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## **VAGINAL MICROBIOME AND THE RISK OF PRETERM BIRTH: PATHOPHYSIOLOGICAL MECHANISMS AND THERAPEUTIC PERSPECTIVES**

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### **NARRATIVE LITERATURE REVIEW**

#### **ABSTRACT**

The vaginal microbiome has been increasingly recognized as a key modulator of female reproductive health, playing a central role in maintaining genital tract homeostasis and protecting against ascending infections. The predominance of Lactobacillus species is associated with a stable vaginal environment, characterized by an acidic pH and the production of antimicrobial metabolites, which are essential for preventing colonization by pathogenic microorganisms. Disruptions in this composition, particularly the reduction of these beneficial microorganisms and the proliferation of anaerobic bacteria, define a state of vaginal dysbiosis, which has been consistently associated with adverse obstetric outcomes, notably preterm birth. This study aimed to analyze, through a narrative literature review, the main pathophysiological mechanisms linking the vaginal microbiome to the risk of prematurity, as well as to discuss emerging therapeutic perspectives in this field. The findings indicate that vaginal dysbiosis may trigger local and systemic inflammatory responses, facilitate the ascension of pathogens into the intrauterine environment, and compromise the integrity of fetal membranes, thereby promoting the premature onset of labor. Furthermore, individual, behavioral, and environmental factors are shown to modulate microbiome composition, rendering this interaction multifactorial and dynamic. Therapeutic strategies such as the use of probiotics, selective antibiotics, and personalized approaches based on microbial profiling have been investigated as promising alternatives for the prevention of prematurity. In conclusion, a deeper understanding of the vaginal microbiome represents a critical frontier in contemporary obstetrics, requiring integrated,



individualized, and evidence-based clinical approaches.

**Keywords:** Vaginal microbiome; Preterm birth; Dysbiosis; Inflammation; Probiotics.

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## 1 INTRODUCTION

Preterm birth remains one of the leading causes of neonatal morbidity and mortality worldwide, representing a persistent challenge for healthcare systems and contemporary obstetric practice. Despite advances in perinatal care, the understanding of the underlying mechanisms of prematurity remains incomplete, particularly regarding the interplay between infectious, immunological, and environmental factors. In this context, the vaginal microbiome has emerged as a central element in the regulation of gestational health, directly influencing the stability of the intrauterine environment (Bayar *et al.*, 2020; Fettweis *et al.*, 2019).

A healthy vaginal microbiome is predominantly composed of *Lactobacillus* species, which exert a protective role through the production of lactic acid, maintenance of an acidic vaginal pH, and inhibition of pathogen colonization. However, disruptions in this balance, characterized by a reduction in these beneficial microorganisms and an increase in anaerobic bacteria, result in a state of vaginal dysbiosis, often associated with conditions such as bacterial vaginosis. This imbalance has been widely linked to adverse obstetric outcomes, including premature rupture of membranes and preterm birth (Gudnadottir *et al.*, 2022; Dubé-Zinatelli *et al.*, 2024).

The relationship between the vaginal microbiome and prematurity involves complex mechanisms, including activation of inflammatory pathways, production of pro-inflammatory cytokines, and ascension of microorganisms into the intrauterine environment. These processes may trigger early uterine contractions, cervical changes, and compromise of the fetal membranes. Furthermore, factors such as maternal genetics, sexual behavior, antibiotic use, and socioeconomic conditions also influence microbial composition, rendering this interaction highly multifactorial (Fettweis *et al.*, 2019; Dunlop *et al.*, 2019).

In light of this context, it is essential to comprehensively understand the mechanisms linking the vaginal microbiome to the risk of preterm birth, as well as to explore therapeutic strategies capable of restoring microbial balance and reducing adverse outcomes. Therefore, this study aims to analyze, through a narrative literature review, the pathophysiological mechanisms underlying this association and to discuss the main emerging therapeutic perspectives for clinical practice (Bayar *et al.*, 2020;



Gudnadottir *et al.*, 2022).

