pregnancy, menopause), age, antibiotic use, oral contraceptives, hygiene habits, sexual activity, and diet ⁽⁸⁾. During pregnancy, the predominance of *Lactobacillus* is accentuated by estrogenic action, but dysbiosis during this period is associated with complications ⁽⁵⁾. Likewise, the intestinal microbiota influences the vaginal microbiota through bacterial migration, highlighting the importance of the gut-vagina axis ⁽⁸⁾.

4. Functions of the vaginal microbiome

Protective function (biological barrier): Lactobacilli produce lactic acid, maintaining an acidic pH (3.5–4.5) that inhibits pathogens. They also generate hydrogen peroxide and bacteriocins, and compete for epithelial adhesion sites ^(2,9).

Immune function: They modulate the local immune response, regulating the production of cytokines and antimicrobial peptides. They interact with Toll-like receptors and prevent excessive inflammatory responses ⁽¹⁰⁾.

Metabolic function: They metabolize epithelial glycogen (stimulated by estrogens) producing lactic acid, which stabilizes the environment ⁽⁹⁾.

Competitive exclusion: They occupy ecological niches and compete for nutrients, preventing pathogen colonization ⁽³⁾.

5. Vaginal dysbiosis: concept, controversies, and clinical associations

Vaginal dysbiosis is defined as an alteration of the microbial balance characterized by a decrease in protective *Lactobacillus* spp. and an increase in anaerobic bacteria ⁽⁷⁾. However, definition solely based on the absence of lactobacilli is problematic, since healthy women from certain ethnic groups naturally have low *Lactobacillus* abundance without pathology ⁽⁷⁾. Therefore, some authors propose a functional definition based on metabolites and inflammatory response ⁽¹¹⁾.

Dysbiosis is associated with:

a. Bacterial vaginosis (BV)

BV is the most frequent pathological expression, with loss of *Lactobacillus* and overgrowth of *Gardnerella vaginalis*, *Prevotella* spp., *Atopobium vaginae*, and *Megasphaera* ^(2,7). It affects between 10-30% of women of childbearing age and is associated with an increased risk of acquiring STIs (HIV, herpes, HPV) ⁽⁷⁾.

b. Obstetric complications

Numerous studies have shown that dysbiosis during pregnancy increases the risk of preterm birth, premature rupture of membranes, and chorioamnionitis ^(5,12). A recent systematic review (2025) including 34 cohort studies found that women with CST IV microbiome in the first trimester have an odds ratio of 2.8 (95% CI 2.1-3.7) for delivery before 34 weeks ⁽¹²⁾. The mechanisms involved include the ascent of pathogens from the vagina to the amniotic cavity, triggering intra-amniotic inflammation ⁽⁵⁾.

c. Human papillomavirus (HPV) infection and cervical cancer

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Recent evidence suggests that vaginal dysbiosis favors the persistence of high-risk HPV and progression to cervical intraepithelial neoplasia (CIN) and cancer^(13,14). A 2025 meta-analysis⁽¹³⁾ including 12 observational studies (n=3,247 women) showed that the presence of *L. crispatus* is associated with HPV clearance (OR 0.42), whereas abundance of *Gardnerella* and *Atopobium* correlates with viral persistence (OR 2.9). A multi-omics study (2024) identified that the vaginal metabolome (especially L-isomer lactic acid levels and certain diols) is the best predictor of the cervical microenvironment, surpassing taxonomic composition⁽¹⁵⁾.

d. Other sexually transmitted infections and assisted reproduction

Vaginal dysbiosis increases susceptibility to *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis*⁽⁷⁾. In the context of assisted reproduction, a 2025 meta-analysis⁽¹⁶⁾ found that women with a non-Lactobacillus-dominated microbiome have a significantly lower implantation rate (RR 0.65; 95% CI 0.52-0.81).

6. Strategies for modulating the vaginal microbiome: towards personalized medicine

Probiotics

Vaginal or oral probiotics with specific strains of *L. rhamnosus*, *L. reuteri*, *L. crispatus*, and *L. acidophilus* have demonstrated efficacy in preventing recurrences of bacterial vaginosis and vulvovaginal candidiasis^(8,17). A 2025 randomized clinical trial⁽¹⁷⁾ showed that oral administration of *L. crispatus* LMG P-32001 for 6 months reduced the BV recurrence rate from 45% to 23% (p<0.01). However, the evidence for preventing preterm birth is still limited and heterogeneous⁽¹⁸⁾.

