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THE IMPORTANCE OF VAGINAL MICROFLORA IN THE PATHOGENESIS OF PREMATURE RUPTURE OF MEMBRANES

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ABSTRACT: Premature rupture of membranes (PROM) remains a significant obstetric complication, contributing to neonatal morbidity and maternal infections. Emerging evidence suggests that alterations in the vaginal microflora play a critical role in the pathogenesis of PROM. This prospective, multicenter observational study aimed to evaluate the composition of vaginal microflora in pregnant women and its association with PROM. A total of 500 pregnant women, including 250 cases with PROM and 250 gestational age–matched controls, were enrolled between January 2018 and December 2020. Vaginal swabs were analyzed using culture methods and molecular techniques (16S rRNA sequencing) to characterize the microflora [1]. Results indicated a significant association between bacterial vaginosis–related organisms (e.g., Gardnerella vaginalis, Atopobium vaginae) and the occurrence of PROM, with an observed disruption in Lactobacillus-dominated flora. Multivariate logistic regression demonstrated that an abnormal vaginal microflora was an independent predictor of PROM (OR 2.8, 95% CI 1.9–4.2, $p < 0.001$). Our findings underscore the need for early screening and targeted interventions to restore normal vaginal flora, which may reduce the incidence of PROM and its associated complications [2].

Keywords: Vaginal microflora, premature rupture of membranes, PROM, bacterial vaginosis, obstetric infection, 16S rRNA sequencing

INTRODUCTION

Background - Premature rupture of membranes (PROM), defined as the rupture of fetal membranes before the onset of labor at term, poses significant risks to both the mother and the neonate. When PROM occurs before 37 weeks of gestation (preterm PROM), the risks are further compounded by prematurity-related complications. A growing body of literature has linked alterations in the vaginal microflora to the pathogenesis of PROM. A normal vaginal microbiome is typically dominated by Lactobacillus species, which help maintain a low pH and inhibit pathogenic bacterial colonization. In contrast, dysbiosis—characterized by the overgrowth of anaerobic bacteria such as Gardnerella vaginalis and Atopobium vaginae—has been implicated in the development of bacterial vaginosis, a known risk factor for PROM [3].

Rationale - The “ascending infection” theory posits that the migration of pathogenic bacteria from the lower genital tract into the uterine cavity can weaken the fetal membranes and trigger premature rupture. Despite numerous studies investigating the microbial etiology of PROM, the specific roles of individual bacterial species and the overall composition of the vaginal microflora in its pathogenesis remain incompletely understood. Identifying key microbial factors could pave the way for preventive strategies, including probiotic or antibiotic interventions

aimed at restoring a healthy vaginal microbiome [4].

Objective - This study was designed to: Characterize the vaginal microflora in pregnant women with and without PROM. Determine the association between specific microbial profiles and the incidence of PROM. Evaluate whether alterations in the vaginal microflora serve as an independent risk factor for PROM after adjusting for known confounders.

MATERIALS AND METHODS

Study Design and Setting - A prospective, multicenter observational study was conducted from January 2018 to December 2020 at three tertiary obstetric centers. The study was approved by the Institutional Review Boards of all participating institutions, and written informed consent was obtained from all participants.

Participants - A total of 500 pregnant women were enrolled and divided into two groups: PROM Group (n = 250): Pregnant women diagnosed with PROM before the onset of labor, confirmed by sterile speculum examination and amniotic fluid tests. Control Group (n = 250): Gestational age–matched pregnant women with intact membranes. Inclusion Criteria: Singleton pregnancy. Gestational age between 28 and 37 weeks. No antibiotic treatment in the two weeks preceding enrollment. Exclusion Criteria: Multiple gestations. Pre-existing immunosuppressive conditions. History of cervical cerclage or uterine anomalies [5].

Data Collection - Vaginal swabs were collected from all participants at the time of enrollment using sterile techniques. Samples were processed for: Culture Analysis: Identification of aerobic and anaerobic bacteria using standard microbiological methods. Molecular Analysis: DNA extraction followed by 16S rRNA gene sequencing to characterize bacterial community composition. In addition, clinical data, including maternal age, body mass index (BMI), obstetric history, and known risk factors for PROM, were recorded using a standardized questionnaire [6].

Outcome Measures - The primary outcome was the association between abnormal vaginal microflora (defined as a deviation from a Lactobacillus-dominated community) and PROM. Secondary outcomes included the identification of specific bacterial taxa linked to PROM and the evaluation of neonatal outcomes (birth weight, Apgar scores, and NICU admissions).

Statistical Analysis - Statistical analysis was performed using SPSS version 27.0. Continuous variables were expressed as mean ± standard deviation (SD) and compared using the Student's t-test, while categorical variables were compared using the chi-square test. Multivariate logistic regression was used to adjust for confounders and determine the independent effect of vaginal microflora on the risk of PROM. A p-value <0.05 was considered statistically significant.

RESULTS

Demographic and Baseline Characteristics - The mean maternal age was 29.8 ± 4.7 years in the PROM group and 29.5 ± 4.5 years in the control group (p = 0.42). Baseline BMI, parity, and gestational age at enrollment were comparable between groups (see Table 1).

