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Correlation of Levels of Serum C-Reactive Protein in Pregnancy with Fetomaternal Outcome

Dr. Geda Hyndavi[1], Dr. Alpana Agrawal[2], Dr. Manisha Gupta[3], Dr. Devika Mor[4]

[1]Junior Resident, Department of Obstetrics & Gynaecology, Santosh Medical College & Hospital, Santosh Deemed to be University, Ghaziabad, India

[2]Professor, Department of Obstetrics & Gynaecology, Santosh Medical College & Hospital, Santosh Deemed to be University, Ghaziabad, India

[3]Professor & HOD, Department of Obstetrics & Gynaecology, Santosh Medical College & Hospital, Santosh Deemed to be University, Ghaziabad, India

[4]Assistant Professor, Department of Obstetrics & Gynaecology, Santosh Medical College & Hospital, Santosh Deemed to be University, Ghaziabad, India

Abstract: ***Background: Maternal systemic inflammation is recognized as a pivotal determinant in the progression and outcome of pregnancy. C-reactive protein (CRP), a pentameric acute-phase reactant synthesized primarily by hepatic parenchyma, serves as a sensitive biomarker for inflammatory activity. The immunological environment of pregnancy requires a delicate equilibrium between fetal tolerance and maternal protection. Disturbances in this balance through exaggerated inflammatory cascades can lead to significant maternal and neonatal complications. Objectives: The primary aim of this study was to meticulously evaluate the association between maternal serum CRP levels during the third trimester and specific fetomaternal outcomes, including premature rupture of membranes (PROM), maternal infection, and neonatal morbidity markers such as Apgar scores and NICU admissions. Methodology: A prospective observational study was conducted at a tertiary care facility involving 255 pregnant women beyond 34 weeks of gestation. Maternal serum CRP was quantified via immunoturbidimetric assay, using a clinical threshold of 10 mg/L to define elevated levels. Statistical analysis was performed using SPSS version 25.0. Results: The study identified that elevated CRP (>10 mg/L) was significantly associated with adverse clinical sequelae. Specifically, the incidence of PROM was drastically higher in the elevated CRP group (60.0%) compared to the normal group (8.3%). Furthermore, neonatal outcomes such as NICU admission rates were markedly increased in the high-CRP cohort (24.0% vs 5.5%). Conclusion: Third-trimester serum CRP estimation provides a robust, cost-effective tool for identifying high-risk pregnancies, enabling timely intervention to mitigate adverse fetomaternal outcomes.***

Keywords: C-Reactive Protein, PROM, Neonatal Morbidity, Maternal Sepsis, NICU.

1. Introduction

The biological miracle of human pregnancy involves a complex, highly regulated series of immunological and physiological adaptations. From the moment of implantation, the maternal immune system must navigate the presence of a semi-allogeneic fetus, necessitating a shift toward humoral-mediated immunity to prevent rejection. While a certain degree of localized inflammation is essential for processes such as implantation, cervical ripening, and the initiation of labor, systemic and exaggerated inflammatory responses are often precursors to pathology.

C-reactive protein (CRP) has long been utilized in clinical medicine as a quintessential marker of systemic inflammation. It is synthesized by hepatocytes in response to circulating pro-inflammatory cytokines, most notably Interleukin-6 (IL-6) and Tumor Necrosis Factor-alpha (TNF-alpha). In the context of obstetrics, CRP levels have been shown to rise in response to subclinical infection, placental stress, and other inflammatory triggers that can jeopardize the health of both the mother and the fetus.

Previous research has suggested that elevated CRP in the early and middle trimesters may be predictive of preeclampsia and gestational diabetes. However, its role in the third trimester—particularly as a predictor for Premature Rupture of Membranes (PROM) and subsequent neonatal outcomes—remains a critical area of investigation. PROM, defined as the rupture of fetal membranes prior to the onset of labor, contributes significantly to preterm birth and maternal-fetal infection. Understanding the biochemical predictors of these events allows clinicians to refine triage protocols and improve prognostic accuracy.

