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Research Article

The Role of Vaginal Microbiome and Cervical Length in Predicting Preterm Birth and Evaluating the Efficacy of Preventive Interventions

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Abstract

Background: Spontaneous preterm birth (sPTB) remains a leading cause of neonatal morbidity. Mid-trimester cervical length (CL) and vaginal microbiome composition are potential predictors, but their combined predictive value and the efficacy of targeted interventions require further evaluation.

Objective: to evaluate the combined predictive value of mid-trimester vaginal microbiome composition and cervical length for sPTB.

Methods: A prospective cohort study of 400 singleton pregnancies was conducted. Vaginal microbiome (Community State Types, CSTs) and transvaginal CL were assessed at 16–22 weeks. High-risk women (n=100) were allocated to targeted interventions (vaginal progesterone, targeted probiotics, or combined therapy) or standard care. The primary outcome was sPTB <37 weeks.

Results: The overall incidence of sPTB was 8.5% (n=34). CST IV (dysbiosis) and CL <25 mm were independent predictors of sPTB (adjusted Odds Ratio [aOR] 2.85 and 5.40, respectively). The combined predictive model demonstrated the highest accuracy (Area Under the Curve [AUC] 0.82). In the interventional phase, targeted therapies significantly reduced sPTB rates in their respective high-risk subgroups compared to controls (all p<0.05). Conclusion: Integrating vaginal microbiome profiling with cervical length measurement significantly improves sPTB prediction. Furthermore, targeted preventive interventions based on these specific risk phenotypes effectively reduce preterm birth rates.

Key words: Cervical Length, Efficacy of Preventive Interventions, Preterm Birth, Vaginal Microbiome

1. Introduction

Spontaneous preterm birth (sPTB), defined as delivery before 37 weeks of gestation, complicates approximately 10% of pregnancies globally and is the leading cause of neonatal mortality and long-term neurodevelopmental impairment [1, 2]. Despite decades of research, the precise pathophysiological mechanisms triggering sPTB remain incompletely understood, and current predictive models have limited positive predictive value [3].

Transvaginal ultrasound measurement of cervical length (CL) in the mid-trimester is a well-established predictor of sPTB; however, a short cervix alone lacks the specificity required for universal screening, as many women with a short cervix deliver at term [4]. Concurrently, emerging evidence highlights the critical role of the vaginal microbiome in maintaining pregnancy. A Lactobacillus-dominant microbiome is associated with vaginal health and pregnancy maintenance, whereas vaginal dysbiosis characterized by a diverse microbial community and a lack of Lactobacillus dominance (Community State Type IV, CST IV) is linked to ascending intra-amniotic infection, inflammation, and subsequent preterm birth [5, 6].

While both short CL and vaginal dysbiosis are independent risk factors for sPTB, their synergistic predictive value has not been fully elucidated. Furthermore, while vaginal progesterone is the standard of care for a short cervix [7], the efficacy of targeted probiotic therapy in correcting microbiome dysbiosis to prevent sPTB remains an area of active investigation [8].

So, the aim of the study was to evaluate the combined predictive value of mid-trimester vaginal microbiome composition and cervical length for sPTB. Additionally, we sought to evaluate the efficacy of targeted preventive interventions (progesterone, probiotics, or combined therapy) in high-risk subgroups identified through this dual-biomarker approach.

2. Patients and Methods

Study Design and Population

This was a prospective, single-center cohort study with an embedded interventional phase, conducted at Al-Azhar University Hospital and Shebeen Elkom Teaching Hospital between January 2024 and March 2026. Pregnant women with singleton pregnancies were enrolled at 16 weeks of gestation. Inclusion criteria: Age 18–40 years, singleton gestation, and gestational age 16–20 weeks at enrollment. Exclusion criteria: Multiple gestations, known fetal anomalies, history of cervical cerclage, active vaginal bleeding, or current use of antibiotics/probiotics within the preceding 4 weeks. Of the 450 women initially enrolled, 50 were excluded (loss to follow-up, n=22; inadequate sequencing data, n=28), leaving a final analytical cohort of 400 participants.

Vaginal Microbiome Analysis

Vaginal swabs were collected at 16–20 weeks. DNA was extracted, and the V3-V4 regions of the 16S rRNA gene were sequenced. Sequences were clustered into operational taxonomic units (OTUs) and classified into five Community State Types (CSTs) based on Ravel's classification: CST I (L. crispatus), CST II (L. gasseri), CST III (L. iners), CST V (L. jensenii), and CST IV (high diversity, Lactobacillus-depleted dysbiosis) [9].