## 2 METHOD

This study consists of a narrative literature review with a qualitative, descriptive-analytical approach, aimed at synthesizing and critically interpreting the scientific evidence related to the vaginal microbiome and its association with the risk of preterm birth. This methodological approach allows for the integration of different study designs, including experimental research, observational studies, and systematic reviews, thereby enabling a comprehensive and contextualized understanding of the phenomenon under investigation.

The literature search was conducted across the PubMed/MEDLINE, Scopus, Web of Science, and ScienceDirect databases, using descriptors combined with Boolean operators, such as “vaginal microbiome,” “preterm birth,” “dysbiosis,” “Lactobacillus,” “inflammation,” and “pregnancy outcomes.” Articles published within the last 10 years in English, Portuguese, and Spanish were included. Editorials, letters to the editor, and studies with low clinical relevance were excluded. The guiding research question, structured according to the PICO strategy, was: “What are the pathophysiological mechanisms and therapeutic interventions related to the vaginal microbiome in the risk of preterm birth?”

## 3 RESULTS

The analysis of the included studies demonstrated that the composition of the vaginal microbiome plays a decisive role in the maintenance of pregnancy, with Lactobacillus dominance being associated with a lower risk of preterm birth. These microorganisms contribute to the stability of the vaginal environment through the production of lactic acid, hydrogen peroxide, and bacteriocins, thereby creating a protective barrier against pathogen colonization. In contrast, vaginal dysbiosis—characterized by an increased abundance of anaerobic bacteria such as Gardnerella vaginalis, Atopobium vaginae, and species of the genus Mobiluncus—is associated with a higher incidence of local inflammation and adverse obstetric outcomes (Fettweis *et al.*, 2019; Kindinger *et al.*, 2017; Ravel *et al.*, 2021).

Furthermore, the studies indicate that vaginal dysbiosis may facilitate the ascension of microorganisms to the upper genital tract, triggering intrauterine inflammatory responses and activating biochemical cascades associated with preterm labor. Increased levels of pro-inflammatory cytokines, collagen degradation in the fetal membranes, and activation of prostaglandins have been observed, all of which contribute to premature rupture of membranes and the early onset of uterine contractions. However, there is heterogeneity among studies regarding the strength of this association, particularly across different populations and clinical contexts (Brown *et al.*, 2019; Freitas *et al.*, 2018).

In light of these findings, the main results of the analyzed studies were systematically organized to identify recurring patterns, gaps in the literature, and methodological divergences across investigations. This synthesis highlights the complexity of the interactions between the microbiome, the immune system, and the gestational environment, reinforcing the need for an integrated analysis of the available evidence (Fettweis *et al.*, 2019). Thus, in order to facilitate comparative visualization of the evidence and support critical interpretation of the findings, Table 1 was developed, summarizing the key elements related to vaginal microbiome composition, underlying pathophysiological mechanisms, and associated obstetric outcomes.

**Table 1.** Main findings on the relationship between the vaginal microbiome and the risk of preterm birth

Author/Year	Study design / Type of evidence	Main focus	Principal findings	Clinical implications
Fettweis <i>et al.</i> (2019)	Prospective cohort study	Vaginal microbiome composition and preterm birth	Demonstrated that specific vaginal microbial profiles are associated with increased risk of spontaneous preterm birth, particularly those characterized by reduced <i>Lactobacillus</i> dominance and higher abundance of anaerobic bacteria.	Supports the use of vaginal microbiome profiling as a potential tool for risk stratification during pregnancy.
Kindinger <i>et al.</i> (2017)	Observational clinical study	Vaginal microbiota, cervical length, and	Showed that depletion of protective <i>Lactobacillus</i> species and increased dysbiosis were associated	Suggests that vaginal microbiota assessment may improve

