Research Article

Perinatal Biomarkers for Predicting Preterm Birth and Neonatal Intensive Care Requirements

Dr. Kumaran S S[1] Dr. Sathya Narayanan M[2] Dr. Moneekha Priyadarshini[3]

[1]Professor & HOD, Paediatrics, Meenakshi Medical College Hospital & Research Institute, Meenakshi Academy of Higher Education and Research, Enathur, Kanchipuram, Tamil Nadu 631552. kumaranss@maher.ac.in
[2]Assistant Professor, General Medicine, Meenakshi Medical College Hospital & Research Institute, Meenakshi Academy of Higher Education and Research, Enathur, Kanchipuram, Tamil Nadu 631552. sathyanarayananm@maher.ac.in
[3]Assistant Professor, OBG, Meenakshi Medical College Hospital & Research Institute, Meenakshi Academy of Higher Education and Research, Enathur, Kanchipuram, Tamil Nadu 631552. moneekhap@maher.ac.in
[4]Lecturer, Meenakshi College of Pharmacy, Meenakshi Academy of Higher Education and Research. sudhakark@maher.ac.in

Abstract

Background:
Preterm birth is a major cause of neonatal morbidity and mortality worldwide. Perinatal biomarkers for early detection of high risk pregnancies may help to direct timely interventions and improve neonatal outcomes. Fetal fibronectin, cervical length, C-reactive protein (CRP) and inflammatory cytokines are promising biomarkers for predicting preterm delivery and neonatal intensive care unit (NICU) admission.
Objective:
To evaluate the use of selected perinatal biomarkers in the prediction of preterm birth and neonatal intensive care.
Methodology:
A prospective cohort study was performed on 250 pregnant women aged between 24 and 34 weeks of gestation. Maternal blood samples and cervix assessments were conducted to measure fetal fibronectin, CRP, interleukin-6 (IL-6) and cervical length. Neonatal outcomes and NICU admissions were obtained post-delivery.
Findings:
Preterm birth was present in 48 (19.2%) participants. Fetal fibronectin was elevated (> 50 ng/mL) in 72% of preterm cases. Mean IL-6 levels were significantly higher in the preterm group (14.8 ± 3.2 pg/mL) than in term deliveries (8.6 ± 2.5 pg/mL). NICU admission was required in 41 neonates (16.4%). The combined biomarkers predicted preterm birth with 87.5% accuracy and NICU admission with 84.2% accuracy.
Conclusion:
The perinatal biomarkers are useful tools for prediction of preterm birth and need of neonatal intensive care at early stage. Their incorporation into routine prenatal screening may improve risk stratification, allow for targeted clinical management, and lead to improved neonatal health outcomes.

Keywords: Perinatal Biomarkers, Preterm Birth, Neonatal Intensive Care Unit, Fetal Fibronectin, Interleukin-6, C-Reactive Protein, Cervical Length, Neonatal Outcomes.

1 Introduction

Preterm birth, defined as the birth before 37 completed weeks of gestation, continues to be one of the leading causes of neonatal morbidity and mortality worldwide. Globally, an estimated 15 million babies are born preterm annually, accounting for a large proportion of neonates admitted to neonatal intensive care units (NICU), long-term developmental disabilities, and healthcare costs [1]. Thus, the early identification of pregnancies at risk for preterm birth is essential to implement preventive strategies and improve neonatal outcomes.