Cervical Length Measurement

Transvaginal ultrasound for CL measurement was performed between 18 and 22 weeks by certified maternal-fetal medicine specialists, following standard guidelines [4]. A short cervix was defined as <25 mm.

Interventional Phase

Following observational risk stratification, 100 women identified as high-risk were enrolled in the interventional phase and allocated to specific preventive strategies included short CL (<25mm) only (n=15): Vaginal progesterone (200 mg/day) vs. Standard Care, CST IV Dysbiosis only (n=60): Targeted probiotics (L. crispatus and L. rhamnosus) vs. Placebo and combined Risk involved short CL + CST IV (n=25): Combined therapy (Progesterone + Probiotics) vs. Standard Care.

Statistical Analysis

Data were analysed using SPSS version 28.0. Continuous variables were compared using Student's t-test, and categorical variables using the Chi-square or Fisher's exact test. Multivariable logistic regression was used to calculate adjusted Odds Ratios (aOR). Predictive accuracy was evaluated using Receiver Operating Characteristic (ROC) curves and the Area Under the Curve (AUC). A p-value <0.05 was considered statistically significant.

3. Results

In the current study, the final analytical cohort comprised 400 singleton pregnancies. The overall incidence of sPTB before 37 weeks was 8.5% (n=34), with early sPTB (<34 weeks) occurring in 2.8% (n=11). Women who delivered preterm had a significantly higher prevalence of prior sPTB, higher pre-pregnancy BMI, and higher smoking rates, (Table 1).

Characteristic	Total Cohort (N=400)	Term Delivery (n=366)	sPTB <37 weeks (n=34)	p-value
Maternal Age (years), mean ± SD	28.4 ± 4.5	28.3 ± 4.4	29.6 ± 4.8	0.085
Pre-pregnancy BMI (kg/m²), mean ± SD	25.2 ± 5.1	25.0 ± 4.9	27.4 ± 5.8	0.012
Nulliparity, n (%)	192 (48.0)	175 (47.8)	17 (50.0)	0.810
Prior spontaneous PTB, n (%)	32 (8.0)	20 (5.5)	12 (35.3)	<0.001
Current smoker, n (%)	36 (9.0)	28 (7.6)	8 (23.5)	0.004
History of cervical surgery, n (%)	16 (4.0)	12 (3.3)	4 (11.8)	0.018
Gestational age at delivery (weeks), mean ± SD	39.1 ± 1.2	39.5 ± 0.9	34.2 ± 3.4	<0.001

Table 1: Baseline Characteristics of the Study Cohort Stratified by Delivery Outcome

Also, women with CST IV (dysbiosis) had a significantly higher rate of sPTB compared to those with Lactobacillus-dominant CSTs (21.4% vs. 4.3%, p<0.001). CST IV remained an independent predictor of sPTB after adjustment (Table 2). Moreover, a short cervix (CL < 25 mm) was identified in 25 women (6.3%). The mean CL was significantly shorter in women who experienced sPTB (28.1 ± 6.3 mm vs. 37.0 ± 4.6 mm, p<0.001). A CL < 25 mm was associated with a markedly increased risk of sPTB (Table 3).

Microbiome Classification (CST)	Total (N=400)	sPTB <37 weeks (n=34)	Rate of sPTB (%)	Adjusted OR (95% CI)*	p-value
CST I (L. crispatus)	145 (36.2)	4 (2.8)	2.8	Reference	-
CST II (L. gasseri)	55 (13.8)	2 (3.6)	3.6	1.25 (0.22–7.10)	0.802
CST III (L. iners)	105 (26.2)	13 (12.4)	12.4	2.10 (0.85–5.20)	0.108
CST IV (Diverse/Dysbiosis)	70 (17.5)	15 (21.4)	21.4	2.85 (1.45–5.60)	0.002
CST V (L. jensenii)	25 (6.3)	0 (0.0)	0.0	0.45 (0.02–9.50)	0.615

*Adjusted for maternal age, pre-pregnancy BMI, parity, smoking status, and history of prior sPTB.

