

## Microbiome Review: Ethnicity, Diet, and Lifestyle in Bad Obstetric History

Dr Samina Kausar Tabassum<sup>1\*</sup>, Dr. Parveen Jahan<sup>2</sup>

<sup>1</sup>Consultant Microbiologist, Premier Hospital, Hyderabad, Telangana, India

<sup>2</sup>Professor, Maulana Azad National Urdu University, Hyderabad, Telangana, India

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\*Corresponding author: Dr Samina Kausar Tabassum

Consultant Microbiologist, Premier Hospital, Hyderabad, Telangana

### Abstract

### Review Article

This systematic review explores the intricate relationship between the maternal microbiome and adverse obstetric outcomes in women with a history of recurrent miscarriages, preterm birth, or stillbirth, collectively known as Bad Obstetric History (BOH). The microbiome, encompassing bacteria, viruses, and fungi, within the reproductive tract is increasingly recognized as a crucial factor in pregnancy maintenance and complications. The study explores BOH's multifactorial causes—genetic, anatomical, endocrine, thrombophilic, immunological, and environmental. Despite one-third of cases being unexplained, it underscores the importance of evaluating uterine macro and microenvironments. Emerging evidence challenges prior beliefs by supporting the existence of an endometrial microbiome, hinting at its impact on pregnancy outcomes. The methodology follows a systematic approach adhering to PRISMA guidelines, incorporating electronic database searches yielding 125 relevant articles, with 47 meeting inclusion criteria. The selected studies focus on human samples from stool, oral, or vaginal swabs, including randomized clinical trials, systematic reviews, and meta-analyses. In conclusion, the review emphasizes the significance of understanding the microbial changes in pregnant females and their potential impact on obstetric outcomes. The findings propose a connection between altered microbiota and maternal complications, highlighting the potential for personalized medicine interventions. Additionally, the study delves into the nuanced relationship between ethnicity, dietary patterns, and the microbiome, underscoring the importance of personalized and culturally sensitive healthcare interventions. Overall, this comprehensive review provides valuable insights into the role of the microbiome in obstetric outcomes, paving the way for future research and targeted interventions to optimize pregnancy outcomes globally.

**Keywords:** Maternal Microbiome, Adverse Obstetric Outcomes, Bad Obstetric History (BOH), Endometrial Microbiome, Personalized Medicine, Ethnicity and Microbiome.

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## INTRODUCTION

The term "microbiome in bad obstetric history" refers to the microbial composition in the reproductive tract of women facing adverse obstetric outcomes, such as recurrent miscarriages, preterm birth, or stillbirth. Bad Obstetric History (BOH) presents challenges for couples and obstetricians. Women at high risk for BOH have a history of  $\geq 2$  consecutive spontaneous miscarriages, Intrauterine Fetal Death (IUFD), stillbirths, Fetal Growth Restriction (FGR), or fetal congenital anomalies [1].

The etiological factors of BOH are multifactorial, involving chromosomal abnormalities, anatomical or structural uterine anomalies, endocrine imbalance, thrombophilia (inherited and acquired), APLA syndrome, immunological factors, and environmental factors. Approximately one-third of cases lack a known cause, falling under the 'unexplained' etiology [3].

Evaluation for miscarriage causes typically involves examining the macro and micro environment within the uterus, recognizing that disruptions in normal embryo-endometrium interaction can lead to pregnancy failure [3]. Contrary to past beliefs in uterine cavity sterility, molecular-based studies reveal the existence of an endometrial microbiome.

Changes in maternal gut microbiota during pregnancy, associated with increased body weight and dietary modifications, are observed. Physiological maternal metabolic adjustments maintain hyperglycemia, providing essential glucose to the growing fetus<sup>4</sup>. Evidence challenges the century-old hypothesis of germ-free birth, suggesting bacterial presence in the fetoplacental unit [6, 7]. Dysbiosis, linked to harmful effects and long-term consequences, is influenced by factors like diet, host environment, and maternal effect, shaping the gut microbiota. However,

the interaction with host genetics remains poorly understood [9, 10].

## METHODOLOGY

The methodology for this study followed a systematic approach, incorporating electronic database searches and adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [11]. The systematic searches were conducted in November 2023, utilizing prominent databases such as PubMed, Science Direct, and Google Scholar. The PRISMA guidelines are recognized standards for conducting and reporting systematic reviews, ensuring transparency and reliability in the review process (accessible at <https://www.prisma-statement.org/>).

To maintain rigor and precision in the information retrieval process, two authors independently conducted the searches in the identified databases. This dual-author approach aimed to enhance the thoroughness and accuracy of the data collected, contributing to the overall quality and reliability of the study's findings.

### Study Selection and Data Selection Process

For this review article, a systematic selection process was employed, initially based on titles and abstracts, resulting in the identification of 125 articles pertaining to the topic of interest. Subsequent application of inclusion and exclusion criteria, along with the removal of duplicates, narrowed down the pool to 47 studies deemed suitable for in-depth analysis.

