Original Article

Relationship between Serum CRP Levels and Fetal Outcomes in Women with Preeclampsia

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ABSTRACT

Introduction: *Preeclampsia (PE) is a type of pregnancy hypertension that affects 4-5% of women. The illness is distinguished by elevated blood pressure and proteinuria after 20 weeks of gestation. Its complications include a major cause of morbidity and mortality in both the mother and the fetus. The study aimed to determine if there is a significant relationship between Serum CRP levels and fetal outcomes in women with preeclampsia women.* ***Methods and materials:*** *This cross-sectional analytical study was conducted at the Department of Obstetrics and Gynaecology at the Institute of Child and Mother Health (ICMH), Matuail, Dhaka. It took place from January to December 2018.* ***Results:*** *The study involved 120 participants evenly distributed across three groups (A, B, and C), predominantly aged 18-25 years, with similar educational and socioeconomic backgrounds. Groups A and B had higher BMIs than C ($p<0.05$). Fetal birth weight varied significantly ($p<0.05$) with 23.3% low birth weight in severe preeclampsia, 16.7% in mild preeclampsia, and 5.0% in normal pregnancies. Maternal CRP levels negatively correlated with newborn birth weights ($r = -0.470$, $p < 0.001$). Low-birth-weight and IUGR babies had higher CRP proportions ($p < 0.001$ and $p < 0.01$, respectively).* ***Conclusion:*** This study emphasizes the crucial connection between elevated CRP levels in preeclampsia and adverse fetal outcomes such as lower birth weights, prematurity,

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and IUGR. It underscores the value of monitoring CRP, particularly in preeclampsia cases, to enable early intervention and enhance fetal well-being.

Key Words: *Serum, CRP, Fetal outcome, Pre-eclampsia.*

INTRODUCTION

Preeclampsia is a pregnancy illness characterized by hypertension and proteinuria that appears after 20 weeks of pregnancy. This illness is estimated to complicate 5 to 7% of pregnancies worldwide, resulting in a massive disease burden [1]. Potential Fetal problems include low birth weight, preterm, and mortality. Maternal problems include renal failure, liver failure, cerebral edema with seizures, and, in rare cases, death [2]. Pre-eclampsia affects between 3% and 5% of all pregnancies and causes more than 60,000 maternal and 500,000 fetal deaths worldwide each year [3]. According to 2005 WHO figures, the incidence of preeclampsia is seven times higher in underdeveloped nations (2.8% of live births) than in industrialized countries (0.4%). Eclampsia is common in industrialized countries like North America and Europe, with an estimated 5-7 occurrences per 10,000 deliveries. In developing countries, however, the incidence of eclampsia ranges greatly, ranging from 1 case per 100 births to 1 case per 1700 pregnancies [4]. In undeveloped countries, the prevalence of preeclampsia ranges from 1.8% to 16.7%. According to reports, Ethiopia, India, Nigeria, Pakistan, Afghanistan, and the Democratic Republic of the Congo account for roughly half of all maternal mortality. Contraception saves an estimated 2.7 million baby lives and 60 million healthy lives worldwide each year. Promoting family planning in high-birth-rate countries has the potential to reduce poverty and hunger, as well as save 32% of all maternal fatalities and nearly 10% of childhood deaths [5]. C-reactive protein (CRP) is a systemic inflammatory marker. High-sensitivity CRP is a protein that can be evaluated using antibodies tagged with an enzyme (ELISA) a fluorescent molecule, or antibody-coated polystyrene beads. It has been proposed that measuring hsCRP is more sensitive than measuring CRP and gives superior sensitivity in confirming inflammation. It has been proposed that determining hsCRP is more sensitive than standard CRP measurement and gives superior sensitivity in confirming inflammation [6]. C-reactive protein (CRP) is a sensitive and specific indicator of the body's overall inflammatory activity. It has a high sensitivity but is not specific. CRP levels are higher in healthy pregnant women than in non-pregnant women, however to a lesser extent than in PE C-reactive protein (CRP), a sensitive sign of tissue damage and inflammation, may be a possible marker and play a role in inducing the inflammatory response seen in preeclampsia [7,8]. Preeclampsia is a well-known risk factor for premature birth and poor fetal growth. It is one of the primary causes of prenatal morbidity and mortality, along with eclampsia [9]. CRP may be utilized as a low-cost inquiry to determine the risk of preeclampsia and its impact on baby birth weight [10]. The aim of this study was to determine if there is a significant relationship between Serum CRP levels and fetal outcomes in pre-eclamptic women

