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Original Research Article

Association of maternal serum c-reactive protein with pre-eclampsia among patients attending in the outpatient department of a tertiary care hospital

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ABSTRACT

Background: Preeclampsia is a pregnancy-specific hypertensive disorder associated with systemic inflammation and endothelial dysfunction. C-reactive protein (CRP), an acute-phase reactant, is a potential biomarker for detecting and assessing preeclampsia severity. This study aimed to evaluate the association between maternal serum c-reactive protein (CRP) levels and preeclampsia.

Methods: This case-control study was conducted in the department of obstetrics and gynecology, Institute of Child and Mother Health (ICMH), Dhaka, Bangladesh, from March 2023 to February 2024. This study included 70 pregnant women with a gestational age of 20-40 weeks. Among them, 35 women diagnosed with pre-eclampsia were assigned as cases, and 35 normotensive pregnant women were taken as controls.

Results: Mean age and height were similar between groups, but preeclamptic women had significantly higher weight compared to controls (67.46±9.85 kg versus 57.26±9.27 kg; $p=0.001$). Elevated serum CRP levels were observed in 94.3% of preeclamptic patients, whereas all controls (100%) had normal CRP levels ($p<0.001$). The mean CRP was significantly higher in cases (25.37±14.70 mg/dl) than controls (4.22±0.92 mg/dl; $p<0.001$). A strong positive correlation was found between CRP and systolic blood pressure ($r=0.822$, $p<0.001$) and diastolic blood pressure ($r=0.792$, $p<0.001$).

Conclusions: This study demonstrated a significant association between elevated maternal serum c-reactive protein (CRP) levels and preeclampsia, with a strong positive correlation to blood pressure. Elevated CRP may serve as a useful biomarker for early detection and monitoring of preeclampsia.

Keywords: Biomarker, CRP, Hypertension, Preeclampsia, Pregnancy

INTRODUCTION

Pregnancy is a physiological state that places considerable stress on the body, resulting in numerous changes in its internal environment. As physiological stress increases, the biochemical alterations that normally occur during pregnancy can become exaggerated in pregnancy-related complications such as preeclampsia and eclampsia. Preeclampsia is a serious, multisystem disorder that typically develops after the 20th week of gestation in previously normotensive and nonproteinuric women. It is characterized by hypertension (blood pressure $\geq 140/90$ mmHg) and proteinuria (≥ 0.3 gm/24-hour urine collection), with or without pathological edema.¹

Globally, preeclampsia affects approximately 5-7% of all pregnancies and is associated with numerous maternal and fetal complications.² Each year, an estimated 500,000 infants die as a result of preeclampsia and related conditions, while approximately 60,000 maternal deaths occur due to the disease.³⁻⁵ The global incidence of preeclampsia continues to rise, particularly in developing countries where limited access to adequate healthcare contributes to more than 50,000 maternal deaths annually.⁵ Preeclampsia accounts for 12-25% of cases of fetal growth restriction and small-for-gestational-age neonates, as well as 15-20% of all preterm births.⁶ Prematurity, in turn, is associated with significant neonatal mortality and long-term morbidity.⁶

Hypertension is often the first clinical manifestation of preeclampsia, commonly appearing before the onset of proteinuria.⁷ Therefore, any pregnant woman presenting with hypertension should be considered at risk of developing preeclampsia and promptly evaluated to prevent maternal and fetal complications. Despite extensive research, the etiology of preeclampsia remains incompletely understood, with multiple theories proposed to explain its pathophysiology.⁸⁻¹⁰ One key mechanism involves the failure of trophoblastic invasion of spiral arteries, leading to maladaptation of maternal arterioles, increased uterine artery resistance, and reduced placental perfusion.¹¹

Emerging evidence suggests a potential association between c-reactive protein (CRP) and pregnancy-induced hypertension (PIH).¹² Among the various hypotheses proposed for the pathogenesis of preeclampsia, immune maladaptation and inflammation play central roles. CRP, an acute-phase protein and key component of the innate immune response, has been linked to other inflammatory markers and to cardiovascular dysfunction associated with preeclampsia.¹³⁻¹⁶ Elevated plasma CRP levels indicate systemic inflammation and tissue injury.^{17,18}

Previous studies have demonstrated that elevated high-sensitivity CRP (hs-CRP) levels correlate with disease severity in preeclampsia.^{19,20} Furthermore, hs-CRP levels have been found to positively correlate with mean arterial pressure and abnormal uterine artery Doppler findings,

suggesting a relationship between endothelial dysfunction, increased vascular resistance, and impaired utero-placental perfusion.²¹ These findings indicate that elevated maternal hs-CRP may serve as a marker of disease severity and poor fetal outcomes. In addition, Best et al reported that specific CRP gene variants (rs876538 and rs3093068), previously associated with cardiovascular disease, showed a suggestive association with preeclampsia in an American Indian population, further supporting a potential genetic and inflammatory role of CRP in preeclampsia.²²

Therefore, the aim of the present study was to determine the association between maternal serum CRP levels with preeclampsia.