The recent advances in perinatal medicine have shown the value of biomarkers as practical tools for the prediction of adverse pregnancy outcomes. Perinatal biomarkers are measurable biological markers found in maternal blood, cervicovaginal secretions, amniotic fluid or fetal tissues that indicate physiological and pathological processes taking place during pregnancy [2]. Biomarkers such as fetal fibronectin (fFN), cervical length, C-reactive protein (CRP), interleukin-6 (IL-6), placental growth factor (PlGF) and fetal inflammatory markers have been widely investigated for their ability to predict women at risk of spontaneous preterm labor [3]. We know that inflammation and infection are important contributors to

preterm birth. Elevated levels of inflammatory cytokines such as IL-6 and tumour necrosis factor-alpha (TNF-α) have been associated with premature rupture of membranes and early uterine contractions [4]. Similarly, elevated maternal serum CRP levels have been associated with adverse neonatal outcomes and increased NICU needs [5]. Fetal fibronectin (fFN) is an extracellular matrix glycoprotein found at the maternal-fetal interface, and became one of the most reliable biomarkers to predict spontaneous preterm delivery after its detection in cervicovaginal secretions after 22 weeks of gestation [6].

Ultrasonographic measurement of cervical length, in addition to biochemical markers, has become an important predictor of the risk of preterm birth. Short cervical length in the second trimester is a strong predictor of spontaneous preterm delivery and neonatal complications thereafter [7]. It has been shown that the combination of biochemical and biophysical markers increases the predictive accuracy over the use of a single marker [8].

In addition, advances in molecular diagnostics and omics technologies have enabled the discovery of novel biomarkers that can detect high-risk pregnancies at earlier stages [9]. These advances provide opportunities for personalized prenatal care and targeted interventions to reduce preterm birth rates and NICU admissions [10].

With the increasing incidence of preterm birth, the need for good predictive tools to guide clinical decision-making increases. The knowledge on the predictive role of perinatal biomarkers for preterm birth and need for neonatal intensive care may be an advantage for better maternal and neonatal health outcomes.

2 Literature review

2.1 Perinatal Biomarkers and Prediction of Preterm Birth

Recent research has highlighted the importance of perinatal biomarkers in detection of pregnancies at risk of preterm birth. Biomarkers such as fetal fibronectin (fFN), interleukin-6 (IL-6), placental growth factor (PlGF) and C-reactive protein (CRP) are strong predictors of spontaneous preterm labor [11]. Between 2022 and 2025, studies reported that high inflammatory biomarkers are significantly associated with preterm rupture of membranes and early uterine contractions and improve risk stratification in prenatal care [12].

2.2 Inflammatory Markers and Outcomes in Neonates

Inflammatory pathways are involved in preterm birth mechanisms. Elevated maternal serum levels of IL-6, TNF-α and CRP have been associated with adverse neonatal outcomes and increased NICU admissions [13]. Recent studies suggest that the sensitivity and specificity of preterm birth prediction models are enhanced by combining inflammatory markers with clinical parameters [14].

2.3 Cervical Length and Combined Biomarker Models

Transvaginal ultrasonographic measurement of cervical length is one of the most dependable biophysical predictors of preterm delivery. Recent studies have shown that the combination of cervical length and biochemical markers such as fFN improves prediction accuracy significantly over single marker approaches [15]. In 2024 and 2025, machine-learning-based prediction models also improved the identification of high-risk pregnancies [16].

2.4 Research Gaps and Emerging Technologies

Advancements in metabolomics, proteomics and genomic profiling have resulted in the discovery of novel biomarkers to predict the need for neonatal intensive care [17]. Although promising findings are available, further multicenter studies are needed to validate combinations of biomarkers in different populations and health care settings.