		progesterone treatment	with cervical shortening and higher risk of preterm birth.	identification of women at greater obstetric risk.
<b>Ravel et al. (2021)</b>	Microbiological and ecological review	Structure and dynamics of the vaginal microbiome	Highlighted the importance of <i>Lactobacillus</i> -dominated communities in maintaining vaginal homeostasis, low pH, and resistance to pathogen colonization.	Reinforces the protective role of eubiotic vaginal microbiota in reproductive health and pregnancy maintenance.
<b>Brown et al. (2019)</b>	Observational study	Vaginal dysbiosis and obstetric complications	Reported that vaginal dysbiosis was associated with increased risk of preterm prelabor rupture of membranes, neonatal sepsis, and unfavorable pregnancy outcomes.	Indicates that vaginal dysbiosis may act as an early warning marker for adverse perinatal outcomes.
<b>Freitas et al. (2018)</b>	Comparative microbiome study	Vaginal microbiome in pregnant and non-pregnant women	Found that pregnant women presented a less diverse yet more stable vaginal microbiome, with lower prevalence of Mollicutes and greater microbial specialization.	Suggests that microbiome stability during pregnancy may represent a protective adaptation against ascending infection.

Source: Prepared by the authors (2026), based on the studies included in the narrative review.

#### 4. DISCUSSION

The recognition of the vaginal microbiome as a central element in the pathophysiology of preterm birth represents a significant shift in the understanding of gestational health, moving from a purely infection-based perspective toward a more ecological and dynamic framework. This emerging paradigm highlights that not only the presence of pathogens, but also the balance between commensal and opportunistic microorganisms, is crucial for the maintenance of pregnancy.

Moreover, this approach broadens the understanding of the gestational process as an integrated biological phenomenon, in which microbiological, immunological, and environmental factors interact continuously. Such a perspective underscores the importance of clinical practices that account for the complexity of these interactions, particularly in the prevention of adverse outcomes such as preterm birth (Fettweis et al., 2019; Gudnadottir et al., 2022; Gerede et al., 2024).



#### 4.1 Pathophysiological Mechanisms of Vaginal Dysbiosis and Preterm Birth

Vaginal dysbiosis can trigger a series of immunological and inflammatory alterations that compromise the integrity of the gestational environment. The reduction of *Lactobacillus* species leads to an increase in vaginal pH, favoring the proliferation of anaerobic microorganisms and the production of inflammatory metabolites. These agents can stimulate the release of cytokines such as IL-6, IL-8, and TNF- $\alpha$ , promoting both local and systemic inflammation. This persistent inflammatory milieu contributes to the dysregulation of maternal immune balance, creating conditions conducive to the premature activation of pathways associated with the onset of labor (Chan *et al.*, 2022; Gomez-Lopez *et al.*, 2022; Gerede *et al.*, 2024).

Furthermore, the ascension of microorganisms to the upper genital tract may result in subclinical infection of the amniotic fluid, triggering intrauterine inflammatory pathways. This process is associated with the production of prostaglandins and matrix metalloproteinases, which contribute to cervical ripening and the rupture of fetal membranes. The integrity of these structures is essential for the maintenance of pregnancy, and their premature degradation is directly linked to preterm birth. This mechanism underscores the importance of the cervical barrier and the vaginal microbiota as essential protective components during pregnancy (Brown *et al.*, 2019; Gomez-Lopez *et al.*, 2022).

Another relevant aspect involves the interaction between the microbiome and the maternal immune system. An exaggerated or dysregulated immune response may amplify the effects of dysbiosis, creating a favorable environment for the initiation of labor. Genetic and environmental factors also modulate this response, highlighting the multifactorial nature of the phenomenon. Additionally, individual maternal characteristics, such as obstetric history and metabolic conditions, may influence the magnitude of this inflammatory response, further contributing to the complexity and individualized nature of the process (Fettweis *et al.*, 2019; Dunlop *et al.*, 2019; Gerede *et al.*, 2024).

#### 4.2 Therapeutic Perspectives and Clinical Implications

From a clinical perspective, the identification of the vaginal microbiological profile may represent an important tool for risk stratification and the prevention of



preterm birth. Strategies such as the use of Lactobacillus-containing probiotics have been investigated with the aim of restoring microbial balance and reducing inflammatory processes. Although the results remain heterogeneous, there is promising evidence regarding their preventive potential. This approach signals a shift in the therapeutic paradigm, with increasing emphasis on microbiota modulation as a strategy for care (Petricevic *et al.*, 2023; Solgi *et al.*, 2022).