This study serves to fill a gap in localized clinical data, examining a large cohort of 255 patients to determine if a simple, inexpensive serum test can serve as a "red flag" for obstetricians in a tertiary care setting. By identifying these risks early, maternal healthcare providers can initiate prophylactic measures, such as corticosteroid administration or antibiotic therapy, with greater precision.

2. Literature Review

The utility of CRP in pregnancy has been a subject of international academic discourse for over two decades. Landmark studies, such as those by Sorensen et al. (2004), established a clear link between early-pregnancy systemic inflammation and the subsequent development of hypertensive disorders. Their findings suggested that inflammation precedes clinical symptoms, making CRP a valuable early screening tool.

The mechanism linking inflammation to preterm labor and membrane rupture was further elucidated by Catov and

colleagues (2007). They proposed that systemic inflammatory markers like CRP reflect a state of intrauterine stress that prematurely activates the fetal hypothalamic-pituitary-adrenal (HPA) axis. This activation triggers a cascade of hormones that lead to uterine contractions and cervical changes well before the term date.

In more recent years, the focus has shifted toward the impact of maternal inflammation on the neonate. Huang et al. (2020) demonstrated that elevated high-sensitivity CRP (hs-CRP) is an independent predictor for neonatal Respiratory Distress Syndrome (RDS). This suggests that the inflammatory environment of the uterus can cross the placental barrier, affecting fetal lung maturity and surfactant production. Furthermore, Sharmin et al. (2017) observed that chronic maternal inflammation is often associated with lower birth weights, likely due to impaired placental perfusion and nutrient transport.

Domestically, researchers like Gahlot and Pandey (2016) have validated the use of CRP in the Indian population, particularly in predicting the success of labor induction and the risk of chorioamnionitis. Their work emphasized the need for standardized thresholds in clinical practice, suggesting that values above 10 mg/L should be treated with high clinical suspicion.

3. Methodology

3.1 Study Setting and Design

This prospective observational research was conducted within the Department of Obstetrics and Gynaecology at Santosh Medical College and Hospital, Ghaziabad. The study period spanned from 2023 to early 2026, capturing a diverse demographic of patients from the Delhi NCR region.

3.2 Ethical Considerations

Prior to commencement, the study protocol was reviewed and approved by the Institutional Ethics Committee. All participants provided written informed consent after receiving a detailed explanation of the study objectives and the non-invasive nature of the serum collection.

3.3 Participant Selection

A total of 255 pregnant women were recruited based on specific inclusion criteria: singleton pregnancy, gestational age exceeding 34 weeks, and willingness to follow up through delivery. Exclusion criteria were rigorously applied to prevent confounding; women with pre-existing chronic inflammatory conditions (e.g., Rheumatoid Arthritis, SLE), active non-obstetric infections, or known fetal chromosomal anomalies were omitted from the study.

3.4 Data Collection and Assay

Upon enrollment, maternal blood samples were collected under sterile conditions. Serum was separated and analyzed for C-reactive protein levels using a quantitative immunoturbidimetric assay. For clinical classification, a threshold of 10 mg/L was utilized, where values >10 mg/L were defined as "elevated" and ≤10 mg/L as "normal". Detailed obstetric history, demographic data, and delivery outcomes were recorded in a structured proforma.

3.5 Statistical Analysis

The data were entered into Microsoft Excel and analyzed using SPSS version 25.0. Categorical variables were expressed as percentages, and associations were tested using Chi-square or Fisher's exact tests. Continuous variables were presented as mean ± standard deviation. A p-value of less than 0.05 was considered statistically significant.

4. Results

4.1 Demographic Characteristics

The study cohort of 255 women had a mean maternal age of 25.4 ± 4.2 years. The majority of participants were between 21 and 30 years of age. Regarding gestational age at the time of testing, the mean was 36.5 weeks. Parity and socioeconomic status did not show a statistically significant difference in the baseline distribution of CRP levels, suggesting that inflammation in this group was primarily driven by obstetric or subclinical factors rather than purely demographic ones.

