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Influence of the maternal vaginal, gut, and placental microbiome on pregnancy outcomes – An observational study

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Abstract:
Introduction: The human microbiome, encompassing various microbial communities residing within and on the human body, has emerged as a critical determinant of health and disease. During pregnancy, the maternal microbiome undergoes dynamic shifts, particularly in the vaginal, gut, and placental regions, which play essential roles in maternal-fetal health. Understanding the intricate interplay between these microbial communities and pregnancy outcomes is of paramount importance for improving prenatal care and maternal health.
Methods: Samples were collected from pregnant women at various gestational ages during routine prenatal visits. Vaginal, gut, and placental samples were collected, and DNA extraction and sequencing were performed to analyze microbial composition. Clinical data including demographic information and pregnancy outcomes were collected from electronic medical records. Statistical analysis was conducted to assess associations between microbial composition and pregnancy outcomes.
Results: Demographic characteristics of the study participants are presented, showing a diverse population in terms of age and education level. Microbial composition analysis revealed distinct profiles in the maternal vaginal, gut, and placental microbiomes. Associations were observed between specific microbial compositions and pregnancy outcomes, including preterm birth, gestational diabetes, and preeclampsia.
Discussion: Our findings highlight the significance of the maternal microbiome in shaping pregnancy outcomes. Associations between microbial dysbiosis and adverse pregnancy outcomes underscore the potential for microbiome-targeted interventions in prenatal care. Comparison with previous studies further supports the importance of considering the maternal microbiome in understanding pregnancy complications.
Conclusion: This study contributes to our understanding of the complex interactions between the maternal microbiome and pregnancy outcomes. By elucidating the role of microbial composition in maternal-fetal health, we pave the way for personalized interventions to optimize pregnancy care and improve maternal and neonatal health outcomes.

Introduction :

The human microbiome, encompassing various microbial communities residing within and on the human body, has emerged as a critical determinant of health and disease. During pregnancy, the maternal microbiome undergoes dynamic shifts, particularly in the vaginal, gut, and placental regions, which play essential roles in maternal-fetal health [1]. Understanding the intricate interplay between these microbial communities and pregnancy outcomes is of paramount importance for improving prenatal care and maternal health.

Pregnancy represents a unique physiological state characterized by profound alterations in the maternal microbiome. The vaginal microbiome, primarily composed of Lactobacillus species, maintains a delicate balance that is crucial for preventing ascending infections and ensuring a healthy uterine environment. Disruptions in this balance, such as bacterial vaginosis, have been associated with adverse pregnancy outcomes including preterm birth and low birth weight [2]. Similarly, the gut microbiome, comprising a diverse array of microorganisms, influences maternal metabolism, immune function, and inflammation. Perturbations in gut microbial composition during pregnancy have been

linked to gestational diabetes, preeclampsia, and maternal obesity, underscoring the importance of a stable gut microbiome for maternal well-being and fetal development [3].

Moreover, recent research has shed light on the presence of a placental microbiome, challenging the traditional notion of the placenta as a sterile organ. The placental microbiome, believed to originate from maternal or environmental sources, has been implicated in various pregnancy complications, including intrauterine infection and inflammation, which can adversely impact fetal growth and development [4].

Despite advancements in microbiome research, comprehensive studies elucidating the collective influence of the vaginal, gut, and placental microbiomes on pregnancy outcomes are limited [5]. Therefore, this observational study aims to investigate the associations between maternal microbial profiles and a spectrum of pregnancy outcomes, including preterm birth, gestational diabetes, preeclampsia, and fetal growth restriction. By leveraging high-throughput sequencing technologies and clinical data, we seek to unravel the complex interactions between maternal microbiota and pregnancy complications, paving the way for personalized interventions and targeted therapies to optimize maternal and neonatal health.

Aim and Objectives:

- To investigate the associations between the composition and diversity of the maternal vaginal, gut, and placental microbiome during pregnancy and a range of pregnancy outcomes, including preterm birth, gestational diabetes, preeclampsia, and fetal growth restriction.

Methods:

Sample Collection: Maternal vaginal, gut, and placental samples were collected from pregnant women at various gestational ages during routine prenatal visits at a tertiary care hospital. Vaginal swabs were obtained using sterile cotton swabs inserted into the vaginal canal and gently rotated to collect microbial samples. Fecal samples were collected in sterile containers provided to participants, and placental samples were collected immediately post-delivery following standard sterile procedures.

DNA Extraction and Sequencing: Total genomic DNA was extracted from the collected samples using a commercial DNA extraction kit following the manufacturer's instructions. The extracted DNA was quantified using a spectrophotometer, and the quality was assessed using gel electrophoresis. The V3-V4 hypervariable regions of the bacterial 16S rRNA gene were amplified using polymerase chain reaction (PCR) with universal primers. Amplicons were purified, quantified, and pooled in equimolar concentrations. Sequencing was performed on the Illumina MiSeq platform using paired-end sequencing protocols.

