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MATERNAL SERUM C-REACTIVE PROTEIN BEFORE 20 WEEKS GESTATION AS A PREDICTOR OF PRETERM DELIVERY: A PROSPECTIVE OBSERVATIONAL STUDY

Obstetrics & Gynaecology

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ABSTRACT

Background: Preterm birth (PTB), defined as delivery before 37 completed weeks of gestation, is a leading cause of neonatal morbidity and mortality worldwide. Inflammation and subclinical infections are recognized contributors to spontaneous preterm labor (PTL). Maternal serum C-reactive protein (CRP), an acute-phase reactant, is a candidate early biomarker for PTB. **Objective:** To determine whether elevated maternal serum CRP levels measured before 20 weeks gestation can predict the risk of preterm delivery and associated neonatal complications in a South Indian tertiary-care population. **Methods:** A prospective observational study at Alluri Sitarama Raju Academy of Medical Sciences, Eluru (May 2024–Oct 2025) enrolled 100 singleton pregnancies <20 weeks. Serum CRP was measured using RHELAX-CRP latex agglutination. Subjects were categorized as CRP-positive (>0.6 mg/dL) or CRP-negative (≤0.6 mg/dL) and followed until delivery. Primary outcome: PTB (<37 weeks). Secondary outcomes: mode of delivery, neonatal complications. **Results:** 30% of participants were CRP -positive. PTB occurred in 84.6% of CRP-positive women versus 15.4% of CRP-negative (p = 0.001). At 0.6 mg/dL cutoff, sensitivity was 84.62% and specificity 89.19% (AUC 0.858). Elevated CRP was significantly associated with neonatal respiratory distress syndrome and sepsis. **Conclusion:** Maternal serum CRP measured before 20 weeks gestation showed strong predictive value for PTB and selected neonatal complications. Early CRP screening may improve antenatal risk stratification and enable targeted preventive strategies.

KEYWORDS

INTRODUCTION

Preterm birth[1] (PTB), delivery before 37 completed weeks of gestation, remains a principal cause of neonatal morbidity and mortality globally and a major driver of long-term neuro-developmental and respiratory sequelae among survivors. The global burden of PTB is estimated at approximately 15 million births per year, with the highest rates in low- and middle-income countries. Early identification of pregnancies at high risk for PTB allows for intensified surveillance and interventions that can reduce neonatal morbidity.

A substantial fraction of spontaneous PTB is initiated or propagated by inflammation arising from ascending intrauterine infection, systemic maternal inflammation or non-infectious inflammatory processes [2,3]. These processes upregulate proinflammatory cytokines (IL-6, IL-1β, TNF-α) that stimulate hepatic synthesis of acute-phase proteins, notably C-reactive protein [8,10,11,13] (CRP). CRP is a stable, widely available laboratory marker that rises predictably in response to inflammatory stimuli and has been evaluated as a potential early biomarker for adverse pregnancy outcomes, including PTB. Compared with direct cytokine assays, CRP is inexpensive, robust, and widely accessible in routine clinical laboratories, making it attractive for low-resource settings.

Despite multiple studies reporting associations between elevated early-pregnancy CRP and PTB, thresholds and diagnostic performance metrics vary across populations and assays. Moreover, few prospective studies have examined this relationship in South Indian cohorts. This prospective observational study was therefore designed to assess the predictive performance of maternal serum CRP measured before 20 weeks gestation for subsequent PTB and selected neonatal outcomes.

MATERIALS AND METHODS

Study Setting and Design: This prospective observational study was conducted at the Department of Obstetrics and Gynaecology, Alluri Sitarama Raju Academy of Medical Sciences, Eluru, Andhra Pradesh.
Study Period: May 2024 to October 2025.
Sample Size and Recruitment: 100 antenatal women with singleton pregnancies between 8+5 and 19+4 weeks gestation were recruited.

Inclusion Criteria
Singleton pregnancy <20 weeks gestation.

Exclusion Criteria
1. Multiple gestation
2. Pre-eclampsia
3. Gestational diabetes
4. Polyhydramnios
5. History of mid-trimester abortions
6. Chronic medical disorders
7. Recent infections
8. Immunocompromised state
9. HBsAg positivity

Laboratory Assessment: Venous blood collected, serum separated, CRP measured using RHELAX-CRP latex agglutination. CRP >0.6 mg/dL considered positive.

Follow-up and Outcomes: Participants were followed through routine antenatal care and until delivery. The primary outcome was preterm birth[8][1](<37 completed weeks). Secondary outcomes included mode of delivery, birth weight, APGAR scores, and neonatal complications[7,8] such as respiratory distress syndrome (RDS), neonatal sepsis, and meconium aspiration syndrome (MAS).

Statistical Analysis
Descriptive statistics summarized baseline characteristics. Associations between CRP status and categorical outcomes were assessed using chi-square tests. Receiver operating characteristic (ROC) analysis evaluated predictive accuracy and generated area under the curve (AUC). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for the chosen cutoff. A p-value <0.05 was considered statistically significant.