### Inclusion Criteria for Study Selection Encompassed the Following Parameters

- Samples sourced from stool, oral, or vaginal swabs,
- Randomized clinical trials, systematic reviews, and meta-analyses,
- Human-focused research, specifically original research articles.

### Exclusion Criteria Were Applied as Follows

- Case reports, conference summaries, and comments,
- Insufficient data availability,
- Unavailability of full-text articles for review,
- Articles not in the English language,
- Research conducted in non-human species.

To ensure comprehensiveness, key review references were meticulously examined to identify any pertinent studies that might have been overlooked during the initial selection process. This systematic approach aimed to curate a robust set of studies for a comprehensive review, ensuring the inclusion of relevant and high-quality research in the analysis.

## Ethnicity and Its Influence on Microbiome

The exploration of the relationship between ethnicity and its influence on the human microbiome represents a fascinating area of research within the field of microbiology and human health. The human microbiome, comprising trillions of microorganisms inhabiting various body sites, plays a crucial role in maintaining health and influencing disease susceptibility. While studies have attempted to elucidate the impact of ethnicity on the composition and function of the microbiome, it is important to approach this topic with a critical lens due to several key considerations [12].

### 1. Diversity within Ethnic Groups:

Ethnicity is a broad and heterogeneous category that encompasses diverse cultural, genetic, and environmental factors. Within any ethnic group, there exists considerable individual variability, making it challenging to draw generalized conclusions about the microbiome based solely on ethnic categorization [13].

### 2. Complex Interplay of Factors:

The microbiome is shaped by a complex interplay of genetic, environmental, dietary, and lifestyle factors. Ethnicity represents only one dimension of this intricate web. It is essential to account for confounding variables and recognize that multiple factors may contribute simultaneously to microbiome variations observed among different ethnic groups [14].

### 3. Geographic and Environmental Influences:

Ethnic groups often exhibit geographic and environmental variations, leading to differences in lifestyle, dietary habits, and exposure to various microorganisms. Disentangling the specific impact of ethnicity from these environmental factors poses a significant challenge and requires meticulous study design and statistical control [15].

### 4. Evolutionary History and Adaptations:

Human populations have undergone evolutionary processes that have shaped genetic adaptations to specific environments. Understanding the microbiome necessitates considering the evolutionary history of populations and how these adaptations may influence microbial communities [16].

### 5. Limited Generalizability of Findings:

Research findings on ethnicity and the microbiome from one population may not be easily extrapolated to other populations. Factors such as genetics, cultural practices, and environmental exposures differ across regions and ethnicities, limiting the generalizability of findings [17].

### 6. Dynamic Nature of the Microbiome:

The microbiome is dynamic and can be influenced by short-term factors such as diet, medication, and illness. Longitudinal studies are crucial for capturing the temporal dynamics of the microbiome and

understanding how ethnicity interacts with these dynamic factors over time [18].

This review explores the influence of ethnic background on the composition of the vaginal microbiome in women who have experienced adverse obstetric outcomes. Recent research suggests that distinct profiles of vaginal microbiota exist across various ethnicities, impacting pregnancy, labor, and postpartum well-being. Through a systematic review of literature, we found consistent evidence indicating unique microbial landscapes among women of different ethnic backgrounds, shaped by genetic, lifestyle, and cultural factors. These variations are not merely academic; they have practical consequences on obstetric outcomes such as preterm birth and neonatal health. Recognizing the intersection of ethnicity and vaginal microbiota is essential for developing personalized and culturally sensitive healthcare interventions, offering the potential to enhance maternal and neonatal well-being across diverse cultural groups [20, 21].

In a study with 163 pregnant Japanese women, vaginal fluid samples were analyzed to explore microbiota composition and its correlation with Bacterial Vaginosis (BV). The presence of *Lactobacillus crispatus* showed a significant association with normal vaginal flora, suggesting its protective role against BV. Conversely, BV-related bacteria were linked to bacterial vaginosis occurrence. Notably, pregnant Japanese women exhibited a lower prevalence of BV-related bacteria compared to non-pregnant American women. This observation raises questions about factors influencing vaginal microbiota during pregnancy across populations, emphasizing the need for further research. The study underscores the importance of understanding microbial dynamics in pregnant individuals, offering insights for preventive and therapeutic approaches to maintain vaginal health during pregnancy [22].

*Lactobacillus iners* (*L. iners*) is a common member of the human vaginal microbiota, distinct within the *Lactobacillus* genus. Unlike other species, such as *L. crispatus* and *L. jensenii*, *L. iners* has a lower prevalence of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) production. This unique trait raises questions about its functional role. Studies have linked *L. iners* to the colonization of bacteria associated with Bacterial Vaginosis (BV) in pregnant Japanese women, shedding light on its specific interactions and implications in the vaginal microbiome. Understanding these dynamics is crucial for developing targeted interventions and preventive strategies [23].