The use of antibiotics, in turn, presents limitations, particularly due to the risk of dysbiosis recurrence and its negative impact on the microbiome. In this context, more personalized approaches, based on individual microbiome characterization, have been proposed as more effective and safer alternatives. Precision medicine applied to the microbiota is emerging as an innovative field within obstetrics. This perspective highlights the need to integrate technological advances with clinical practice, aiming for more targeted and effective interventions (Klebanoff *et al.*, 2023; Gerede *et al.*, 2024).

Additionally, educational interventions and qualified prenatal care are essential for the proper management of these conditions. The integration of microbiological diagnosis, clinical assessment, and individualized therapeutic strategies may significantly contribute to reducing prematurity, consolidating the vaginal microbiome as a relevant target in contemporary clinical practice. Furthermore, public health policies focused on education and access to prenatal care may enhance the impact of these interventions at the population level (Gerede *et al.*, 2024; Gudnadottir *et al.*, 2022).

## 5 CONCLUSION

The vaginal microbiome plays a central role in the maintenance of pregnancy, with its composition representing a key determinant in the risk of preterm birth. Vaginal dysbiosis is associated with complex inflammatory mechanisms that may trigger adverse events, including membrane rupture and the premature onset of labor.

Although scientific advances have improved the understanding of these processes, important gaps remain regarding the standardization of diagnostic methods and the effectiveness of available therapeutic interventions. The heterogeneity of



existing studies further underscores the need for additional research, particularly studies with robust designs and longitudinal follow-up.

Therefore, the integration of knowledge about the vaginal microbiome into clinical practice should be guided by a critical, individualized, and evidence-based approach, aiming to promote maternal–fetal health and reduce the incidence of prematurity.

## REFERENCES

BAYAR, E. *et al.* The pregnancy microbiome and preterm birth. **Journal of Reproductive Immunology**, Shannon, v. 142, p. 103209, 2020. DOI: 10.1007/s00281-020-00817-w. Available at: <https://pubmed.ncbi.nlm.nih.gov/32797272/>. Accessed on: 11 Mar. 2026.

BROWN, R. G. *et al.* Vaginal dysbiosis increases risk of preterm fetal membrane rupture, neonatal sepsis and is exacerbated by erythromycin. **BMC Medicine**, London, v. 17, n. 1, p. 9, 2019. DOI: 10.1186/s12916-018-1249-7. Available at: <https://pubmed.ncbi.nlm.nih.gov/30646934/>. Accessed on: 09 Mar. 2026.

CHAN, D. *et al.* Microbial-driven preterm labour involves crosstalk between the innate and adaptive immune response. **Nature Communications**, London, v. 13, p. 975, 2022. DOI: 10.1038/s41467-022-28620-1. Available at: <https://www.nature.com/articles/s41467-022-28620-1>. Accessed on: 11 Mar. 2026.

DUBÉ-ZINATELLI, E.; CAPPELLETTI, L.; ISMAIL, N. Vaginal microbiome: environmental, biological, and racial influences on gynecological health across the lifespan. **American Journal of Reproductive Immunology**, Hoboken, v. 92, n. 6, e70026, 2024. DOI: 10.1111/aji.70026. Available at: <https://pubmed.ncbi.nlm.nih.gov/39670915/>. Accessed on: 10 Mar. 2026.

DUNLOP, A. L. *et al.* Stability of the vaginal, oral, and gut microbiota across pregnancy among African American women: the effect of socioeconomic status and antibiotic exposure. **PeerJ**, London, v. 7, e8004, 2019. DOI: 10.7717/peerj.8004. Available at: <https://pubmed.ncbi.nlm.nih.gov/31772833/>. Accessed on: 01 Feb. 2026.