METHODS

This case-control study was conducted in the department of obstetrics and gynecology, Institute of Child and Mother Health (ICMH), Dhaka, Bangladesh, from March 2023 to February 2024. In this study, A total of 70 pregnant women with a gestational age of 20-40 weeks, attending the department of obstetrics and gynecology, ICMH, Dhaka, during the study period, were included in this study. Among them, 35 women diagnosed with preeclampsia were assigned as cases, and 35 normotensive pregnant women were taken as controls.

These were the following criteria for eligibility as study participants:

Inclusion criteria

Pregnant women with a gestational age of 20-40 weeks. Pregnant women diagnosed with pre-eclampsia, as well as normotensive, non-proteinuric pregnant women attending the department of obstetrics and gynecology, ICMH, during the study period. Singleton pregnancy. Patients willing to provide informed written consent.

Exclusion criteria

Multiple pregnancies. Pregnancies complicated by chronic medical conditions, such as diabetes mellitus, renal disease, asthma, cardiac disease, chronic hypertension, or hemorrhagic disorders. Pregnancies with acute medical illnesses, including urinary tract infections, viral infections, tuberculosis, or other significant infections.

Data collection procedure

Participant selection was conducted using purposive sampling, based on the defined inclusion and exclusion criteria. The study population included pregnant women with a gestational age of 20-40 weeks, both with preeclampsia and normotensive, attending the department of obstetrics and gynecology, ICMH, Dhaka, Bangladesh during the study period.

After confirming eligibility, informed written consent was obtained from all participants. Primary data, including sociodemographic characteristics, obstetric and gynecological history, were collected through structured interviews and patient records.

Blood samples were then obtained for serum CRP measurement. Reports were collected and recorded for both study groups for further analysis. A semi-structured, pre-tested questionnaire was employed to collect relevant information through history taking, physical examination, and laboratory investigations. All data were collected directly by the researcher to ensure consistency and accuracy.

Statistical analysis

All data were recorded systematically in a pre-formatted data collection form. Continuous variables were summarized as means with standard deviations, while

categorical variables were presented as frequencies and percentages. The difference between the findings were ascertained by obtaining p values from t-test for continuous variables and from Chi-square for categorical variables. A p value <0.05 was considered significant. Statistical analysis was performed by using SPSS 26 (Statistical Package for Social Sciences). This study was ethically approved by the institutional review board (IRB) of Institute of Child and Mother Health (ICMH), Dhaka, Bangladesh.

RESULTS

This case-control study was conducted in the department of obstetrics and gynecology, Institute of Child and Mother Health (ICMH), Dhaka. After obtaining a detailed history, performing physical examinations, and conducting relevant investigations according to the inclusion and exclusion criteria, serum CRP samples were collected from a total of 70 participants.

Table 1: Distribution of baseline characteristics between cases and controls (n=70).

Variables	Type of participants		P value
	Cases (n=35)	Controls (n=35)	
Age (years)	N (%)	N (%)	
18-28	23 (65.7)	29 (82.9)	0.101
29-39	12 (34.3)	6 (17.1)	
Total	35 (100.0)	35 (100.0)	
Mean±SD	26.09±5.39	24.94±4.08	0.321
Height (cm)	154.77±3.91	152.94±3.73	0.050
Weight (kg)	67.46±9.85	57.26±9.27	0.001
Para	1.03±1.15	1.06±1.05	0.914
Gravida	2.03±1.15	2.06±1.05	0.914
Gestational age (weeks)	32.31±4.52	31.37±4.91	0.407

Table 2: Comparison of serum CRP between cases and controls.

Variables	Type of participants		P value
	Cases (n=35) N (%)	Controls (n=35) N (%)	
Serum CRP (mg/dl)			
Normal (<6 mg/dl)	2 (5.7)	35 (100.0)	0.001
High (>6 mg/dl)	33 (94.3%)	0 (0.0)	
Mean±SD	25.37±14.70	4.22±0.92	0.001

Cases (n=35): pregnant women with a gestational age of 20-40 weeks diagnosed with pre-eclampsia, attending the department of obstetrics and gynecology, ICMH, Dhaka during the study period.