The exploration of microbiota in Japanese women, particularly within vaginal flora, reveals a diverse array of *Lactobacillus* species, including *L. crispatus*, *L. jensenii*, and *L. gasseri*, known for their association with a healthy vaginal environment. These species are traditionally linked to a balanced microbial community. The study also identifies BV-related

bacteria like BVAB2, *Megasphaera*, *Leptotrichia*, and an Eggerthella-like bacterium, shedding light on their presence in the vaginal microbiota and association with bacterial vaginosis. This nuanced profiling emphasizes the coexistence of beneficial and potentially pathogenic bacteria, providing valuable insights into the dynamic equilibrium within the vaginal ecosystem and implications for targeted interventions in Japanese women [22].

In the gut microbiota of pregnant women in South China, *Bacteroidetes* emerged as the predominant bacterium, accounting for a substantial proportion ranging from 47.57% to 52.35%. Interestingly, as pregnancy progressed, there was an observed increase in *Tenericutes*, while *Verrucomicrobia* exhibited a notable decline, nearly disappearing in late pregnancy. In the context of Pre-eclampsia (PE) patients, a distinct alteration in the gut microbial landscape was identified. Notably, there was a general escalation in pathogenic bacteria, with notable increases in *Clostridium perfringens* and *Bulleidia moorei*, alongside a reduction in the abundance of the probiotic bacterium *Coprococcus catus*. These findings collectively suggest a substantial structural shift in the gut microbiota of PE patients, implying a potential association between these microbial changes and the onset and progression of the disease. This research underscores the intricate relationship between gut microbiota composition and pregnancy-related complications, offering insights that could pave the way for targeted interventions and therapeutic strategies for individuals at risk of or affected by Pre-eclampsia [24].

In a study involving pregnant women in Denmark, an investigation into the gut microbiota revealed distinctive differences between those with gestational diabetes mellitus (GDM) and normoglycemic pregnant women. Notably, at the phylum level, *Actinobacteria* exhibited a higher abundance in the GDM cohort compared to their normoglycemic counterparts. Similarly, at the genus level, the GDM group showed elevated levels of *Collinsella*, *Rothia*, and *Desulfovibrio*. Further scrutiny at the operational taxonomic units (OTUs) level uncovered specific microbial variations in the GDM cohort, characterized by an enrichment of species affiliated with *Faecalibacterium* and *Anaerotruncus*, alongside a depletion of species annotated to *Clostridium* and *Veillonella*. These findings suggest a discernible dysbiosis in the gut microbiota of pregnant women with gestational diabetes mellitus, emphasizing the potential significance of these microbial alterations in the context of GDM pathophysiology. Understanding these microbial dynamics holds promise for advancing targeted interventions and therapeutic strategies to mitigate the impact of gestational diabetes mellitus on maternal health [25].

A nested case-control study was conducted on 107 well-phenotyped cases of spontaneous preterm birth

(sPTB) within a cohort of 2000 pregnant women in Philadelphia, United States. The investigation revealed distinctive contributions of the cervicovaginal microbiota to sPTB, with a particular emphasis on the differences between African American (AA) and non-AA pregnant women. The study highlighted variations in the frequency of specific cervicovaginal microbiota community state types (CSTs) in AA and non-AA women. Additionally, differences were observed in the

association between certain bacterial taxa and the risk of sPTB. These disparities, rooted in race and ethnicity, underscore the significance of understanding cervicovaginal microbiota composition in diverse population groups. The findings emphasize the necessity of considering race and ethnicity-based factors in both research and clinical approaches to comprehensively address and mitigate the risk of spontaneous preterm birth [26].

**Table 1: Factors Influencing Ethnic Disparities in Obstetric Outcomes**

Influencing Factors	Impact on Obstetric Outcomes
Genetic Factors	Ethnic variations in genetics may influence the risk of complications like gestational diabetes or preeclampsia.
Inherited Conditions	Varied prevalence of inherited conditions or genetic disorders among ethnic groups can impact pregnancy outcomes.
Socio-Economic Factors	Socio-economic factors linked to ethnicity affect access to healthcare, education, and resources, influencing prenatal care quality and overall outcomes.
Cultural Practices	Ethnic-specific cultural practices, dietary habits, and attitudes towards healthcare can impact maternal and fetal health during pregnancy.
Prevalence of Chronic Conditions	Ethnic disparities in the prevalence of chronic conditions (e.g., diabetes, hypertension, obesity) contribute to differing rates of pregnancy complications.
Healthcare Disparities	Disparities in healthcare access and quality contribute to variations in obstetric outcomes among different ethnic groups.
Healthcare Provider Approach	Discussions about ethnicity and obstetric outcomes should be approached with sensitivity, considering individual medical history, genetics, and lifestyle.
Addressing Disparities	Efforts to address healthcare disparities, promote cultural competence, and ensure equitable access to prenatal care can enhance obstetric outcomes for all ethnic groups.

