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Review Article

HIDDEN PLAYERS IN PRETERM BIRTH: EXPLORING THE VAGINAL MICROBIOME’S ROLE IN RISK AND PREVENTION

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ABSTRACT

Preterm birth (PTB), defined as delivery before 37 weeks of gestation, remains a leading cause of neonatal morbidity and mortality worldwide, particularly in low- and middle-income countries. Despite advances in obstetric care, its global burden remains high, necessitating exploration of underlying mechanisms beyond traditional risk factors. This review examines the role of the vaginal microbiome as a critical yet under recognized contributor to PTB. A structured narrative review with systematic elements was conducted using databases including PubMed, Scopus, Web of Science, and Google Scholar, covering studies published from 2000 onwards. Eligible studies included observational studies, systematic reviews, and meta-analyses focusing on vaginal microbiome composition, mechanisms, biomarkers, and preventive strategies. Findings indicate that a Lactobacillus-dominated vaginal microbiome is associated with reduced PTB risk, while dysbiosis characterized by increased microbial diversity and anaerobic bacteria such as *Gardnerella*, *Prevotella*, and *Atopobium* is strongly linked to adverse outcomes. Mechanistically, ascending infections and inflammation mediated by cytokines contribute to preterm labor. Microbial biomarkers and community state types show promise for early prediction, supported by advances in sequencing technologies and machine learning models. Additionally, modifiable factors including nutrition, hygiene practices, antibiotic use, and socioeconomic status significantly influence microbiome composition and PTB risk. Preventive strategies such as probiotics, prebiotics, and microbiome-targeted interventions show potential but require further validation. Overall, the vaginal microbiome plays a pivotal role in PTB pathogenesis and prevention. Integrating microbiome research with clinical and public health strategies may enable early risk identification and reduce the global burden of preterm birth.

Keywords: Preterm birth, Vaginal microbiome, Dysbiosis, Lactobacillus, Bacterial vaginosis.

INTRODUCTION

Preterm birth (PTB), defined as delivery before 37 completed weeks of gestation, remains one of the most pressing challenges in maternal and neonatal health worldwide. It is a leading cause of neonatal morbidity and mortality, accounting for nearly one million deaths annually and contributing significantly to long-term complications such as neurodevelopmental impairment, chronic lung disease, and metabolic disorders (World Health Organization [WHO], 2018; Goldenberg, Culhane, Iams, & Romero, 2008). In spite of considerable advancements in obstetric care, the global burden of preterm birth has not declined substantially, particularly in low- and middle-income countries (LMICs), where healthcare disparities, maternal undernutrition, infections, and limited access to antenatal care exacerbate the risk (Goldenberg *et al*., 2008). Countries like India contribute significantly to the global incidence of PTB, highlighting the urgent need for improved understanding of its underlying causes and development of effective preventive strategies (WHO, 2018). Traditionally, preterm birth has been associated with well-established risk factors such as maternal age, multiple pregnancies, previous history of PTB, infections, and lifestyle factors (Romero *et al*., 2006). However, these factors do not fully explain the complexity and variability observed in PTB cases. In recent years, attention has increasingly shifted toward the role of the human microbiome as a critical yet often overlooked contributor to pregnancy outcomes (Aagaard *et al*., 2014; Ma, Forney, & Ravel, 2012). Among various microbial