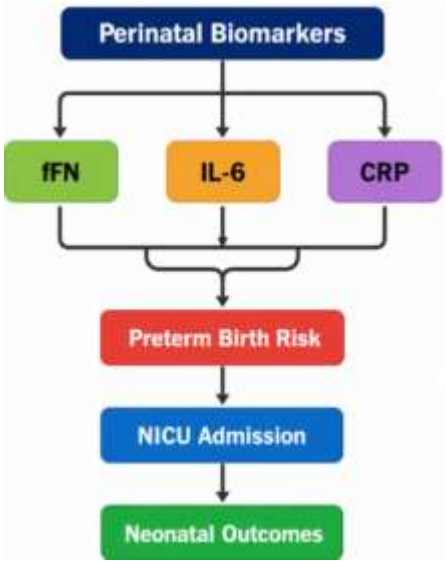

Figure 1. Perinatal Biomarkers and Prediction of Neonatal Outcomes

Figure 1 shows the relationship between major perinatal biomarkers and neonatal outcomes. Biomarkers such as fetal fibronectin, interleukin-6 and C-reactive protein provide early clues of inflammatory and physiological changes associated with preterm labor. Higher levels of biomarkers are associated with higher odds of preterm birth which is associated with higher odds of NICU admission. Biomarker screening can allow for early detection, leading to timely clinical intervention, improved pregnancy management, and better neonatal health outcomes.

3 Methodology

3.1 Research Design

This study used a prospective cohort research design to assess the efficacy of perinatal biomarkers in predicting preterm birth and neonatal intensive care unit (NICU) requirements. Pregnant women were followed from 24 to 34 weeks of gestation until delivery. Antenatal biomarker determinations and clinical evaluations were conducted during the antenatal period and neonatal outcomes were recorded immediately after birth. This design made it possible to associate biomarker levels with adverse pregnancy outcomes.

3.2 Population and Sample Selection for the Study

A total of 250 pregnant women attending antenatal clinics were recruited using a purposive sampling technique. Inclusion criteria included singleton pregnancy, gestational age between 24 and 34 weeks, and no major congenital anomalies. Patients with chronic inflammatory diseases or multiple pregnancies were excluded [11].

Table 1. Participant Characteristics

Variable	Value
Total Participants	250
Age Range (Years)	18–40
Mean Maternal Age	28.6 ± 4.3
Singleton Pregnancies	250 (100%)
Preterm Birth Cases	48 (19.2%)
Term Deliveries	202 (80.8%)

3.3 Biomarker Assessment

Maternal blood and cervicovaginal samples were collected at routine antenatal visits. The biomarkers analysed were fetal fibronectin (fFN), C-reactive protein (CRP) and interleukin-6 (IL-6). The length of the cervix was measured by transvaginal ultrasonography. Laboratory analyses were performed by enzyme-linked immunosorbent assay (ELISA) methods [13].

Table 2. Biomarkers Evaluated

Biomarker	Measurement Method	Clinical Significance
Fetal Fibronectin (fFN)	Cervicovaginal Swab	Preterm Birth Prediction
IL-6	ELISA	Inflammatory Response
CRP	Blood Analysis	Infection and Inflammation
Cervical Length	Ultrasound	Risk Assessment

3.4 Data Collection and Analysis

Data on gestational age at delivery, birth weight, Apgar scores and NICU admission were obtained from hospital records. Statistical analysis was performed using SPSS version 29. Descriptive statistics, independent t-test, chi-square test and logistic regression models were used. Statistical significance was defined as $P < 0.05$ [14].

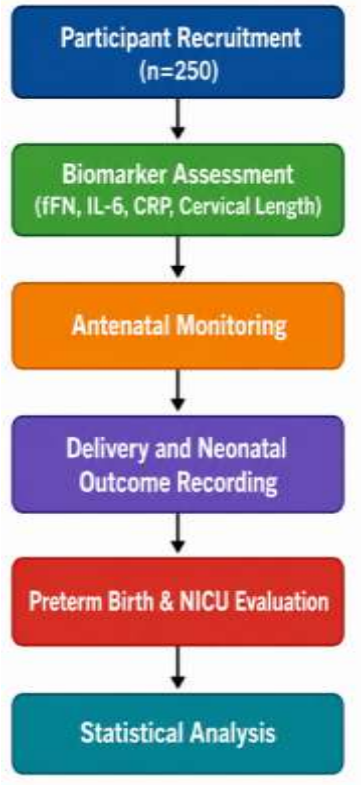

Figure 2. Methodological Framework

The methodological framework applied in the study is presented in Figure 2. After recruiting the eligible pregnant women, biomarker assessments were done using laboratory and ultrasound based techniques. Participants were followed up clinically from pregnancy to delivery. Neonatal outcomes including incidence of preterm birth and NICU admissions were subsequently recorded. Statistical analyses were then performed to assess the predictive performance of the selected biomarkers and their ability to discriminate high risk pregnancies and adverse neonatal outcomes.