Understanding the impact of distinct microbial compositions among different ethnic groups on reproductive health is crucial for tailored strategies to enhance maternal and infant outcomes. Research reveals that changes in vaginal microbiota significantly influence pregnancy-related complications such as preterm birth and miscarriage [27, 28]. This emphasizes the necessity for interventions considering unique microbial dynamics in diverse ethnicities, contributing to more effective approaches for maternal and infant well-being. Examining these changes is vital for early identification and developing interventions to improve outcomes. Personalized treatment approaches focusing on regulating the vaginal microbiome during pregnancy and postpartum are essential, offering potential for improved health outcomes for mothers and newborns [29, 30].

While geography traditionally dominated gut microbiota research, recent studies highlight the significant impact of ethnicity, even within shared geographical locations. Analysing the HLIUS cohort (2,084 participants) identifies ethnic-specific gut microbiota patterns, emphasizing ethnicity's independent effect on diversity [31]. Similarly, a Malaysian study (214 participants) finds ethnicity as the primary driver of gut microbiota differences, suggesting shared cultural and lifestyle practices associated with ethnicity significantly shape microbial communities [31].

Beyond the gut, the vaginal microbiome also exhibits intriguing links with ethnicity. A UK study of 42 pregnant women reveals postpartum shifts in the vaginal microbiome, emphasizing biogeographical and ethnic specificity [32]. These findings collectively depict the multifaceted influence of ethnicity on human microbiota. Shared cultural practices associated with ethnicity play a significant role in shaping microbial communities, underscoring the importance of comprehensive studies acknowledging diverse populations and their unique ethnic backgrounds. Future research should explore the interplay between ethnicity, microbiota composition, and health outcomes across demographics and geographical contexts [33].

### Role of Diet in Regulating Microbiome

The role of diet in regulating the human microbiome has become a focal point in research, offering insights into how dietary choices impact microbial composition and function within the body [34]. While numerous studies suggest a profound connection between diet and the microbiome, it is essential to approach this relationship critically, considering the following key aspects:

#### Individual Variability:

Individuals exhibit substantial variability in their microbiome composition, and this diversity is influenced by factors beyond diet, including genetics, environment, and lifestyle. Recognizing the individuality



of microbiome responses to diet is crucial, and sweeping generalizations may oversimplify this intricate relationship [35].

#### Dietary Patterns and Diversity:

The microbiome's response to diet extends beyond individual nutrients, emphasizing the importance of overall dietary patterns and diversity. Comprehensive dietary assessments are crucial in microbiome studies to capture the synergistic effects of a varied and balanced diet.

#### Short-Term vs. Long-Term Effects:

While short-term dietary changes impact the microbiome, understanding the stability of these effects requires longitudinal studies. Distinguishing transient alterations from enduring shifts in microbial communities provides a nuanced view of diet-microbiome interactions.

#### Host-Specific Responses:

Given the host-specific nature of the microbiome, individual physiological and genetic

characteristics influence diet-microbiome interactions. Recognizing host-specific responses is essential for accurate interpretation.

#### Microbial Adaptability:

Microbial communities adapt to diet changes, mitigating immediate impacts. Unraveling the mechanisms behind microbial adaptability is crucial for understanding complex dynamics.

#### Resilience and Stability:

The human microbiome displays resilience and stability, recovering from disturbances, including dietary changes. Examining how the microbiome maintains stability after perturbations is vital for understanding the long-term consequences of diet on microbial communities [36].

**Table 2: Dietary Influences on Pregnancy Outcomes: A Comprehensive Overview [37]**

Pregnancy Outcomes	Impact on Obstetric Health
Neural Tube Defects	Inadequate folic acid intake raises neural tube defect risk; emphasizes B-vitamin importance.
Low Birth Weight	Insufficient maternal nutrition, lacking essential nutrients, contributes to low birth weight.
Gestational Diabetes	Poor dietary habits, excessive high-sugar and high-fat foods, contribute to gestational diabetes. Risk of complications during pregnancy, delivery, and type 2 diabetes later in life.
Preeclampsia	Diets high in sodium and low in specific nutrients linked to increased preeclampsia risk.
Preterm Birth	Inadequate maternal nutrition, coupled with key nutrient deficiencies, raises preterm birth risk.
Macro and Micronutrient Deficiencies	Insufficient intake impacts fetal development, increases complication risk.
Dietary Recommendations	Pregnant women advised well-balanced diet, rich in fruits, vegetables, whole grains, lean proteins, and dairy. Prenatal vitamins address nutritional gaps.
Prenatal Care Guidance	Healthcare professionals provide tailored dietary guidance, considering individual needs. Women with history of bad obstetric outcomes or specific health conditions may receive additional nutritional counseling for a healthier pregnancy and delivery.