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niches in the body, the vaginal microbiome has emerged as a key player in maintaining reproductive health and influencing the risk of preterm birth (Ravel *et al*., 2011). The vaginal microbiome is a dynamic and complex ecosystem composed of bacteria, fungi, and viruses that coexist in a delicate balance. In healthy reproductive-age women, this ecosystem is typically dominated by Lactobacillus species, which play a protective role by producing lactic acid, maintaining a low vaginal pH, and preventing colonization by pathogenic microorganisms (Ravel *et al*., 2011; Ma *et al*., 2012). This Lactobacillus dominant state is considered optimal for reproductive health and is associated with favorable pregnancy outcomes (Freitas *et al*., 2017). However, this microbial balance is not static and can be influenced by various factors, including hormonal changes, sexual activity, hygiene practices, antibiotic use, and socioeconomic conditions (van de Wijgert *et al*., 2014). Disruption of the normal vaginal microbiome, known as dysbiosis, is characterized by a reduction in Lactobacillus species and an overgrowth of diverse anaerobic bacteria such as Gardnerella, Prevotella, Atopobium, and Mycoplasma (van de Wijgert *et al*., 2014). This altered microbial state is commonly associated with bacterial vaginosis (BV), a condition that is often asymptomatic but has been strongly linked to adverse pregnancy outcomes, including preterm birth (Verstraelen & Swidsinski, 2013). Emerging evidence suggests that women with dysbiotic vaginal microbiomes are at significantly higher risk of PTB compared to those with Lactobacillus-dominated microbiota (Fettweis *et al*., 2019; Romero *et al*., 2014), emphasizing the importance of microbial balance during pregnancy.

The mechanisms through which the vaginal microbiome contributes to preterm birth are multifaceted and involve complex interactions between microorganisms and the host immune system. One of the primary pathways is ascending infection, where pathogenic bacteria from the lower genital tract migrate into the upper reproductive tract, leading to intra amniotic infection and inflammation (Romero *et al*., 2006). This triggers a cascade of immune responses, including the activation of inflammatory pathways and the release of cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). These inflammatory mediators can induce cervical ripening, weakening of fetal membranes, and uterine contractions (Romero *et al*., 2006; Vinturache *et al*., 2016). In addition to infection-driven inflammation, microbial metabolites and biofilm formation also play significant roles in disrupting the vaginal environment. Certain pathogenic bacteria produce enzymes and toxins that degrade the mucosal barrier, facilitating microbial invasion and amplifying inflammatory responses. Biofilms formed by organisms such as Gardnerella vaginalis further enhance microbial persistence and resistance to host defenses, making infections more difficult to eradicate (Verstraelen & Swidsinski, 2013). These findings highlight the intricate biological pathways linking the vaginal microbiome to preterm birth and underscore its importance as a “hidden player” in this condition. Beyond its role in pathogenesis, the vaginal microbiome also holds promise as a predictive tool for identifying women at risk of preterm birth. Conventional methods for predicting PTB, such as cervical length measurement and biochemical markers, often detect risk relatively late in pregnancy. In contrast, changes in the vaginal microbiome can occur early in gestation (Callahan *et al*., 2017; DiGiulio *et al*., 2015), offering a potential window for early detection and intervention. Advances in high-throughput sequencing technologies have enabled detailed characterization of microbial communities, leading to the identification of specific bacterial signatures and community state types (CSTs) associated with increased PTB risk (Ravel *et al*., 2011). For instance, increased microbial diversity and reduced dominance of Lactobacillus species have been consistently linked to adverse outcomes (Fettweis *et al*., 2019). Importantly, the composition of the vaginal microbiome is influenced not only by biological factors but also by social, environmental, and behavioral determinants. Factors such as nutrition, hygiene practices, antibiotic use, and socioeconomic status can significantly impact microbial composition and diversity (van de Wijgert *et al*., 2014).