METHODS & MATERIALS

This cross-sectional analytical study was conducted at the Department of Obstetrics and Gynaecology at the Institute of Child and Mother Health (ICMH), Matuail, Dhaka. It took place from January to December 2018. The study population comprised 120 pregnant women within the gestational age of 28-40 weeks. The women were categorized into three groups: Group A (control) consisted of normotensive pregnant women, Group B included pregnant women with mild pre-eclampsia, and Group C comprised pregnant women with severe pre-eclampsia. Purposive convenient sampling was employed. Data was collected through a detailed history, physical examinations, and relevant tests, with diagnosis based on established criteria. Ethical considerations were adhered to, with ethical clearance obtained from the Institutional Review Board and informed consent obtained from each participant. Data analysis employed SPSS-22, encompassing calculations of means, standard deviations, frequencies, and percentages, and statistical tests such as Chi-Square, t-test, and ANOVA. The results were presented using tables, figures, charts, and textual summaries while safeguarding participant rights, confidentiality, and the option to withdraw from the study.

Inclusion criteria:

- Normotensive patient between 28 to 40 weeks of pregnancy.
- Preclamptic women between 28 to 40 weeks of pregnancy.
- Age between 18 to 40 years.
- Prime and multi-para with singleton pregnancy

Exclusion criteria:

- Patient with chronic hypertension
- Patient with obstetrics complication.
- Patients with medical diseases like diabetes, renal disease, cardiovascular disease, hemorrhagic disorders or PROM.

RESULTS

Table I: Distribution of participants by their demographic profile ((n=120)

Variables	Group			p-value
	A(n=60%)	B(n=30%)	C(n=30%)	
Age				
18-25	45(75.0)	22(73.3)	19(63.3)	0.364
26-30	12(20.0)	4(13.3)	9(30.0)	
31-35	12(20.0)	4(13.3)	9(30.0)	
Mean±SD	24.26±3.07	24.23±4.52	24.73±4.01	0.83
BMI				
Underweight	1(1.7)	0	0	0.039
Normal (18.5-	50(83.3)	19(63.3)	16(53.3)	
Overweight (25-29.9)	9(15.0)	10(33.3)	12(40.0)	
Obese (≥30)	0	1(3.3)	2(6.7)	
Education				

Illiterate	11(18.3)	9(30.0)	6(20.0)	0.424
Primary	24(40.0)	10(33.3)	10(33.3)	
Secondary	9(15.0)	7(23.3)	9(30.0)	
Higher	16(26.7)	4(13.3)	5(16.7)	
Occupation				
Housewife	43(71.7)	22(73.3)	23(76.7)	0.811
Service holder	7(11.7)	4(13.3)	5(16.7)	
Day labor	5(8.3)	2(6.7)	0	
Student	5(8.3)	2(6.7)	2(6.7)	
Socioeconomic Status				
Poor	30(50.0)	18(60.0)	18(60.0)	0.811
Middle income	18(30.0)	8(26.7)	8(26.7)	
Rich	12(20.0)	4(13.3)	4(13.3)	

P-value determined by the Chi-square test and one-way ANOVA.

Table I shows the distribution of demographic characteristics among the participants. The majority of the patients from all groups were aged between 18-25 years (75.0,73.3 and 63.3%) respectively of groups A, B and C). The mean age of group A, B and C participants were respectively 24.26±3.07, 24.23±4.52 years and 24.73±4.01 years. The distribution was similar across groups (p>0.05). BMI was significantly higher in group A and B patients than in group C. The majority of the patients from all groups attended primary education (classes one to five). Among group A, B and C patients respectively 40.0,33.3 and 33.3% of patients completed were educated between classes one to five. Among groups A, B and C respectively 18.3,30 and 20% of patients were illiterate. The distribution was similar across groups. Most of the patients were housewives in all groups. The distribution of occupation was similar across groups. The frequency of socioeconomic class is described in Table I. However, the distribution was similar across groups(p>0.05).