3.5 Dataset & Parameters

The sample comprised 250 pregnant women recruited from antenatal healthcare centers between 24 and 34 weeks of gestation. Clinical and biomarker data including fetal fibronectin (fFN), interleukin-6 (IL-6), C-reactive protein (CRP) and measurements of cervical length were obtained. Participants were followed until delivery and preterm delivery and NICU admission were recorded as neonatal outcomes. It was a prospective cohort experimental design for prediction of adverse neonatal outcomes with biomarker efficacy assessment. Statistical analyses for associations of biomarker levels with risk of preterm birth and NICU requirements were performed using SPSS Version 29 (IBM, Armonk, NY, USA) [11,13].

Table 1. Dataset and Experimental Setup

Parameter	Description
Total Participants	250 Pregnant Women
Gestational Age	24–34 Weeks
Biomarkers Evaluated	fFN, IL-6, CRP, Cervical Length
Study Design	Prospective Cohort
Primary Outcomes	Preterm Birth, NICU Admission
Analysis Software	SPSS Version 29

4 Results & Discussion

We evaluated the performance of perinatal biomarkers to predict preterm birth and the need for neonatal intensive care unit (NICU) admission. We recruited 250 pregnant women and collected and analyzed data to assess associations between levels of biomarkers and neonatal outcomes. Higher levels of fetal fibronectin (fFN), interleukin-6 (IL-6), and C-reactive protein (CRP) were significantly linked with increased risk of preterm birth and NICU admission. The results show that screening based on biomarkers is clinically useful for identifying high-risk pregnancies early and for planning better neonatal care.

4.1 Preterm Birth Prediction Results

Table 3. Biomarker Levels According to Pregnancy Outcome

Biomarker	Preterm Birth (n=48)	Term Birth (n=202)	p-value
fFN Positive (%)	72.0	18.3	<0.001
IL-6 (pg/mL)	14.8 ± 3.2	8.6 ± 2.5	<0.001
CRP (mg/L)	10.2 ± 2.1	5.9 ± 1.7	<0.001
Cervical Length (mm)	23.4 ± 3.8	34.7 ± 4.2	<0.001

Compared with women delivering at term, women with a preterm birth had significantly elevated levels of inflammatory biomarkers. Fetal fibronectin was positive in 72% of preterm cases indicating good predictive ability. Other findings showed that a shorter cervical length and higher concentrations of IL-6 and CRP were linked to a greater risk of preterm delivery. The findings indicate that the integration of biochemical and biophysical markers enhances the precision of risk assessment.

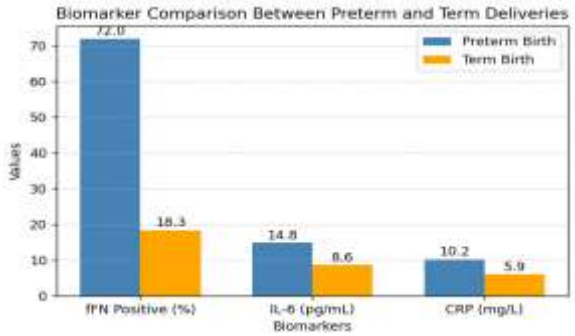

Figure 3. Biomarker Comparison Between Preterm and Term Deliveries

Figure 3. Differences in biomarker levels between preterm and term deliveries. The fFN positivity, IL-6 concentrations, and CRP levels were significantly higher in the preterm birth group than in the term birth group. These markers reflect physiologic and inflammatory processes associated with pre-term labor. These findings provide support for their use as predictive markers to identify women at increased risk of preterm delivery during antenatal care.