In LMIC settings, where challenges such as poor sanitation, limited access to healthcare, and high prevalence of infections are common, these factors may contribute to a higher burden of vaginal dysbiosis and, consequently, preterm birth. In India, for example, maternal malnutrition, anemia, and inappropriate antibiotic use are widespread and may indirectly influence the vaginal microbiome, although research in this area remains limited. Given the growing recognition of the vaginal microbiome’s role in preterm birth, there is increasing interest in developing microbiome-targeted preventive strategies. Current approaches, such as antibiotic treatment for bacterial vaginosis, have shown limited success in reducing PTB rates (Kindinger *et al*., 2017) and may disrupt beneficial microbial communities. As a result, alternative strategies such as probiotics, prebiotics, and microbiome modulation are being explored (Kindinger *et al*., 2017; Vinturache *et al*., 2016). Probiotics, particularly those containing Lactobacillus strains, aim to restore microbial balance and enhance the natural defense mechanisms of the vaginal environment (Ma *et al*., 2012; Ravel *et al*., 2011). While preliminary findings are promising, further research is needed to establish their efficacy and safety in diverse populations (Kindinger *et al*., 2017). The vaginal microbiome represents a critical yet under recognized factor in the complex etiology of preterm birth (Fettweis *et al*., 2019; Romero *et al*., 2014). Its influence extends from underlying biological mechanisms to potential applications in early prediction and prevention (Callahan *et al*., 2017; DiGiulio *et al*., 2015). Understanding the interplay between microbial communities and host factors, particularly in diverse global and local contexts, is essential for developing effective interventions (van de Wijgert *et al*., 2014). This review aims to explore the role of the vaginal microbiome as a “hidden player” in preterm birth, with a focus on its contribution to risk, identification of microbial patterns, and emerging strategies for prevention (Fettweis *et al*., 2019; Romero *et al*., 2014). By integrating insights from microbiology, immunology, and public health, this work seeks to contribute to a more comprehensive approach to reducing the global burden of preterm birth (WHO, 2018; Goldenberg *et al*., 2008).

MATERIALS AND METHODS

Study Design

This review was conducted to comprehensively examine the role of the vaginal microbiome in preterm birth, with emphasis on microbial composition, mechanisms of disease, predictive biomarkers, and preventive strategies. A structured narrative review approach with systematic elements was adopted to ensure a rigorous, transparent, and reproducible process of literature identification, selection, and synthesis. The methodology was guided by established recommendations for review articles, including adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework where applicable.

Search Strategy

A comprehensive and systematic literature search was carried out across multiple electronic databases to identify relevant studies. The primary databases included PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. Additional sources such as reference lists of selected articles and relevant review papers were also manually screened to identify any studies that may have been missed during the initial search. The search covered publications from January 2000 to the most recent available studies to ensure inclusion of both foundational and contemporary research. A combination of keywords and Medical Subject Headings (MeSH) terms was used to enhance the sensitivity and specificity of the search. The following search terms were used in various combinations using Boolean operators (AND, OR): “vaginal microbiome” OR “vaginal microbiota” “preterm birth” OR “preterm labor” “dysbiosis” “Lactobacillus” “bacterial vaginosis” “microbial diversity” OR “community state types” “biomarkers” OR “prediction” “pregnancy outcomes” “probiotics” OR “antibiotics” “nutrition” OR “hygiene” OR “socioeconomic factors” Search filters were applied to include studies involving human subjects and articles published in the English language.

Study Selection Process

The study selection process was conducted in a stepwise manner to ensure methodological rigor. Initially, all identified records were imported into a reference management system, and duplicates were removed. The remaining articles were screened in three stages: Title Screening: Titles were reviewed to exclude clearly irrelevant studies. Abstract Screening**:** Abstracts of potentially relevant articles were assessed against the inclusion and exclusion criteria. Full-Text Review**:** Full texts of selected studies were thoroughly evaluated for eligibility. A PRISMA flow diagram was used to document the selection process, including the number of studies identified, screened, excluded, and included in the final analysis.

Data Extraction

Data from the selected studies were systematically extracted using a standardized data extraction form to ensure consistency and completeness. The following information was collected: Author(s) and year of publication, Study design and sample size. Study population characteristics (age, gestational age, geographic location). Methods used for microbiome analysis (e.g., culture-based methods, 16S rRNA gene sequencing, metagenomics). Key findings related to vaginal microbiome composition and diversity. Identified bacterial species or community patterns associated with preterm birth. Reported mechanisms linking microbiome alterations to adverse outcomes. Influence of external factors such as nutrition, hygiene, antibiotic use, and socioeconomic status. Preventive or therapeutic interventions evaluated

Quality Assessment

The methodological quality of the included studies was assessed using validated tools appropriate to the study design. Observational studies were evaluated using the Newcastle–Ottawa Scale (NOS), which assesses selection, comparability, and outcome domains. Systematic reviews and meta-analyses were assessed using the AMSTAR (A Measurement Tool to Assess Systematic Reviews) checklist. Each study was categorized as high, moderate, or low quality based on predefined scoring criteria. Quality assessment was used to inform the interpretation of findings and to highlight potential biases or limitations in the available evidence.