Maintaining a balanced diet with essential nutrients is crucial for maternal health and fetal development. Prenatal care, including dietary guidance and the use of recommended prenatal vitamins, plays a vital role in optimizing pregnancy outcomes. Healthcare professionals tailor advice to individual needs, particularly for women with a history of adverse obstetric outcomes or specific health conditions, promoting a healthier pregnancy and delivery.

#### 7. Interplay with Other Factors

Diet interacts with factors like medications, physical activity, and stress, collectively influencing the microbiome. Isolating diet's effects from these variables poses methodological challenges; comprehensive research must consider these multifaceted interactions.

In summary, while diet's role in regulating the microbiome is significant, a critical perspective is vital to navigate complexities. Understanding individual variability, the holistic impact of dietary patterns, and the dynamic nature of the microbiome contributes to a nuanced comprehension of the intricate interplay with diet [38].

Dietary interventions, like high-fiber diets in pregnancy, impact the gut microbiome, potentially influencing maternal and neonatal health. Specific fiber types, e.g., arabinoxylans and  $\beta$ -glucans, may benefit gestational diabetes mellitus (GDM) patients based on individual microbial patterns [40].

Fiber-rich diets associate with increased SCFA-producing bacteria, such as *Holdemania*, *Roseburia*,

Lachnospira, and Coprococcus, and reduced Collinsella and Sutterella with heightened dietary fiber intake.<sup>39</sup> This highlights the complex relationship between dietary choices, gut microbial composition, and potential health outcomes during pregnancy.

In GDM, diet shapes the gut microbiota, impacting insulin resistance and inflammation dynamics. Maternal dietary choices, especially saturated fats, influence offspring microbiome and immune system, possibly leading to long-term health effects. Despite interest, specific dietary recommendations for GDM prevention and treatment remain inconclusive [40].

Probiotics during pregnancy elevate anti-inflammatory molecules in breast milk, influencing infant gut maturation and immune responses. Probiotics, with beneficial Lactobacillus strains and prebiotics, show potential in balancing and maintaining a healthy vaginal microbiome [44].

The intricate relationship between diet, microbiota, and health during pregnancy highlights the need for personalized dietary interventions. While dietary modifications and probiotics show promise for gestational diabetes mellitus and maternal-neonatal health, further research is essential for precise and evidence-based recommendations. Probiotics, though promising, require further investigation for their specific role in modulating the maternal microbiome.

## CONCLUSION

Dietary interventions, emphasizing high-fiber, fruit, and vegetable-rich diets with limited animal fats, show promise for gestational diabetes mellitus (GDM) management by influencing microbial composition and short-chain fatty acid production. However, specific dietary recommendations for GDM lack robust evidence, necessitating further research. Probiotics exhibit potential in enhancing anti-inflammatory molecules, influencing immune pathways, and restoring a healthy vaginal environment, yet their specific role in modulating the maternal microbiome requires deeper understanding before definitive recommendations can be established.

### Lifestyle Interventions for Better Microbiome Health

Excitement about lifestyle interventions for microbiome health faces challenges. Individual responses vary, long-term effects are unclear, and genetics play a role. Untangling lifestyle components, from diet to stress, is tricky. The microbiome's adaptability raises questions about intervention

durability. Ethical considerations arise, and environmental factors complicate the picture. Embracing a nuanced approach recognizing the intricate dance between lifestyle and microbiome is essential for developing effective and ethical strategies for gut health [45].

Promoting healthy lifestyle practices, including well-rounded nutrition, sufficient hydration, and avoiding behaviors disrupting the vaginal microbiome, is integral for fostering a favorable microbial environment during pregnancy [44].

In pregnancies with gestational diabetes mellitus (GDM), distinct gut microbiota composition differences include increased Parabacteroides distasonis, Klebsiella variicola, Ruminococcus, Eubacterium, Prevotella, Collinsella, Rothia, Desulfovibrio, Actinobacteria, Firmicutes, coupled with reduced gut richness of Methanobrevibacter smithii, Alistipes species, Bifidobacterium species, Eubacterium species, Akkermansia, Bacteroides, Parabacteroides, Roseburia, and Dialister [46].

Additionally, gestational weight gain correlates with specific gut microbiota alterations, such as higher concentrations of Bacteroides species, Staphylococcus, Enterobacteriaceae, and Escherichia coli, along with a reduction in the abundance of Bifidobacterium and Akkermansia muciniphila, resulting in lower  $\alpha$ -diversity [46]. Women with gestational obesity exhibit increased Bacteroides and Bifidobacterium, alongside decreased Enterobacteriaceae and Escherichia coli [47].

These findings highlight connections between lifestyle factors, gut microbiota dynamics, and challenges posed by conditions like gestational diabetes mellitus and gestational obesity during pregnancy. Implementing tailored lifestyle modifications and nutritional strategies holds potential for positively impacting maternal and neonatal health outcomes. Maintaining a healthy lifestyle during pregnancy is crucial for a balanced vaginal microbiome and potentially mitigating complications. Recognizing these associations holds promise for targeted interventions to optimize the gut microbiome during pregnancy. Future research should focus on elucidating precise mechanisms by which diet, lifestyle, and weight gain influence the microbiome, paving the way for personalized strategies for maternal and fetal health. Acknowledging the interplay between lifestyle, the microbiome, and pregnancy outcomes advances personalized prenatal care for optimal health across diverse populations [48].