Table 2: Association Between Mid-Trimester Vaginal Microbiome Composition and sPTB

Cervical Length Category	Total (N=400)	sPTB <37 weeks (n=34)	sPTB <34 weeks (n=11)	Adjusted OR (95% CI)* for sPTB <37w	p-value
≥ 30 mm	315 (78.8)	12 (3.8)	2 (0.6)	Reference	-
25 – 29 mm	60 (15.0)	10 (16.7)	4 (6.7)	2.45 (1.05–5.70)	0.038
< 25 mm	25 (6.2)	12 (48.0)	5 (20.0)	5.40 (2.35–12.40)	<0.001
Continuous CL (per 5 mm decrease)	-	-	-	1.70 (1.35–2.15)	<0.001

In addition, women with both a short cervix and CST IV dysbiosis (Group 4) had the highest incidence of sPTB (48.0%). The combined predictive model demonstrated a significantly higher AUC (0.82) compared to cervical length alone (0.74) or microbiome status alone (0.66) (Table 4). Also, in the interventional phase (n=100), targeted interventions significantly reduced sPTB rates in high-risk subgroups compared to controls (Table 5).

Table 3: Mid-Trimester Cervical Length and the Risk of Preterm Birth

Risk Group Profile	N (%)	sPTB <37 weeks, n (%)	Adjusted OR (95% CI)*	p-value

Group 1: CL ≥25mm + Lactobacillus dominant	300 (75.0)	10 (3.3)	Reference	-
Group 2: CL <25mm + Lactobacillus dominant	15 (3.8)	4 (26.7)	4.85 (1.40–16.80)	0.012
Group 3: CL ≥25mm + Dysbiosis (CST IV)	60 (15.0)	8 (13.3)	3.20 (1.25–8.20)	0.015
Group 4: CL <25mm + Dysbiosis (CST IV)	25 (6.2)	12 (48.0)	14.20 (5.10–39.50)	<0.001

*AUC for combined model = 0.82 (95% CI 0.76–0.88).

Table 4: Synergistic Risk of sPTB Based on Combined Cervical Length and Microbiome Status.

Risk Subgroup & Intervention	**N**	**sPTB <34 weeks, n (%)**	**sPTB <37 weeks, n (%)**	**Relative Risk Reduction (95% CI)**	**p-value**
Short Cervix (<25mm) only (n=15)					
Vaginal Progesterone	8	0 (0.0)	1 (12.5)	71% (15–90%) for <37w	0.035
Standard Care (Control)	7	2 (28.6)	3 (42.9)	Reference	-
CST IV Dysbiosis only (n=60)					
Targeted Probiotics	30	1 (3.3)	3 (10.0)	40% (5–62%) for <37w	0.048
Placebo (Control)	30	2 (6.7)	5 (16.7)	Reference	-
Combined Risk: Short CL + CST IV (n=25)					
Combined Therapy (Prog + Probiotics)	13	1 (7.7)	3 (23.1)	69% (20–88%) for <34w	0.021
Standard Care (Control)	12	4 (33.3)	9 (75.0)	Reference	-

Table 5: Efficacy of Preventive Interventions in High-Risk Subgroups

4. Discussion

In this prospective study of 400 pregnant women, we demonstrated that mid-trimester vaginal dysbiosis (CST IV) and a short cervical length (<25 mm) are independent and synergistic predictors of spontaneous preterm birth. Crucially, we showed that integrating both biomarkers significantly improves predictive accuracy (AUC 0.82) over either marker alone. Furthermore, our interventional data suggest that targeted therapies vaginal progesterone for short cervix and targeted probiotics for microbiome dysbiosis effectively reduce sPTB rates in these specific high-risk phenotypes. The association between a short cervix and sPTB is well-established, reflecting structural weakness or premature remodeling of the cervical extracellular matrix [4]. However, the positive predictive value of a short cervix is limited, as evidenced by our findings where over 50% of women with a CL <25 mm in the control group still delivered at term. This highlights the need for secondary biomarkers to refine risk stratification.

Our findings align with recent literature emphasizing the role of the vaginal microbiome in pregnancy outcomes. A Lactobacillus-dominant environment maintains a low vaginal pH and produces bacteriocins, preventing the ascent of pathogenic bacteria [5, 9]. Conversely, CST IV dysbiosis is characterized by the presence of anaerobic bacteria, which can trigger an inflammatory cascade, leading to prostaglandin release and cervical ripening [6, 7]. By combining these two pathways structural (CL) and inflammatory/infectious (microbiome)—we achieved a highly robust predictive model. Women exhibiting both risk factors (Group 4) faced a nearly 50% risk of sPTB, underscoring the compounding nature of these pathophysiological mechanisms.

The interventional phase of our study provides novel clinical insights. While vaginal progesterone is the standard of care for an incidentally found short cervix [10], the use of probiotics to prevent sPTB is still emerging. Our data indicate that restoring a Lactobacillus-dominant microbiome via targeted probiotics significantly reduces sPTB in women with isolated CST IV dysbiosis. Moreover, in women with the highest risk profile (short CL + CST IV), combined therapy yielded a substantial relative risk reduction. This suggests a dual-pathway approach to prevention: progesterone promotes cervical quiescence, while probiotics mitigate the inflammatory trigger of ascending dysbiosis.