Data Synthesis

A qualitative synthesis approach was employed to integrate findings from the included studies. Due to heterogeneity in study designs, populations, and microbiome analysis methods, a meta-analysis was not performed. Instead, results were organized into thematic categories to provide a comprehensive understanding of the topic. The main themes included: Composition and diversity of the vaginal microbiome. Mechanisms linking microbiome alterations to preterm birth. Identification of microbial biomarkers and community patterns. Influence of environmental and behavioral risk factors. Preventive strategies targeting the vaginal microbiome.

Analysis of Microbial Patterns

Studies reporting microbiome data were analyzed to identify consistent patterns associated with preterm birth. Particular attention was given to: Dominance of Lactobacillus species and their protective role. Presence of anaerobic bacteria associated with dysbiosis. Variations in microbial diversity and community state types (CSTs).

Reproducibility of microbial biomarkers across different populations

Assessment of Risk Factors

Evidence related to modifiable risk factors such as nutrition, hygiene practices, antibiotic use, and socioeconomic status was critically evaluated. The review examined how these factors influence the vaginal microbiome and contribute to preterm birth risk, with particular focus on findings from low- and middle-income countries.

Limitations

This review has certain limitations. Variability in microbiome analysis techniques, differences in study populations, and heterogeneity in outcome definitions may affect comparability across studies. Additionally, limited data from certain regions, particularly LMICs, may restrict the generalizability of findings. Despite these limitations, efforts were made to include a diverse range of high-quality studies to ensure a balanced and comprehensive synthesis.

RESULTS AND DISCUSSION

The literature search identified a substantial number of studies examining the association between the vaginal microbiome and preterm birth (PTB). After screening and applying eligibility criteria, studies comprising cohort, case-control, cross-sectional designs, and systematic reviews were included in the final synthesis. These studies represented diverse populations across high-income countries and low- and middle-income countries (LMICs), enabling a comprehensive evaluation of microbial patterns, risk factors, and preventive strategies. Most studies utilized advanced molecular techniques such as 16S rRNA gene sequencing, allowing detailed characterization of microbial communities. Across the reviewed studies, a consistent association was observed between vaginal microbiome composition and the risk of preterm birth. Women with a Lactobacillus dominated microbiome, particularly those enriched with *Lactobacillus crispatus* and *Lactobacillus jensenii*, were found to have a lower risk of PTB. These species contribute to maintaining an acidic vaginal environment through lactic acid production, which inhibits the growth of pathogenic microorganisms. In contrast, a shift toward a dysbiotic microbiome characterized by reduced Lactobacillus abundance and increased microbial diversity was strongly associated with higher PTB risk. This dysbiotic state often included anaerobic bacteria such as *Gardnerella vaginalis*, *Prevotella spp.*, *Atopobium vaginae*, and *Mycoplasma hominis*. Several studies reported that women with such microbial profiles had significantly higher odds of experiencing preterm delivery compared to those with stable Lactobacillus dominant communities. Furthermore, the concept of community state types (CSTs) emerged as an important framework for understanding microbial variation. CSTs dominated by Lactobacillus species (CST I, II, III, and V) were generally associated with healthy pregnancy outcomes, whereas CST IV, characterized by high microbial diversity and low Lactobacillus presence, was consistently linked to increased PTB risk.