**Table 3: Pregnancy-Related Complications: Impact of Lifestyle Factors**

Lifestyle Factor	Impact on Pregnancy
Smoking	Increased risk of miscarriage, preterm birth, low birth weight, stillbirth, and complications like placental abruption.

Lifestyle Factor	Impact on Pregnancy
Alcohol Consumption	Heavy consumption linked to fetal alcohol syndrome, leading to developmental and physical abnormalities in the baby.
Illicit Drug Use	Cocaine, heroin, or methamphetamine use during pregnancy associated with preterm birth, low birth weight, developmental issues, and neonatal withdrawal symptoms.
Poor Nutrition	Inadequate maternal nutrition can lead to neural tube defects, intrauterine growth restriction, and preterm birth. Lack of essential nutrients, such as folic acid and iron, can impact fetal development.
Obesity	Maternal obesity increases the risk of gestational diabetes, preeclampsia, macrosomia (large birth weight), and other complications during pregnancy and delivery.
Inadequate Prenatal Care	Lack of regular prenatal care contributes to complications that may affect pregnancy outcomes.
Stress and Mental Health	Chronic stress and mental health conditions may contribute to preterm birth and other complications during pregnancy.
Chronic Medical Conditions	Lifestyle-related chronic conditions like diabetes and hypertension can increase the risk of adverse pregnancy outcomes if not properly managed.

Adopting healthy habits, receiving proper prenatal care, and effective medical management are crucial for mitigating pregnancy complications. Women with a history of adverse obstetric outcomes should embrace positive lifestyle changes and adhere to recommendations for a healthy pregnancy. Open discussions with healthcare teams are vital for receiving personalized advice. Acknowledging the multifactorial impact of ethnicity on obstetric outcomes, healthcare providers must consider individual medical histories, genetics, and lifestyles. Initiatives targeting healthcare disparities and ensuring equal access to prenatal care are pivotal for enhancing outcomes across diverse ethnic groups. Tailored prenatal care fosters improved communication, understanding, and adherence to recommended interventions, promoting the well-being of both mother and baby.

### Impact of Microbiome on Obstetric Outcomes

The exploration of the microbiome's impact on obstetric outcomes has gained momentum, holding substantial implications for maternal and neonatal health [49]. Convincing evidence points to the influential role of the maternal microbiome, especially within reproductive and gestational tracts, in shaping pregnancy outcomes. However, the complexity of these contributions requires cautious consideration, influenced by individual variations, environmental factors, and microbial community dynamics [49]. Methodological challenges, encompassing sample collection variability and confounding variables, underscore the importance of meticulous interpretation. The translation of microbiome research into clinical practice, aiming to enhance obstetric outcomes, demands a comprehensive understanding of intricate interactions during pregnancy, birth, and postpartum health.

Imbalances in the microbiota can contribute to various pregnancy complications, including gestational diabetes, preterm delivery, and preeclampsia. The development of gestational diabetes mellitus (GDM) involves insulin resistance and inflammation, both

modulated by the gut microbiota during GDM pregnancies [46]. Emerging evidence suggests that specific nutrients exert varying effects on metabolic outcomes, influenced by individual microbial patterns. This implies that the impact of the same food may differ among individuals based on their gut microbiota composition [46].

In the context of gestational diabetes, women with GDM exhibit an altered abundance of microbial species. An increased prevalence of Firmicutes, *Klebsiella variicola*, *Collinsella*, *Rothia*, *Ruminococcus*, and *Actinobacteria* is observed, accompanied by a decreased abundance of *Parabacteroides distasonis* and *Desulfovibrio*. These microbial variations underscore the intricate relationship between the gut microbiota, specific nutrient influences, and the development of gestational diabetes, holding promise for targeted interventions to mitigate associated complications [47].

Exploring the landscape of spontaneous preterm birth (sPTB) unveils a complex interplay of immune and microbial factors, particularly impactful for African American women (26). Seven bacterial taxa are distinctly associated with a heightened risk of sPTB, providing a nuanced perspective on the multifactorial nature of this phenomenon (26). Surprisingly, even in cervicovaginal microbiota dominated by *Lactobacillus* spp., low levels of  $\beta$ -defensin-2 are linked with an increased risk of sPTB. These discoveries hold promise for advancing early pregnancy diagnostics, enabling the identification of women at risk for sPTB.

Changes in vaginal microbiota during pregnancy are identified as potential precursors to vaginal infections, such as bacterial vaginosis, escalating the risk of preterm birth<sup>42</sup>. This insight underscores the need for heightened vigilance in monitoring and managing vaginal microbiota to mitigate associated risks.