Bioinformatic Analysis: Raw sequencing data were processed using QIIME2 software. Paired-end reads were quality-filtered, denoised, and merged to generate amplicon sequence variants (ASVs). Taxonomic classification of ASVs was performed against the Greengenes database using the q2-feature-classifier plugin. Alpha and beta diversity metrics were calculated to assess the within-sample and between-sample diversity, respectively. Differential abundance analysis was performed to identify microbial taxa associated with specific pregnancy outcomes.

Clinical Data Collection: Demographic, clinical, and pregnancy outcome data were extracted from electronic medical records. Variables of interest included maternal age, gestational age at delivery, mode of delivery, birth weight, presence of gestational diabetes, preeclampsia, and preterm birth. Data were anonymized and stored securely for subsequent analysis.

Statistical Analysis: Statistical analysis was performed using SPSS statistical software (version 23.0). Descriptive statistics were calculated for demographic and clinical variables. Associations between microbial composition and pregnancy outcomes were assessed using appropriate statistical tests, including chi-square tests, t-tests, and multivariate regression analysis, adjusting for potential confounders.

Results:

The table provides demographic information about the study participants, including their age, trimester at enrollment, gestational age, and education level. The mean age of the participants was 29.2 years, with a standard deviation of 3.8 years. The majority of participants were enrolled during the second trimester of pregnancy, with gestational ages ranging from 18 to 24 weeks. Regarding education level, the distribution was diverse, with the majority holding a Bachelor's degree (35%),

followed by Some College (30%), High School or Less (15%), Master's Degree (12.5%), and Doctorate or Higher (7.5%).

Table 1: Baseline characteristics of the study participants

Characteristic	Value n=200
Mean Age (years)	29.2 (SD = 3.8)
Trimester at Enrolment	Second Trimester
Age Range	20 - 40 years
Gestational Age at Enrolment (weeks)	18 - 24 weeks
Education Level (n, %)	
- High School or Less	30 (15%)
- Some College	60 (30%)
- Bachelor's Degree	70 (35%)
- Master's Degree	25 (12.5%)
- Doctorate or Higher	15 (7.5%)

This table outlines the dominant phyla, genera, and abundance percentages of microbial communities in the maternal vaginal, gut, and placental microbiomes. Lactobacillus species, particularly Lactobacillus crispatus and Lactobacillus iners, were predominant in the vaginal microbiome. The gut microbiome was characterized by Firmicutes and Bacteroidetes, with Faecalibacterium and Bacteroides being prevalent genera. In contrast, the placental microbiome exhibited lower microbial diversity, with Proteobacteria, Firmicutes, and Actinobacteria being the dominant phyla.

Table 2: Microbial Composition of Maternal Vaginal, Gut, and Placental Microbiomes

Microbiome Location	Dominant Phyla	Dominant Genera	Abundance (%)
Vaginal	Lactobacillus	Lactobacillus crispatus	45
		Lactobacillus iners	30
		Other	25
Gut	Firmicutes	Faecalibacterium	35
		Bacteroidetes	30
		Other	35
Placental	Proteobacteria		20
	Firmicutes		30
	Actinobacteria		15
	Other		35

This table summarizes the associations between specific microbial compositions and pregnancy outcomes. Higher abundance of Gardnerella vaginalis in the vaginal microbiome was significantly associated with an increased risk of preterm birth (OR = 2.67, 95% CI 1.42-5.03, $p < 0.001$). Participants with gestational diabetes had a significantly lower Firmicutes to Bacteroidetes ratio in their gut microbiome compared to non-diabetic participants (mean ratio 0.72 vs. 1.18, $p = 0.003$). Moreover, analysis revealed a higher abundance of Proteobacteria in the placental microbiome of women who developed preeclampsia compared to those who did not (mean relative abundance 20.5% vs. 14.2%, $p = 0.012$). However, no significant associations were observed between maternal microbial composition and fetal growth restriction.

Table 3: Association Between Microbial Composition and Pregnancy Outcomes

Pregnancy Outcome	Microbial Composition	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Preterm Birth	Gardnerella vaginalis (Vaginal Microbiome)	2.67	1.42 - 5.03	< 0.001
Gestational Diabetes	Firmicutes to Bacteroidetes ratio (Gut Microbiome)	0.72 vs. 1.18	-	0.003
Preeclampsia	Proteobacteria (Placental Microbiome)	Mean relative	-	0.012

		abundance: 20.5% vs. 14.2%		

Discussion:

The findings of this study shed light on the intricate relationship between maternal microbial composition and pregnancy outcomes, providing valuable insights into the potential role of the microbiome in maternal-fetal health. Our analysis revealed distinct microbial profiles in the maternal vaginal, gut, and placental microbiomes, underscoring the dynamic nature of microbial communities during pregnancy.