A key objective of the reviewed studies was to identify specific microbial signatures that could serve as biomarkers for preterm birth. Several bacterial taxa were repeatedly identified as being associated with adverse outcomes. For example, the presence and dominance of *Gardnerella vaginalis* and *Atopobium vaginae* were strongly correlated with bacterial vaginosis and increased PTB risk. Similarly, elevated levels of *Prevotella*, *Sneathia*, and *Ureaplasma* species were associated with inflammation and poor pregnancy outcomes. In addition to individual taxa, microbial diversity indices were also found to be important predictors. Increased alpha diversity (within-sample diversity) and altered beta diversity (between sample differences) were commonly observed in women who later developed preterm birth. These findings suggest that not only the presence of specific pathogens but also the overall structure of the microbial community plays a critical role in determining risk. Recent studies have also explored the use of machine learning models to integrate microbial data and identify predictive signatures. Models incorporating microbial composition, diversity metrics, and clinical variables demonstrated promising predictive accuracy, with some studies reporting area under the curve (AUC) values exceeding 0.80. These findings highlight the potential of microbiome-based biomarkers as non-invasive tools for early risk stratification.

Nutritional status emerged as a significant factor influencing the vaginal microbiome and its association with preterm birth. Studies indicated that maternal malnutrition, particularly deficiencies in micronutrients such as iron, folate, and vitamin D, was associated with altered microbial composition and increased susceptibility to dysbiosis. Poor nutritional status may impair immune function, thereby facilitating the overgrowth of pathogenic bacteria. Dietary patterns also played a role in shaping the microbiome. Diets lacking in essential nutrients and fiber were associated with increased microbial diversity and reduced Lactobacillus dominance. In contrast, balanced diets rich in fruits, vegetables, and probiotics were associated with more stable and protective microbial communities. These findings were particularly relevant in LMIC settings, where maternal undernutrition remains prevalent and may contribute to higher PTB rates. Hygiene practices were found to significantly influence the vaginal microbiome. Poor genital hygiene, use of unclean menstrual products, and lack of access to improved sanitation facilities were associated with increased risk of vaginal infections and dysbiosis. Studies conducted in resource-limited settings highlighted the role of environmental exposure and sanitation in shaping microbial communities. Conversely, certain hygiene practices, such as excessive vaginal washing or douching, were also associated with disruption of the normal microbiome. These practices can alter vaginal pH and remove protective Lactobacillus species, thereby increasing susceptibility to pathogenic colonization. The findings suggest that both inadequate and excessive hygiene practices can negatively impact vaginal health and increase PTB risk.

Antibiotic use during pregnancy was identified as a double-edged sword in relation to the vaginal microbiome and preterm birth. While antibiotics are commonly used to treat infections such as bacterial vaginosis, their impact on PTB prevention has been inconsistent. Several studies reported that antibiotic treatment did not significantly reduce PTB rates and, in some cases, was associated with recurrence of dysbiosis. The broad-spectrum nature of many antibiotics can disrupt beneficial Lactobacillus populations, leading to an imbalance in the microbial ecosystem. This disruption may create an for opportunistic pathogens to proliferate. Additionally, inappropriate or excessive use of antibiotics, particularly in LMICs, was associated with increased microbial resistance and long-term alterations in microbiome composition. Socioeconomic status (SES) was consistently identified as an important determinant of vaginal microbiome composition and PTB risk. Women from lower socioeconomic backgrounds were more likely to experience factors such as poor nutrition, limited access to healthcare, inadequate sanitation, and higher exposure to infections, all of which can influence microbial balance. Studies comparing populations across different geographic regions demonstrated significant variability in microbiome composition, suggesting that environmental and social determinants play a crucial role. In LMICs, higher prevalence of dysbiotic microbiomes and bacterial vaginosis was observed, potentially contributing to the increased burden of preterm birth in these settings.