In the context of preeclampsia, studies reveal shifts in the gut microbiota, featuring an increased abundance of pathogenic bacteria like *Bulleidia moorei* and *Clostridium perfringens*, alongside a decreased abundance of the probiotic *Coprococcus catus* in affected individuals compared to healthy pregnant women [50]. These findings underscore the potential link between gut microbiota composition and the pathophysiology of preeclampsia, offering avenues for further exploration and targeted interventions [50].

Recognizing the impact of hormonal changes on the vaginal microbiome, it is proposed that appropriate medical interventions regulating hormonal dynamics may serve as a valuable strategy to maintain a favorable microbial balance during pregnancy<sup>44</sup>. This inference highlights the potential for hormonal modulation as an adjunctive approach to preserving maternal health through maintaining a healthy vaginal microbiome during pregnancy.

The delicate dance between pregnancy and the microbiome holds immense influence over maternal and fetal well-being. Imbalances within this intricate ecosystem can disrupt metabolic and immune pathways, leading to a cascade of complications like gestational diabetes, preterm delivery, and preeclampsia.

#### **Gestational Diabetes:**

- Insulin resistance and inflammation play key roles in GDM, and the gut microbiome significantly impacts their modulation.
- Specific nutrients influence metabolic outcomes differently depending on individual microbial patterns, highlighting the need for personalized dietary approaches.
- Increased Firmicutes, *Klebsiella variicola*, *Collinsella*, *Rothia*, *Ruminococcus*, and Actinobacteria, and decreased Parabacteroides distasonis and *Desulfovibrio* are observed in women with GDM.

#### **Spontaneous Preterm Birth:**

- Distinct combinations of immune and microbial factors are linked to sPTB risk, particularly impacting African American women.
- Even in Lactobacillus-dominated cervicovaginal microbiota, low  $\beta$ -defensin-2 levels elevate sPTB risk, offering potential for early pregnancy diagnostics.
- Changes in the vaginal microbiome during pregnancy can increase the risk of bacterial vaginosis and subsequent preterm birth.

#### **Preeclampsia:**

- Preeclampsia women exhibit increased gut abundance of pathogenic bacteria (*Bulleidia moorei* and *Clostridium perfringens*) and

decreased probiotics (*Coprococcus catus*) compared to healthy women.

#### **Maintaining a Balanced Microbiome:**

- Encouraging healthy lifestyle practices like balanced nutrition, adequate hydration, and avoiding disruptive behaviors fosters a favorable microbial environment.
- Hormonal regulation through appropriate medical interventions, when necessary, can help maintain a balanced vaginal microbiome during pregnancy.

By unraveling the intricate web of the microbiome's influence on pregnancy, we pave the way for personalized interventions that optimize maternal and fetal health. Future research should delve deeper into the precise mechanisms by which specific factors like diet, lifestyle, and hormones shape the microbiome, ultimately leading to personalized prenatal care strategies for optimal pregnancy outcomes across diverse populations.

#### **Understanding Bad Obstetric History Cases through the Lens of Microbiome**

Understanding the maternal microbiome during pregnancy is crucial for identifying risk factors associated with adverse outcomes. Monitoring the gut microbiome aids in recognizing susceptibility to *Listeria monocytogenes* infection and preterm delivery, while surveillance of the vaginal microbiome helps identify women at risk for preterm birth, preeclampsia, and stillbirths. Insights into the maternal microbiome's role in immune responses and metabolic processes inform interventions, such as prebiotic supplementation, to enhance gut barrier integrity and reduce permeability. These findings underscore the importance of maternal microbiome research in advancing proactive strategies for maternal and fetal well-being during pregnancy.

#### **Gut Microbiome:**

The gut microbiome undergoes significant modifications during pregnancy, including changes in diversity, composition, and metabolic activity. Studies indicate increased Proteobacteria/Actinobacteria abundance and decreased  $\alpha$ -diversity, with alterations in specific bacterial species. These changes are influenced by hormonal, immunological, and metabolic factors in pregnancy. Elevated estrogen and progesterone levels, identified as factors perturbing the gut microbiome, may render women more susceptible to *Listeria monocytogenes* infection, contributing to heightened risks of preterm delivery or stillbirth. The interplay between hormonal dynamics and the gut microbiome highlights multifaceted factors influencing microbial



changes during pregnancy, shedding light on potential pathways contributing to adverse outcomes [46-43].

#### Oral Microbiome:

The oral microbiome of pregnant women exhibits elevated bacterial counts, particularly notable during the first trimester, featuring the presence of bacteria such as Porphyromonas, Neisseria, Treponema, and certain pathogenic strains. Imbalances within the oral microbiome during pregnancy have been associated with various disorders, including gestational diabetes, as well as adverse outcomes like stillbirths and preterm births. These findings underscore the significance of oral microbial health in maternal well-being and the potential implications for pregnancy-related complications [42, 43].