Controls (n=35): pregnant women with a gestational age of 20-40 weeks with normotensive pregnancies, attending the outpatient department of obstetrics and gynecology, ICMH, Dhaka during the study period.

Table 1 presents the comparison of sociodemographic and obstetric characteristics between the two study groups. The

mean age of the participants was slightly higher among cases (26.09±5.39 years) compared to controls (24.94±4.08 years), though the difference was not statistically significant (p=0.321). The mean height was comparable between groups (p=0.050), whereas mean weight was significantly higher among pre-eclamptic women (67.46±9.85 kg) compared to controls (57.26±9.27 kg) (p=0.001). Parity, gravidity, and gestational age did not differ significantly between the two groups.

Table 2 demonstrates that the majority of participants in the case group, 33 (94.3%), had elevated serum CRP

levels, whereas all participants in the control group, 35 (100.0%), had normal CRP levels. This difference was statistically significant ($p<0.001$). The mean serum CRP level was also significantly higher among cases (25.37 ± 14.70 mg/dl) compared to controls (4.22 ± 0.92 mg/dl) ($p<0.001$).

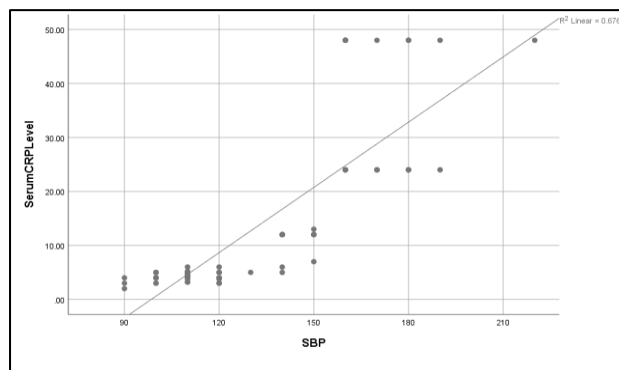


Figure 1: Scatter diagram showing the correlation between maternal serum CRP and SBP (systolic blood pressure).

Figure 1 demonstrates a strong positive correlation between maternal serum CRP levels and systolic blood pressure (SBP) ($r=0.822$), which was statistically significant ($p<0.001$). This finding indicates that serum CRP levels increase proportionally with rising SBP among the study participants.

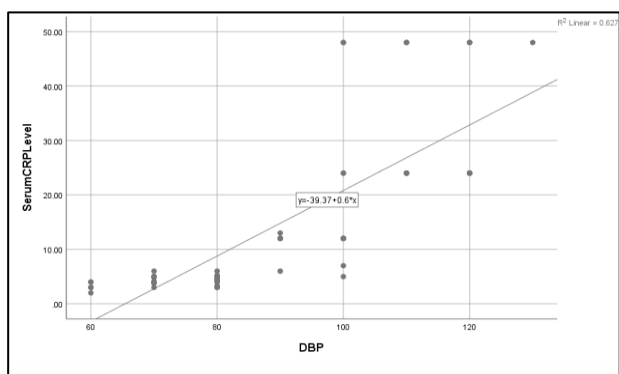


Figure 2: Scatter diagram showing the correlation between maternal serum CRP and DBP (diastolic blood pressure).

Figure 2 illustrates a strong positive correlation between maternal serum CRP levels and diastolic blood pressure (DBP) ($r=0.792$), which was statistically significant ($p<0.001$). This indicates that serum CRP levels tend to increase with rising DBP among the study participants.

DISCUSSION

Preeclampsia remains one of the most serious complications of pregnancy, posing significant risks to both maternal and fetal health. It is a condition associated

with endothelial cell injury and dysfunction. Increasing evidence suggests that preeclampsia is characterized by a state of systemic inflammation.²³ Studies have demonstrated that markers of endothelial activation and inflammation play a key role in its pathophysiology.¹⁹ C-reactive protein (CRP), an acute-phase reactant and sensitive indicator of tissue injury and inflammation, has been proposed to contribute to the characteristic inflammatory response observed in preeclampsia.²³ The present study aimed to evaluate the association between maternal serum CRP levels and preeclampsia.