The potential of the vaginal microbiome as a predictive tool for preterm birth was a major focus of recent research. Early pregnancy microbial profiling, particularly during the first and second trimesters, was shown to provide valuable insights into PTB risk. Specific microbial patterns, such as reduced Lactobacillus dominance and increased abundance of anaerobic bacteria, were identified as early indicators of adverse outcomes. Non-invasive sampling methods, such as vaginal swabs, make microbiome-based screening feasible in clinical settings. Integration of microbial data with clinical and demographic factors further enhanced predictive accuracy. These findings support the development of personalized risk assessment models that could enable early intervention and improved pregnancy outcomes. The review identified several emerging strategies aimed at modulating the vaginal microbiome to reduce PTB risk.

Probiotic interventions, particularly those containing Lactobacillus strains, were among the most widely studied approaches. These interventions aim to restore microbial balance and enhance the protective functions of the vaginal environment. While some studies reported positive outcomes, results were variable, and further research is needed to establish standardized protocols. Other approaches included the use of prebiotics, dietary modifications, and lifestyle interventions to support microbial health. Novel strategies such as vaginal microbiome transplantation and targeted antimicrobial therapies are also being explored, although they remain in early stages of research. Importantly, public health interventions addressing underlying risk factors such as nutrition, hygiene, and access to healthcare were emphasized as essential components of prevention, particularly in resource-limited settings. This review highlights the critical yet often under recognized role of the vaginal microbiome as a key determinant in the risk and prevention of preterm birth (PTB). The findings consistently demonstrate that the composition and stability of the vaginal microbiome are closely linked to pregnancy outcomes, reinforcing the concept that microbial ecosystems act as “hidden players” in maternal and neonatal health. A major observation across the reviewed studies is the protective role of a Lactobacillus-dominated vaginal microbiome. Species such as *Lactobacillus crispatus* and *Lactobacillus jensenii* contribute to maintaining a low vaginal pH through lactic acid production, thereby inhibiting the growth of pathogenic organisms. In contrast, a shift toward a dysbiotic microbiome characterized by reduced Lactobacillus abundance and increased diversity of anaerobic bacteria such as *Gardnerella*, *Prevotella*, and *Atopobium* is strongly associated with an increased risk of PTB. These findings align with the growing body of evidence suggesting that microbial imbalance plays a central role in the pathogenesis of preterm labour. The mechanisms underlying this association are multifactorial and involve complex host microbe interactions.

Ascending infection remains one of the most widely accepted pathways, whereby pathogenic microorganisms migrate from the lower genital tract to the upper reproductive tract, triggering inflammatory responses. The release of pro-inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha, promotes cervical ripening, membrane weakening, and uterine contractions, ultimately leading to preterm birth. Additionally, microbial metabolites and biofilm formation further exacerbate epithelial disruption and immune activation, highlighting the intricate biological pathways linking the vaginal microbiome to adverse pregnancy outcomes. An important contribution of this review is the identification of specific microbial patterns and biomarkers associated with PTB risk. The consistent association of taxa such as *Gardnerella vaginalis*, *Atopobium vaginae*, and *Prevotella* species with adverse outcomes suggests their potential utility as diagnostic or predictive markers. Moreover, increased microbial diversity and the presence of non-Lactobacillus-dominant community state types have emerged as reliable indicators of dysbiosis. Advances in sequencing technologies and bioinformatics have enabled more precise characterization of these microbial signatures, paving the way for microbiome-based risk prediction models. However, variability across populations and study designs underscores the need for standardized methodologies and validation in diverse settings. The influence of external factors such as nutrition, hygiene practices, antibiotic use, and socioeconomic status further underscores the multifactorial nature of vaginal microbiome dynamics. Poor nutritional status, particularly micronutrient deficiencies, may impair immune function and predispose women to dysbiosis. Similarly, inadequate sanitation and hygiene practices can increase exposure to pathogenic microorganisms, while excessive practices such as vaginal douching may disrupt protective microbial communities. Antibiotic use, although essential for treating infections, may inadvertently alter the vaginal microbiome by reducing beneficial Lactobacillus populations and promoting recurrence of dysbiosis. These findings highlight the importance of considering both biological and social determinants in understanding PTB risk. From a global health perspective, the burden of PTB is disproportionately higher in low- and middle-income countries, where adverse socioeconomic conditions, limited access to healthcare, and high prevalence of infections contribute to increased risk. The interplay between these factors and the vaginal microbiome is particularly relevant in such settings. However, there remains a significant gap in region-specific research, particularly in countries like India, where large-scale microbiome studies are limited. Addressing this gap is essential for developing context-specific interventions that are both effective and feasible. The potential for microbiome-based prevention strategies represents a promising avenue for reducing PTB.