#### Vaginal Microbiome:

Changes in the vaginal microbiome during pregnancy, characterized by an increased dominance of Lactobacillus species, have significant implications for maternal immune responses and susceptibility to infections. Fluctuations in hormone levels, particularly estrogen and progesterone, exert a substantial impact on the structure and function of the microbiome. Imbalances in the vaginal microbiome during pregnancy carry the potential to elevate the risk of vaginal infections, such as bacterial vaginosis, with subsequent implications for adverse pregnancy outcomes [42, 43].

Recent studies have further highlighted the association between alterations in the vaginal microbiota and preterm birth. The unique composition of the vaginal microbiome in pregnant women, distinct from that of women in other life stages, has been correlated with various reproductive, obstetric, and perinatal outcomes. These insights emphasize the dynamic nature of the vaginal microbiome during pregnancy and its significant role in influencing maternal and neonatal health [52, 53].

#### Deciphering Dynamic Shifts:

Understanding dynamic shifts within the maternal microbiome during pregnancy holds immense potential for revolutionizing prenatal care and optimizing maternal and fetal health. Monitoring these changes offers a promising avenue for early risk identification and targeted interventions, paving the way for personalized dietary, hygienic, and therapeutic strategies tailored to each woman's unique needs.

The journey ahead involves unraveling the precise mechanisms by which specific maternal and environmental factors influence the microbiome and its impact on pregnancy outcomes. Continued research within this dynamic field holds the key to unlocking transformative interventions, ensuring the well-being of

mothers and their babies throughout pregnancy and beyond.

#### Concluding Remarks: Microbiome, Ethnicity, Diet, and Lifestyle in Obstetrics

Candidate gene approaches reveal host genomic loci influence gut microbial diversity [54]. Vaginal microbiome composition varies by race and ethnicity, influenced by genetic, environmental, and cultural factors, emphasizing the need for personalized healthcare [44]. In bad obstetric history cases, the microbiome may link to adverse pregnancy outcomes, highlighting the importance of monitoring the vaginal microbiome to mitigate risks [55-44]. Understanding the diet-gut microbiota-GDM relationship emphasizes personalized dietary interventions for more effective management of gestational diabetes [46].

#### Recommendations for Future Research on Microbiome in Obstetrics

Tailoring interventions based on individual microbial profiles and genetic factors may offer personalized strategies to optimize the vaginal microbiome and mitigate the risk of adverse pregnancy outcomes [44].

To alleviate the substantial health burden associated with these outcomes, microbial and immune factors linked to sPTB could serve as diagnostic signatures for early identification of women at risk. This could enable personalized counselling and therapeutic approaches such as microbiome-based therapeutics and immune modulators.

The review suggests that the gut microbiota might contribute to gestational metabolic changes through different mechanisms, although further studies on this topic are necessary [46].

Overall, the research on the maternal microbiome during pregnancy highlights the importance of monitoring and understanding these changes for optimal maternal and fetal health outcomes, and may inform interventions to prevent or manage obstetrical complications.

#### CONCLUSION: ETHNIC MICROBIOME AND OBSTETRIC OUTCOMES - A NUANCED PERSPECTIVE

This systematic review highlights the intricate relationship between ethnicity, lifestyle, and the human microbiome, with a specific focus on the impact of the vaginal microbiota on obstetric outcomes. Ethnic background significantly influences microbial composition, necessitating a nuanced understanding of microbiome variations across diverse populations. Genetic, cultural, and environmental factors contribute to this complexity, emphasizing the need for personalized and culturally sensitive healthcare interventions. Distinct

microbial profiles associated with adverse obstetric outcomes in different ethnic groups underscore the importance of recognizing ethnic-specific microbial dynamics, providing a foundation for targeted interventions globally.

The study delves into the complex interplay between diet, the human microbiome, and pregnancy outcomes. While dietary interventions and probiotic supplementation show promise, the study calls for continued research to establish comprehensive evidence for precise dietary recommendations. The potential for personalized, microbiome-based interventions tailored to individual dietary patterns and microbial profiles is recognized as a promising avenue for optimizing pregnancy outcomes.

Additionally, the study addresses the complexities of lifestyle interventions for microbiome health, emphasizing challenges posed by individual variability, unclear long-term effects, and intricate interactions with genetics. Exploring gestational diabetes mellitus and obesity during pregnancy reveals distinct shifts in gut microbiota composition linked to these conditions, highlighting the crucial role of a healthy lifestyle in maintaining a balanced vaginal microbiome and mitigating pregnancy complications. Recognizing associations between lifestyle factors, gut microbiota dynamics, and pregnancy outcomes opens avenues for targeted interventions. The study advocates for personalized prenatal care, urging healthcare providers to consider individualized medical histories, genetics, and lifestyles for improved obstetric outcomes. Initiatives focused on reducing healthcare disparities, cultural competence, and equitable access to prenatal care are crucial for promoting maternal and neonatal health on a broader scale.

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