In this case-control study, the mean age of the preeclamptic group was 26.09 ± 5.39 years, while that of the control group was 24.94 ± 4.08 years, showing no statistically significant difference ($p>0.05$). The majority of participants in both groups were aged 18-28 years (65.7% in cases and 82.9% in controls). Similar findings were reported by Sharmin et al, who found no significant difference in mean age between the study (24.58 ± 4.05 years) and control groups (23.92 ± 3.72 years).²⁴ Mirzaie et al also observed no statistically significant difference in maternal age across groups.²⁵

In the present study, the mean height was 154.77 ± 3.91 cm in the case group and 152.94 ± 3.73 cm in the control group ($p=0.050$), while the mean weight was significantly higher among cases (67.46 ± 9.85 kg) compared to controls (57.26 ± 9.27 kg) ($p<0.05$). The mean gestational age at diagnosis was 32.31 ± 4.52 weeks in cases and 31.37 ± 4.91 weeks in controls ($p>0.05$). In contrast, Mirzaie et al found a significant difference in gestational age between groups ($p=0.0001$).²⁵ Similarly, in another study by Samira et al, it was observed that pre-eclamptic patients delivered at a significantly lower gestational age ($t=2.216$, $p=0.030$), indicating that delivery occurred at an earlier stage of pregnancy compared to normotensive women ($p<0.041$).²⁶

In this study, the mean serum CRP level in the preeclampsia group (25.37 ± 14.70 mg/dl) was significantly higher than that in the control group (4.22 ± 0.92 mg/dl) ($p<0.001$). Most of the preeclamptic participants (94.3%) had elevated CRP levels, whereas all normotensive participants (100%) had normal CRP levels ($p<0.001$). These findings are consistent with those reported by Sharmin et al, who found significantly higher mean CRP levels in preeclamptic women (10.48 ± 6.93 mg/l) compared to controls (3.45 ± 1.71 mg/l) ($p=0.000$).²⁴ In that study, 68% of preeclamptic women had elevated CRP levels compared to only 2% of normotensive controls ($p<0.001$). Mirzaie et al also reported markedly higher serum CRP levels in preeclamptic women than in healthy pregnant controls.²⁵ Similar findings have been reported by other studies, further supporting the association between elevated serum CRP and preeclampsia.^{23,27}

While Sharmin et al found no significant difference in CRP levels between mild and severe preeclampsia ($p=0.76$), other studies have reported a significant variation, with higher CRP levels observed in severe cases ($p=0.001$).^{24,26}

Several studies have also demonstrated that CRP levels in preeclamptic women are significantly higher than those in normal pregnancies, reinforcing the role of inflammation in the disease process.²⁸

In the present study, correlation analysis revealed a strong positive correlation between maternal serum CRP and both systolic ($r=0.822$, $p<0.001$) and diastolic blood pressure ($r=0.792$, $p<0.001$). These findings are consistent with the results of Deveci et al, who reported a significant correlation between mean arterial pressure and serum CRP levels in pregnancies complicated by preeclampsia ($r=0.372$, $p=0.002$).²⁹ The elevated CRP levels observed in preeclamptic patients who delivered earlier in pregnancy may reflect the severity of the disease and an exaggerated inflammatory response.³⁰

The present study findings confirm that preeclampsia is associated with elevated serum CRP levels, supporting the role of systemic inflammation and endothelial dysfunction in its pathogenesis. Although CRP levels are naturally higher in normal pregnancy compared to non-pregnant women, markedly elevated levels in preeclamptic women indicate a pathologic inflammatory response. All participants in this study were matched for maternal age and were free from acute or chronic illnesses or infections that could confound CRP elevation.²⁰

Overall, the significantly higher serum CRP levels observed in preeclamptic women indicate that CRP may serve as a valuable biomarker for assessing the inflammatory component of preeclampsia. Therefore, measurement of serum CRP could assist clinicians in the early detection, risk assessment, and ongoing monitoring of patients with preeclampsia.

This study has several limitations. The sample size was relatively small, which may limit the generalizability of the findings to a larger population. The single-center design and retrospective nature of the study could also affect the overall strength and applicability of the results. Furthermore, purposive sampling was used, which may introduce selection bias and potentially influence the study outcomes.

CONCLUSION

In this study, the association between maternal serum c-reactive protein (CRP) levels and pre-eclampsia was evaluated. The findings support the hypothesis that pre-eclampsia is associated with endothelial dysfunction and systemic inflammation. A significant association was observed between elevated maternal serum CRP and pre-eclampsia, with strong positive correlations between CRP levels and blood pressure. The pre-eclampsia group showed markedly higher mean serum CRP levels compared to the normotensive group. Therefore, elevated maternal serum CRP may serve as a valuable biomarker for the early detection and monitoring of pre-eclampsia.

Further study with a prospective and longitudinal study design, including a larger sample size, needs to be done to validate the findings of this study

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Ethical approval: The study was approved by the Institutional Ethics Committee

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