Consistent with previous research, the vaginal microbiome was predominantly dominated by Lactobacillus species, particularly Lactobacillus *crispatus* and Lactobacillus *iners*, which play a crucial role in maintaining vaginal homeostasis and preventing ascending infections. Our observation of a higher relative abundance of Gardnerella *vaginalis* in the vaginal microbiome being significantly associated with an increased risk of preterm birth corroborates existing evidence linking bacterial dysbiosis to adverse pregnancy outcomes. The presence of pathogenic bacteria such as Gardnerella *vaginalis* may disrupt the delicate balance of the vaginal microbiota, leading to inflammation and the onset of preterm labor.

In the gut microbiome, we observed a significant association between the Firmicutes to Bacteroidetes ratio and gestational diabetes. Participants with gestational diabetes exhibited a lower Firmicutes to Bacteroidetes ratio compared to non-diabetic participants, suggesting alterations in the gut microbial composition may contribute to the development of metabolic disorders during pregnancy. These findings are consistent with previous studies implicating gut dysbiosis in the pathogenesis of gestational diabetes, highlighting the potential for microbiome-targeted interventions in mitigating metabolic complications during pregnancy.

Furthermore, our analysis revealed a higher abundance of Proteobacteria in the placental microbiome of women who developed preeclampsia compared to those who did not. This observation suggests a potential link between placental microbial dysbiosis and the pathogenesis of preeclampsia, a hypertensive disorder of pregnancy associated with significant maternal and fetal morbidity. Although the exact mechanisms underlying this association remain unclear, it is conceivable that dysregulated immune responses triggered by microbial imbalances in the placenta may contribute to the systemic inflammation and endothelial dysfunction characteristic of preeclampsia.

Romero et al. conducted a study investigating the composition and stability of the vaginal microbiota in pregnant women compared to non-pregnant women [6]. They found that the vaginal microbiome of pregnant women was significantly different from that of non-pregnant women, with decreased Lactobacillus abundance and increased microbial diversity [7]. Our study aligns with Romero et al.'s findings regarding the dynamic changes in the vaginal microbiome during pregnancy. Both studies highlight the importance of Lactobacillus species in maintaining vaginal health and suggest that disruptions in the vaginal microbiome composition may contribute to adverse pregnancy outcomes.

Koren et al. investigated changes in the gut microbiome during pregnancy and its association with maternal metabolic changes. They observed alterations in gut microbial composition, characterized by decreased Firmicutes abundance and increased Proteobacteria abundance, which correlated with metabolic changes such as insulin resistance and inflammation [8]. Our study corroborates Koren et al.'s findings regarding the dynamic changes in the gut microbiome during pregnancy. Both studies highlight the potential role of gut dysbiosis in the development of metabolic disorders such as gestational diabetes and emphasize the importance of microbiome modulation in mitigating metabolic complications during pregnancy.

Antony et al. examined the association between the placental microbiome and pregnancy outcomes in preterm births. They found differences in placental microbial composition between preterm and term births, with a higher abundance of specific bacterial taxa such as Proteobacteria and Fusobacteria in preterm placentas [9]. Our study parallels Antony et al.'s findings regarding the association between placental microbial dysbiosis and adverse pregnancy outcomes. Both studies highlight the potential role of the placental microbiome in contributing to pregnancy complications such as preterm birth and underscore the importance of further research in this area.

Despite the compelling associations observed between maternal microbial composition and specific pregnancy outcomes, it is essential to acknowledge the limitations of our study. The observational nature of the study precludes establishing causality, and additional longitudinal studies are warranted to elucidate the temporal dynamics of microbial changes during pregnancy and their impact on maternal and neonatal health [10,11]. Moreover, factors such as maternal diet, lifestyle, and medication use may influence microbial composition and were not comprehensively accounted for in our analysis.

Conclusion:

Our study provides valuable insights into the influence of the maternal vaginal, gut, and placental microbiome on pregnancy outcomes. Through comprehensive analysis of microbial composition and its associations with specific pregnancy complications, we have contributed to the growing body of knowledge surrounding the role of the microbiome in maternal-fetal health. The dynamic changes observed in the vaginal microbiome, characterized by shifts in Lactobacillus abundance and microbial diversity, underscore its significance in maintaining vaginal health and preventing adverse pregnancy outcomes such as preterm birth. Similarly, alterations in the gut microbiome composition, particularly the Firmicutes to Bacteroidetes ratio, highlight its potential role in the pathogenesis of metabolic disorders such as gestational diabetes.

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