FETTWEIS, J. M. *et al.* The vaginal microbiome and preterm birth. **Nature Medicine, New York**, v. 25, n. 6, p. 1012–1021, 2019. DOI: 10.1038/s41591-019-0450-2. Available at: <https://pubmed.ncbi.nlm.nih.gov/31142849/>. Accessed on: 05 Mar. 2026.

FREITAS, A. C. *et al.* The vaginal microbiome of pregnant women is less rich and diverse, with lower prevalence of Mollicutes, compared to non-pregnant women. **Scientific Reports**, London, v. 8, p. 1–12, 2018. DOI: 10.1038/s41598-018-24414-8. Available at: <https://pubmed.ncbi.nlm.nih.gov/29618863/>. Accessed on: 08 Mar. 2026.



GEREDE, A. *et al.* Vaginal microbiome and pregnancy complications. **Journal of Clinical Medicine**, Basel, v. 13, n. 13, p. 3875, 2024. DOI: 10.3390/jcm13133875. Available at: <https://pubmed.ncbi.nlm.nih.gov/38999442/>. Accessed on: 06 Mar. 2026.

GOMEZ-LOPEZ, N. *et al.* The immunobiology of preterm labor and birth: intra-amniotic inflammation or breakdown of maternal-fetal homeostasis. **Frontiers in Immunology**, Lausanne, v. 13, p. 911455, 2022. DOI: 10.3389/fimmu.2022.911455. Available at: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9233101/>. Accessed on: 08 Mar. 2026.

GUDNADOTTIR, U. *et al.* The vaginal microbiome and the risk of preterm birth: a systematic review and network meta-analysis. **Scientific Reports**, London, v. 12, p. 7926, 2022. DOI: 10.1038/s41598-022-12007-9. Available at: <https://www.nature.com/articles/s41598-022-12007-9>. Accessed on: 03 Mar. 2026.

KINDINGER, L. M. *et al.* The interaction between vaginal microbiota, cervical length, and vaginal progesterone treatment for preterm birth risk. **Microbiome**, London, v. 5, n. 1, p. 6, 2017. DOI: 10.1186/s40168-016-0223-9. Available at: <https://pubmed.ncbi.nlm.nih.gov/28069033/>. Accessed on: 20 Feb. 2026.

KLEBANOFF, M. A. *et al.* Antibiotic treatment of bacterial vaginosis to prevent preterm delivery: systematic review and individual participant data meta-analysis. **Paediatric and Perinatal Epidemiology**, Oxford, v. 37, n. 3, p. 239–251, 2023. DOI: 10.1111/ppe.12947. Available at: <https://pubmed.ncbi.nlm.nih.gov/36651636/>. Accessed on: 11 Mar. 2026.

PETRICEVIC, L. *et al.* Effect of vaginal probiotics containing *Lactobacillus casei* rhamnosus (Lcr regenerans) on vaginal dysbiotic microbiota and pregnancy outcome: prospective, randomized study. **Scientific Reports**, London, v. 13, p. 7129, 2023. DOI: 10.1038/s41598-023-34275-9. Available at: <https://pubmed.ncbi.nlm.nih.gov/37130874/>. Accessed on: 05 Mar. 2026.

RAVEL, J. *et al.* Vaginal microbiome of reproductive-age women. **Proceedings of the National Academy of Sciences**, Washington, v. 118, n. 12, 2021. DOI: 10.1073/pnas.2018164118. Available at: <https://pubmed.ncbi.nlm.nih.gov/33782039/>. Accessed on: 11 Mar. 2026.

SOLGI, E. *et al.* Vaginal and oral probiotics effect in the prevention of preterm delivery in patients visiting Kamali Hospital, Karaj, Iran in 2020. **European Journal of Obstetrics & Gynecology and Reproductive Biology: X**, Amsterdam, v. 16, p. 100169, 2022. DOI: 10.1016/j.eurox.2022.100169. Available at: <https://pubmed.ncbi.nlm.nih.gov/36312324/>. Accessed on: 09 Mar. 2026.