RESULTS

Participant Characteristics:
- The mean maternal age was 22.86 ± 3.8 years.
- The mean gestational age at time of CRP testing was 14+2 weeks.

- 30% women were CRP-positive (>0.6 mg/dL), and 70% were CRP-negative.

Association with Preterm Birth:
- Overall, 26% (n = 26) of the cohort [7,8] delivered preterm.
- Preterm delivery occurred in 22 of 30 (73.3%) CRP-positive women compared with 4 of 70 (5.7%) CRP-negative women — reflecting a statistically significant association (p = 0.001). Using the prespecified 0.6 mg/dL cutoff, ROC analysis produced an AUC of 0.858 (95% CI 0.760–0.957). Sensitivity was 84.62%, specificity 89.19%, PPV 73.3%, and NPV 94.3%.

Neonatal Outcomes:
- Mean birth weight across the cohort [7,8] was 2.74 ± 0.53 kg.
- Elevated maternal CRP [2] was associated with a higher incidence of neonatal respiratory distress syndrome (RDS) and culture-proven or clinically suspected sepsis (p = 0.001 for both).
- No statistically significant association was observed between antenatal CRP[2] status and meconium aspiration syndrome.

Mode of Delivery: There was a higher rate of emergency cesarean sections in the CRP-positive group, most commonly for non-reassuring fetal status or failed induction; however, the study was not powered to detect differences in mode of delivery.

CRP Status	Preterm n (%)	Term n (%)	Total n
>0.6 mg/dL	22 (84.6%)	8 (10.8%)	30
≤0.6 mg/dL	4 (15.4%)	66 (89.2%)	70

DISCUSSION

This prospective study demonstrates that elevated maternal serum CRP [2] measured before 20 weeks gestation is strongly associated with subsequent preterm birth [8][1] in a South Indian tertiary-care cohort. At the chosen threshold of 0.6 mg/dL, the test showed excellent discrimination (AUC 0.858) and favorable sensitivity and specificity, suggesting practical utility as an early screening tool.

Comparison with Previous Literature: Multiple prospective and nested case-control studies internationally have reported similar associations between elevated early-pregnancy CRP [2] and increased risk of PTB[1]. Lohsoonthorn et al. observed increased odds of PTB [1] among women in the highest CRP [2] quartile when measured before 20 weeks; this association was particularly strong for very preterm birth[8] [1]. Waranuch et al. reported that markedly elevated early CRP[2] was associated with higher risk of spontaneous PTB[1]. Nikbakht and colleagues reported comparable diagnostic accuracy (AUC ~0.83) with early pregnancy CRP[2] predicting PTB[1] and small-for-gestational-age outcomes. A 2024 BMC Pregnancy Childbirth study from a South Asian population also highlighted first-trimester systemic inflammation[7,8,9] [2,3] as a significant predictor of PTB [1], reinforcing our findings in a nearby regional context. These consistent results across populations strengthen the hypothesis that maternal systemic inflammation[7,8,9] [2,3], captured by CRP[2], precedes and may contribute to PTB [1] pathogenesis.

Biological Plausibility: Inflammatory activation — whether driven by ascending genital tract infection, periodontal disease, subclinical urinary tract infections, or sterile inflammation [2,3] — increases circulating cytokines (e.g., IL-6), prostaglandin synthesis, and matrix metalloproteinase activity, promoting cervical remodeling, membrane weakening, and uterine contractility. CRP as an IL-6 responsive acute-phase protein, provides an integrative signal of systemic inflammatory burden; hence, early elevation plausibly reflects intrauterine and systemic processes that predispose to PTB.

Clinical Implications: The high NPV observed (94.3%) suggests that a negative early CRP test could reassure clinicians and reduce unnecessary intensive surveillance in low-risk women, while a positive result could prompt targeted interventions such as closer cervical length[5,11] surveillance, microbiological screening (high vaginal swab, urine culture, periodontal assessment), and consideration of prophylactic or therapeutic measures (e.g., progesterone[9],[6] therapy where indicated, targeted antibiotics if infection identified, timely corticosteroids for threatened preterm labor). In resource-constrained settings, CRP testing represents an affordable screening modality that could be integrated into routine early antenatal panels.

Limitations and Future Directions: The study is single-center with a moderate sample size and a single CRP measurement. Assay variability and differing CRP thresholds across studies limit direct comparability. Future research should evaluate serial CRP measurements, explore combined predictive models incorporating cervical length[5,11], fetal fibronectin[5,11], and inflammatory cytokines, and test whether interventions guided by early CRP[2] reduce PTB [1] rates in randomized trials. Additionally, mechanistic studies linking maternal CRP[2] to placental histopathology, the maternal microbiome, and neonatal immune outcomes would clarify causal pathways.

CONCLUSION

Maternal serum CRP[2] measured before 20 weeks gestation demonstrated strong predictive performance for PTB[1] and selected adverse neonatal outcomes in this cohort[7,8]. Early CRP[2] screening is inexpensive, feasible, and may enhance antenatal risk stratification. Integration into routine prenatal care warrants further evaluation through larger multicenter and interventional studies.

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