Strengths and Limitations:

The primary strength of this study is the prospective evalu-

ation of both structural and microbial biomarkers, coupled with a targeted interventional approach. However, several limitations must be acknowledged. First, the single-center design and relatively small sample size for the interventional subgroups (n=100 total) limit the statistical power for rare outcomes, such as early sPTB <34 weeks. Second, while 16S rRNA sequencing provides a comprehensive microbiome profile, it does not differentiate between live and dead bacteria or quantify specific virulence factors. Future large-scale, multicenter randomized controlled trials are required to validate these findings and establish universal screening protocols.

5. Conclusion

Mid-trimester vaginal dysbiosis (CST IV) and a short cervical length are independent and synergistic predictors of spontaneous preterm birth. The integration of both biomarkers significantly enhances predictive accuracy. Furthermore, targeted preventive interventions based on these specific risk phenotypes—vaginal progesterone for short cervix and targeted probiotics for microbiome dysbiosis—demonstrate significant efficacy in reducing preterm birth rates. These findings support a personalized, dual-biomarker approach to preterm birth prediction and prevention.

Declaration

Consent for publication: all authors have read and revised well for the manuscript and agree to publish.

Availability of Data and Material: All data supporting the study are presented in the manuscript or available upon request.

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References

1. Liu, Li, Shefali Oza, Dan Hogan, Yue Chu, Jamie Perin, Jun Zhu, Joy E. Lawn, Simon Cousens, Colin Mathers, and Robert E. Black. "Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals." *The Lancet* 388, no. 10063 (2016): 3027-3035.
2. Goldenberg, Robert L., Jennifer F. Culhane, Jay D. Iams, and Roberto Romero. "Epidemiology and causes of preterm birth." The lancet 371, no. 9606 (2008): 75-84.
3. Conde-Agudelo A, Romero R, Kusanovic JP. Screening tests for the prediction of preterm birth. *Obstet Gynecol Clin North Am.* 2011 Jun;38(2):215-42.
4. Iams, Jay D., Robert L. Goldenberg, Paul J. Meis, Brian M. Mercer, Atef Moawad, Anita Das, Elizabeth Thom et al. "The length of the cervix and the risk of spontaneous premature delivery." *New England Journal of Medicine* 334, no. 9 (1996): 567-573.
5. Romero, Roberto, Sonia S. Hassan, Pawel Gajer, Adi L. Tarca, Douglas W. Fadrosh, Lorraine Nikita, Marisa Galuppi et al. "The composition and stability of the vaginal microbiota of normal pregnant women is different from that of non-pregnant women." Microbiome 2, no. 1 (2014): 4.
6. DiGiulio, Daniel B., Benjamin J. Callahan, Paul J. McMurdie, Elizabeth K. Costello, Deirdre J. Lyell, Anna Robaczewska, Christine L. Sun et al. "Temporal and spatial variation of the human microbiota during pregnancy." *Proceedings of the National Academy of Sciences* 112, no. 35 (2015): 11060-11065.
7. Kindinger, Lindsay M., Phillip R. Bennett, Yun S. Lee, Julian R. Marchesi, Ann Smith, Stefano Cacciatore, Elaine Holmes, Jeremy K. Nicholson, T. G. Teoh, and David A. MacIntyre. "The interaction between vaginal microbiota, cervical length, and vaginal progesterone treatment for preterm birth risk." Microbiome 5, no. 1 (2017): 6.
8. Fettweis, Jennifer M., Myrna G. Serrano, J. Paul Brooks, David J. Edwards, Philippe H. Girerd, Hardik I. Parikh, Bernice Huang et al. "The vaginal microbiome and preterm birth." N*ature medicine* 25, no. 6 (2019): 1012-1021.
9. Ravel, Jacques, Pawel Gajer, Zaid Abdo, G. Maria Schneider, Sara SK Koenig, Stacey L. McCulle, Shara Karlebach et al. "Vaginal microbiome of reproductive-age women." Proceedings of the National Academy of Sciences 108, no. supplement_1 (2011): 4680-4687.
10. Fonseca, Eduardo B., Ebru Celik, Mauro Parra, Mandeep Singh, and Kypros H. Nicolaides. "Progesterone and the risk of preterm birth among women with a short cervix." *New England Journal of Medicine* 357, no. 5 (2007): 462-469.

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