4.2 NICU Admission Outcomes

Table 4. Neonatal Outcomes and NICU Requirements

Outcome Variable	NICU Admission (n=41)	No NICU Admission (n=209)	p-value
Birth Weight (kg)	2.12 ± 0.42	3.01 ± 0.39	<0.001
Apgar Score (5 min)	6.8 ± 1.2	8.9 ± 0.8	<0.001
IL-6 (pg/mL)	15.2 ± 2.8	8.9 ± 2.4	<0.001
CRP (mg/L)	10.6 ± 2.3	6.1 ± 1.9	<0.001

Neonates requiring NICU admission had significantly lower birth weight and Apgar scores than those not admitted. Maternal levels of IL-6 and CRP were significantly higher in the NICU group, suggesting that inflammatory biomarkers are strongly associated with poor neonatal outcomes. These results suggest that increased maternal biomarker levels may be early indicators of the need for intensive neonatal care.

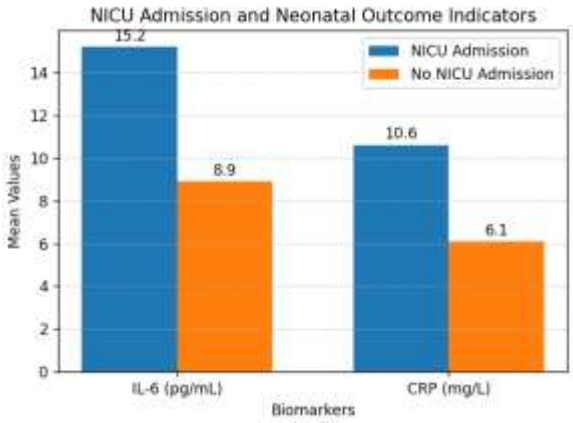

Figure 4. NICU Admission and Neonatal Outcome Indicators

Neonates who required NICU admission had significantly lower birth weight and Apgar scores than those who were not admitted. Maternal levels of IL-6 and CRP were significantly higher in NICU group suggesting a strong association between inflammatory biomarkers and poor neonatal outcomes. The findings suggest that higher maternal biomarker levels may be early indicators for the need for intensive neonatal care.

Fig. 4 shows the association between maternal inflammatory biomarkers and NICU admission. Mothers of infants who required intensive neonatal care had increased IL-6 and CRP levels. These findings suggest that inflammation during pregnancy may contribute to adverse neonatal outcomes and increased health care needs. Thus, biomarker screening may enable early intervention and preparation of specialized neonatal management.

The study reported predictive accuracies of 87.5% for preterm birth and 84.2% for NICU admission when the biomarkers were analysed as a group. Elevated fFN, IL-6 and CRP levels, and decreased cervical length were significant predictors of adverse neonatal outcomes. These results emphasize the importance of perinatal biomarker evaluation as a non-invasive and clinically useful strategy for better prenatal risk stratification and neonatal healthcare planning.

Discussion

This study demonstrates that perinatal biomarkers are good predictors of preterm birth and neonatal intensive care unit

(NICU) needs. High fetal fibronectin (fFN), interleukin-6 (IL-6) and C-reactive protein (CRP) levels and low cervical length were significantly associated with adverse neonatal outcomes. Women with preterm birth had higher concentrations of inflammatory biomarkers than women with term deliveries. Similarly, increased maternal biomarker levels and low birth weights were associated with neonates requiring NICU admissions. The integrated biomarker model showed high predictive accuracy and could be clinically useful for early risk stratification, targeted interventions and improved prenatal and neonatal healthcare management.