Vaginal microbiota transplantation (VMT)

Inspired by fecal transplantation, VMT consists of inoculating vaginal fluid from a healthy donor with eubiotic microbiota into a recipient with recurrent dysbiosis. A phase II study published in *Nature Medicine* (2025) demonstrated that VMT (with CST I donors) achieved an 82% cure rate for recurrent BV at 6 months, with sustained engraftment of *L. crispatus*⁽¹⁹⁾. Additionally, a 2026 randomized controlled trial in postmenopausal women with vaginal atrophy showed significant improvement in pH, vaginal maturation index, and symptoms after VMT⁽²⁰⁾.

Other interventions

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Dietary modulation (increased prebiotic fiber, reduced simple sugars) and the use of topical lactic acid are being explored as adjunctive therapies ^(8,11). The vaginal virome (bacteriophages) is also emerging as a key regulator of the bacterial community, opening new therapeutic avenues ⁽²¹⁾.

DISCUSSION

This narrative review synthesizes the current evidence on the composition, functions, and dysbiosis of the vaginal microbiome, as well as modulation strategies aimed at personalized medicine. The main findings confirm the central role of *Lactobacillus* spp. in preserving vaginal health and the consistent association between dysbiosis and adverse outcomes such as preterm birth, persistent HPV infection, and cervical cancer ^(2,3,5,7,13,14).

The results presented are consistent with the large systematic reviews by France et al. ⁽³⁾ and Dubé Zinatelli et al. ⁽⁷⁾ regarding the heterogeneity of the microbiome among ethnic groups and the need for a functional definition of dysbiosis. However, our review offers a more applied approach to the Latin American reality and the context of a healthcare system with limited resources, something not addressed in depth by the international literature.

Most of the primary studies are observational and cross-sectional, with a risk of selection bias and residual confounding. Clinical trials on probiotics are still small and heterogeneous in terms of strains, dosages, and outcomes. Furthermore, 16S rRNA sequencing does not capture the metabolic function or activity of fungi and viruses. Available meta-analyses show high statistical heterogeneity ($I^2 > 70\%$ in several cases) ^(12,13,16).

It is acknowledged that the literature search was not systematically exhaustive (the search strategy was not registered in PROSPERO, nor was a PRISMA diagram performed), which may introduce selection bias in favor of the most accessible or frequently cited articles. Additionally, prioritizing literature in English, Spanish, and Portuguese may have excluded relevant findings published in other languages. The critical synthesis relies on the authors' judgment, although this was mitigated through independent review by two researchers.

Longitudinal cohort studies in Latin American/Cuban populations are needed to define normal ranges for the vaginal microbiome and to evaluate the predictive value of dysbiosis for preterm birth and HPV persistence. Phase III clinical trials with probiotics and TMV adapted to the diversity of CST are also needed.

In resource-limited settings, the integration of vaginal microbiome analysis should be phased in: initially by measuring vaginal pH and detecting lactobacilli by microscopy; in the medium term, by using quantitative PCR for key species; and ideally, by using next-generation sequencing in tertiary hospitals. Identifying women with subclinical dysbiosis (especially during pregnancy) would allow for personalized preventive interventions (specific probiotics, lifestyle modifications).

The Cuban National Health System, with its emphasis on prevention and primary care, is in a privileged position to implement pilot programs for vaginal dysbiosis screening in gynecology and obstetrics clinics. Training residents in microbiome studies and collaborating with Latin American research centers (Brazil, Mexico, Argentina) that already have sequencing capabilities are realistic and cost-effective strategies ⁽²²⁾.

CONCLUSIONS

The vaginal microbiome constitutes a complex ecosystem dominated, under healthy conditions, by *Lactobacillus* species (*L. crispatus*, *L. iners*, *L. gasseri*, *L. jensenii*), which perform barrier, immunomodulatory, and metabolic regulatory functions. Its alteration (dysbiosis), characterized by the loss of lactobacilli and the increase of anaerobes such as *Gardnerella*, *Prevotella*, and *Atopobium*, is associated with bacterial vaginosis, preterm birth, premature rupture of membranes, persistence of the human papillomavirus, and progression to cervical neoplasia. Although modulating strategies such as specific probiotics and vaginal microbiota transfer have shown promising results, further studies are needed to standardize their clinical use. The incorporation of microbiome analysis using scalable tools (pH, PCR, sequencing) would allow for personalized medicine in gynecology. It is imperative to develop local research in Cuban and Latin American populations to characterize their microbiome and evaluate interventions adapted to their context.

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AUTHORSHIP CONTRIBUTIONS

YNA: Conceptualization, formal analysis, methodology, project management, drafting, revision, and editing.

DVE: Conceptualization, data curation, research, supervision, and drafting.

KOP: Conceptualization, methodology, supervision, revision, and editing.

ACGM: Conceptualization, methodology, supervision, revision, and editing.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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The authors declare that no artificial intelligence was used in the writing of this manuscript.