Table 1. Baseline Characteristics of the Study Population (n = 500)

Variable	**PROM Group (n = 250)**	**Control Group (n = 250)**	**p-value**
Mean Age (years)	29.8 ± 4.7	29.5 ± 4.5	0.42
BMI (kg/m²)	25.1 ± 3.2	24.9 ± 3.0	0.55
Primiparity (%)	48%	50%	0.68

Gestational Age at Enrollment (weeks)	32.1 ± 2.3	32.3 ± 2.4	0.30

Vaginal Microflora Composition - Culture and 16S rRNA sequencing revealed significant differences in the vaginal microbial communities between the two groups: Lactobacillus Dominance: 72% of controls exhibited a Lactobacillus-dominated flora compared with 45% of the PROM group ($p < 0.001$). Bacterial Vaginosis–Associated Bacteria: The PROM group showed a higher prevalence of Gardnerella vaginalis, Atopobium vaginae, and Mobiluncus spp. ($p < 0.001$). Diversity Index: Shannon diversity index was significantly higher in the PROM group, indicating greater microbial diversity and dysbiosis ($p < 0.01$).

Association with PROM - Multivariate logistic regression analysis adjusted for maternal age, BMI, and smoking status demonstrated that an abnormal vaginal microflora (non-Lactobacillus dominant) was an independent predictor of PROM (OR 2.8, 95% CI 1.9–4.2, $p < 0.001$). Additionally, the presence of Gardnerella vaginalis was strongly associated with PROM (OR 3.1, 95% CI 2.0–4.8, $p < 0.001$).

Neonatal Outcomes - Neonatal outcomes were adversely affected in the PROM group: Birth Weight: The mean birth weight was significantly lower in the PROM group (2850 ± 420 g) compared with controls (3050 ± 380 g, $p = 0.001$). Apgar Scores: The 5-minute Apgar score was marginally lower in neonates born fter PROM (7.6 ± 0.8 vs. 8.1 ± 0.7, $p = 0.01$). NICU Admissions:
NICU admission rates were higher in the PROM group (15% vs. 8%, $p = 0.02$).

DISCUSSION

Principal Findings - This study confirms that alterations in the vaginal microflora are significantly associated with the occurrence of PROM. Pregnant women with PROM were more likely to have a disrupted vaginal ecosystem, characterized by reduced Lactobacillus dominance and an overgrowth of bacterial vaginosis–associated organisms. These dysbiotic changes were independently associated with an increased risk of PROM even after adjusting for known confounding factors [7].

Pathophysiological Implications - The integrity of the fetal membranes is believed to be compromised by ascending infections from the lower genital tract. In a healthy vaginal environment, Lactobacillus species produce lactic acid and bacteriocins that inhibit pathogenic bacteria. Dysbiosis, on the other hand, creates an inflammatory milieu that may weaken the collagen structure of the fetal membranes, predisposing them to premature rupture. Our findings support the hypothesis that targeting vaginal dysbiosis could serve as a preventive strategy against PROM.

Clinical Implications - Early screening for vaginal dysbiosis during pregnancy may identify women at higher risk for PROM. Interventions such as probiotic therapy, targeted antibiotic treatment, or vaginal microbiome modulation could potentially restore a healthy microflora and reduce the incidence of PROM. Additionally, understanding the microbial profiles associated with PROM can inform clinical decision-making and prompt closer monitoring of at-risk pregnancies.

Comparison with Previous Studies - Our results are consistent with previous studies linking bacterial vaginosis and abnormal vaginal microflora to PROM. However, the use of advanced molecular techniques in this study allowed for a more detailed characterization of the microbial community, underscoring the importance of microbial diversity as a factor in PROM pathogenesis. The strong association of Gardnerella vaginalis with PROM aligns with the findings of other recent investigations.

Limitations - This study has several limitations: Observational Design: The design precludes establishing a causal relationship between microflora alterations and PROM. Single-Time Point

Sampling: Microbial profiles were assessed at enrollment, and longitudinal changes were not evaluated. Potential Confounders: Although multivariate analysis was performed, residual confounding cannot be entirely ruled out.

Future Directions - Future research should focus on longitudinal studies to monitor changes in the vaginal microflora throughout pregnancy and assess the impact of therapeutic interventions on PROM risk. Randomized controlled trials evaluating probiotic or antimicrobial therapies aimed at restoring normal vaginal flora are warranted. Moreover, investigations into the molecular mechanisms linking microbial dysbiosis and membrane integrity may provide further insights into PROM pathogenesis.

CONCLUSION

Our findings indicate that abnormal vaginal microflora, particularly the reduction of Lactobacillus dominance and overrepresentation of bacterial vaginosis–associated organisms, is significantly associated with an increased risk of PROM. Early identification and targeted correction of vaginal dysbiosis may represent a promising strategy to reduce the incidence of PROM and improve perinatal outcomes. This study highlights the importance of integrating microbial diagnostics into prenatal care to identify at-risk pregnancies and tailor preventive interventions accordingly.

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