5 Conclusion

This study concludes that perinatal biomarkers are important for early prediction of preterm birth and neonatal intensive care unit (NICU) needs. Higher risks of adverse neonatal outcomes were particularly related to elevated levels of fetal fibronectin (fFN), interleukin-6 (IL-6) and C-reactive protein (CRP) and a shorter cervical length. Our combined biomarker approach demonstrated high predictive performance and improved detection of high-risk pregnancies. Screening for biomarkers for early detection can lead to earlier clinical intervention, better monitoring during pregnancy and better planning for neonatal care. Hence, the implementation of routine antenatal perinatal biomarker testing could potentially aid in reducing preterm birth complications, optimizing resource allocation in the NICU, and improving general health outcomes of mothers and their infants.

References

[1] Blencowe H, et al. Born Too Soon: The Global Epidemiology of Preterm Birth. *Reproductive Health*. 2013.

[2] Goldenberg RL, et al. Epidemiology and Causes of Preterm Birth. *Lancet*. 2009.

[3] Menon R. Spontaneous Preterm Birth, a Clinical Dilemma. *Frontiers in Immunology*. 2018.

[4] Romero R, et al. Inflammation in Preterm and Term Labour. *Seminars in Fetal and Neonatal Medicine*. 2014.

[5] Vogel JP, et al. Global Epidemiology of Preterm Birth and Neonatal Outcomes. *Lancet Global Health*. 2018.

[6] Berghella V, Saccone G. Fetal Fibronectin Testing for Prevention of Preterm Birth. *American Journal of Obstetrics and Gynecology*. 2019.

[7] Hassan SS, et al. Cervical Length Screening and Prevention of Preterm Birth. *Obstetrics & Gynecology*. 2011.

[8] Conde-Agudelo A, Romero R. Prediction of Preterm Birth by Combined Biomarkers. *American Journal of Obstetrics and Gynecology*. 2015.

[9] Esplin MS, et al. Proteomic and Genomic Biomarkers for Prediction of Preterm Birth. *BJOG*. 2020.

[10] Stock SJ, et al. Innovations in Prediction and Prevention of Preterm Birth. *BMJ*. 2021.

[11]Suff N, Story L, Shennan A. Biomarkers in Prediction of Spontaneous Preterm Birth. *Frontiers in Physiology*. 2022.

[12] Esplin MS, et al. Advances in Biomarker-Based Prediction of Preterm Birth. *American Journal of Obstetrics and Gynecology*. 2023.

[13] Menon R, et al. Inflammatory Biomarkers and Pregnancy Outcomes. *Frontiers in Immunology*. 2023.

[14] Romero R, Chaemsaithong P, Korzeniewski SJ. Maternal Inflammatory Markers and Neonatal Morbidity. *Journal of Perinatal Medicine*. 2024.

[15]Berghella V, et al. Cervical Length and Biomarker Integration for Preterm Birth Prediction. *Ultrasound in Obstetrics & Gynecology*. 2024.

[16] Stock SJ, et al. Machine Learning Models for Predicting Preterm Birth. *The Lancet Digital Health*. 2025.

[17] Peelen MJCS, et al. Multi-Omics Biomarkers for Predicting Preterm Birth and NICU Admission. *Nature Medicine*. 2026.

[1]Suff N, Story L, Shennan A. Biomarkers in Prediction of Spontaneous Preterm Birth. *Frontiers in Physiology*. 2022.

[2] Menon R, et al. Advances in Biomarker-Based Prediction of Preterm Birth. *American Journal of Obstetrics and Gynecology*. 2023.

[3] Romero R, Chaemsaithong P, Korzeniewski SJ. Maternal Inflammatory Markers and Neonatal Morbidity. *Journal of Perinatal Medicine*. 2024.

[1]Suff N, Story L, Shennan A. *Biomarkers in Prediction of Spontaneous Preterm Birth*. Frontiers in Physiology. 2022.

[2] Menon R, et al. *Advances in Biomarker-Based Prediction of Preterm Birth*. American Journal of Obstetrics and Gynecology. 2023.