Probiotic interventions aimed at restoring Lactobacillus dominance have shown encouraging results, although inconsistencies in study outcomes highlight the need for further clinical trials. Emerging approaches such as prebiotics, dietary modifications, and microbiome-targeted therapies offer additional opportunities for intervention. Importantly, integrating these strategies with broader public health measures such as improving maternal nutrition, promoting appropriate hygiene practices, and rationalizing antibiotic use may provide a more comprehensive approach to prevention. Heterogeneity in study designs, differences in microbiome assessment techniques, and variability in population characteristics limit the comparability of findings. Furthermore, most studies establish associations rather than causality, emphasizing the need for longitudinal and mechanistic research. Future studies should focus on integrating multi-omics approaches, including metagenomics and metabolomics, to better understand the functional role of the microbiome in pregnancy. In conclusion, the vaginal microbiome plays a pivotal role in the risk and prevention of preterm birth, acting as a complex and dynamic interface between environmental exposures and host physiology. Recognizing its importance as a “hidden player” provides new insights into the etiology of PTB and opens avenues for early prediction and targeted interventions. A multidisciplinary approach that integrates microbiological, clinical, and public health perspectives will be essential to translate these findings into improved maternal and neonatal outcomes.

CONCLUSION

Preterm birth (PTB), defined as delivery before 37 weeks of gestation, remains a major global health concern and a leading cause of neonatal morbidity and mortality. In spite of advancements in maternal healthcare, the burden of PTB continues to be high, particularly in low- and middle-income countries such as India. Traditional risk factors alone do not fully explain the complexity of PTB, leading to increasing interest in the role of the vaginal microbiome as a critical yet often overlooked contributor. This review highlights that the vaginal microbiome plays a significant role in maintaining reproductive health and influencing pregnancy outcomes. A healthy vaginal environment is typically dominated by Lactobacillus species, which protect against infections by maintaining an acidic pH. In contrast, dysbiosis characterized by reduced Lactobacillus and increased anaerobic bacteria such as *Gardnerella*, *Prevotella*, and *Atopobium* is strongly associated with an increased risk of preterm birth. These microbial imbalances can trigger inflammatory pathways, ascending infections, and immune responses that ultimately lead to preterm labor. The review also identifies key microbial patterns and biomarkers associated with PTB.

Increased microbial diversity and non-Lactobacillus dominant community types have emerged as important indicators of risk. Advances in sequencing technologies and bioinformatics have enabled the development of microbiome-based predictive models, offering potential for early detection and intervention during pregnancy. Importantly, the vaginal microbiome is influenced by multiple modifiable factors, including nutrition, hygiene practices, antibiotic use, and socioeconomic status. Poor maternal nutrition, inadequate sanitation, and inappropriate antibiotic use can disrupt microbial balance and increase susceptibility to dysbiosis. These factors are particularly relevant in resource-limited settings, where they contribute to higher PTB rates. Preventive strategies targeting the vaginal microbiome are gaining attention. Probiotics, prebiotics, and lifestyle modifications show promise in restoring microbial balance, although evidence remains inconsistent and requires further validation. Public health interventions addressing underlying determinants such as nutrition and hygiene are equally essential for effective prevention. In conclusion, the vaginal microbiome represents a “hidden player” in preterm birth, influencing risk through complex biological and environmental interactions. Understanding these relationships offers new opportunities for early prediction and targeted prevention. Integrating microbiome research with clinical practice and public health strategies may significantly reduce the global burden of preterm birth and improve maternal and neonatal outcomes.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

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AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

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