4.2 Prevalence of Elevated CRP

Out of the 255 participants, 70.6% (n=180) exhibited normal CRP levels (≤10 mg/L), while 29.4% (n=75) were found to have elevated CRP levels (>10 mg/L). This significant minority of patients formed the "high-risk" group for subsequent analysis.

4.3 Maternal Outcomes

The analysis revealed a profound correlation between serum CRP and the incidence of Premature Rupture of Membranes (PROM). In the elevated CRP group, sixty percent (60.0%) of the women experienced PROM. In stark contrast, only eight point three percent (8.3%) of women in the normal CRP group experienced this complication. This association was highly significant with a p-value of less than 0.001. Additionally, clinical maternal infection was observed in twenty- six point six percent (26.6%) of the high-CRP group compared to only two- point seven percent (2.7%) of the normal group.

4.4 Obstetric Interventions

Patients with elevated CRP were also more likely to require medical intervention. The need for prolonged hospitalization (exceeding five days) was noted in forty percent (40.0%) of the high-CRP group, whereas it was required in only five point five percent (5.5%) of the normal group. This trend was consistent across the requirement for intravenous antibiotic therapy.

4.5 Neonatal Outcomes

The impact of maternal inflammation extended significantly to the neonates. Babies born to mothers with elevated CRP

faced a twenty-four percent (24.0%) NICU admission rate, compared to a five point five percent (5.5%) admission rate for those in the normal group. Respiratory Distress Syndrome (RDS) was diagnosed in fourteen point six percent (14.6%) of neonates in the high-CRP group vs. three point eight percent (3.8%) in the control. Furthermore, neonatal sepsis was significantly more prevalent in the elevated group (12.0% vs 1.6%). Low Apgar scores at one minute (less than 7) were also significantly more common in neonates whose mothers had high CRP levels.

5. Discussion

The results of this prospective study confirm that maternal serum CRP in late pregnancy is a powerful predictor of adverse fetomaternal outcomes. The most striking finding is the six-fold increase in PROM risk among women with elevated CRP levels. This can be explained through the biochemical pathways of parturition. Inflammation triggers the release of pro-inflammatory cytokines such as IL-1beta and TNF-alpha, which in turn upregulate the production of Matrix Metalloproteinases (MMPs)- specifically MMP-9. These enzymes are responsible for the degradation of collagen within the amniotic membranes, leading to their structural weakening and eventual rupture.

The neonatal findings support the concept of Fetal Inflammatory Response Syndrome (FIRS). Our data showed that even in near-term pregnancies, maternal inflammation significantly increases the risk of RDS. This supports the hypothesis that maternal cytokines cross the placenta and interfere with the type II pneumocytes' ability to produce adequate surfactant. The higher rates of NICU admission and neonatal sepsis further emphasize the systemic nature of this inflammatory threat.

From a clinical governance perspective, these findings advocate for the integration of CRP screening in high-risk obstetric triage. Unlike more expensive or invasive markers, CRP is a routine, inexpensive test available in most clinical laboratories. Identifying an elevated CRP level (>10 mg/L) allows the obstetric team to prepare for potential PROM, ensure NICU availability, and potentially initiate early antibiotic prophylaxis to prevent maternal and neonatal sepsis.

While this study provides robust data from 255 patients, it is not without limitations. As a single-point measurement study, it does not capture the kinetics of CRP over time. Furthermore, being conducted at a tertiary care center, there may be a degree of referral bias toward more complicated cases. Future research should focus on longitudinal CRP monitoring throughout the third trimester to determine the optimal timing for intervention.

6. Conclusion

Maternal serum C-reactive protein levels in the third trimester serve as a significant clinical marker for predicting adverse pregnancy outcomes. Elevated CRP (>10 mg/L) is strongly correlated with a higher incidence of PROM, maternal infection, and neonatal complications including RDS and increased NICU admissions. Given its accessibility and reliability, CRP estimation should be considered a vital component of the antenatal evaluation to stratify risk and optimize fetomaternal health.

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