Table II: Distribution of the study participants by obstetric profile (n=120)

Variable	Group A n=60(%)	Group B n=30(%)	Group C n=30(%)	p-value
Parity				
Primipara	45(75.0)	23(76.6)	27(90.0)	0.222
Multipara	15(25.0)	7(23.4)	3(10.0)	
Gestational Age(weeks)				
<33	3(5.0)	1(3.3)	4(13.3)	0.022
33-36	22(36.7)	13(43.3)	12(40.0)	
37-40	24(40.0)	16(53.3)	14(46.7)	
>40	11(18.3)	0	0	
Mode of Delivery				
Normal Vaginal	47(78.3)	11(36.7)	6(20.0)	<0.001

Delivery				
Caesarian Section	9(15.0)	17(56.7)	24(80.0)	
Assisted Vaginal Delivery	4(6.7)	2(6.7)	0	

p value determined by the Chi-square test

The **Table II** shows the obstetric profile distribution of the participants. The distribution of parity was also similar across groups. Gestational age was significantly lower in mild and severe preeclampsia in comparison to normal pregnant mothers (p <0.05). According to the Mode of Delivery Caesarian Section delivery was significantly more common among preeclamptic mothers than that normal and assisted vaginal delivery(p<0.001).

Table III: Frequency distribution of study subjects according to CRP status (n=120)

CRP level	Group A n=60(%)	Group B n=30(%)	Group C n=30(%)	p value
Normal(≤5mg/dl)	56(93.34%)	8(26.7%)	2(6.7%)	
Raised (>5mg/dl)	4(6.7%)	22(73.3%)	28(93.3%)	<0.001

The **Table III** shows the CRP status among the participants. Among 30 patients with severe preeclampsia, 93.3% had raised CRP and 6.7% had normal CRP levels. Respectively 6.7,73.3 and 93.3% of participants with normal blood, mild pre-eclampsia and severe preeclampsia blood pressure had raised CRP. The differences among and between groups were statistically significant (p<0.05).

Table IV: Comparison of serum CRP level and birth weight between different groups (n=120)

Variable	Group A (n=60)	Group B (n=30)	Group C (n=30)	P-value
CRP level(mg/dl)	3.07±1.15	9.67±5.49	13.15±4.01	<0.001
Birth Weight(kg)	2.95±.48	2.68±.49	2.61±.40	<0.05
Comparison P-value				
Group	A vs B	A vs C	B vs C	
Serum CRP	<0.001	<0.001	<0.001	
Birth Weight	<0.05	<0.05	<0.05	

P-value determined by one-way ANOVA with the Bonferroni test

The **Table IV** compares the serum CRP level and birth weight between different groups. The average CRP level of group A, group B, and group C participants was respectively 3.07±1.15, 9.67±5.49 and13.15±4.10 mg/dl. ANOVA and independent samples t-test show that CRP

levels are significantly different from each other.

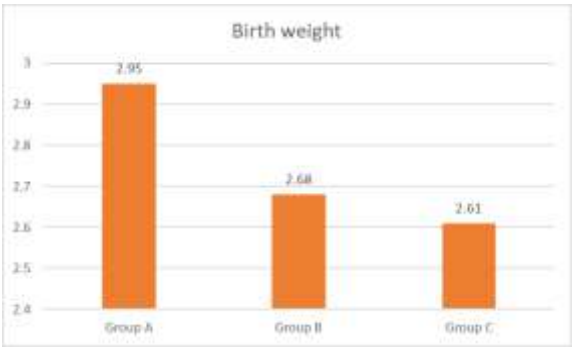

Figure 1: Simple Bar diagram showing mean fetal birth weight among different groups of the study population

In the **figure 1**, the fetal birth weight for Group A is recorded as 2.95, for Group B it is 2.68, and for Group C it is 2.61.

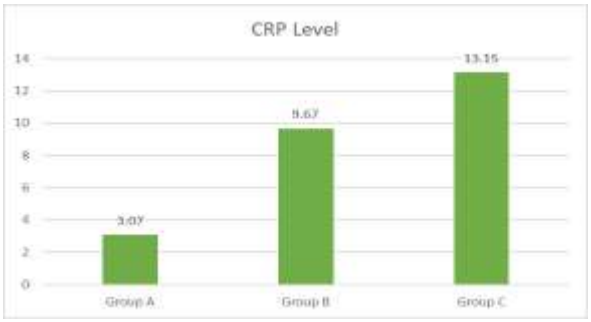

Figure 2: Simple Bar diagram showing mean serum CRP level among different groups of the study population

In **figure 2**, it can be seen that Group A had the lowest mean CRP level at 3.07, while Group B exhibited a higher mean CRP level of 9.67. Group C shows the highest mean CRP level among the three groups, measuring 13.15.

Table V: Frequency distribution of study subjects according to CRP status (n=120)

CRP level	Group A	Group B	Group C	p value
	n=number	n=number (%)	n=number (%)	
Normal(≤5mg/dl)	56(93.34%)	8(26.7)	2(6.7)	
Raised (>5mg/dl)	4(6.7%)	22(73.3)	28(93.3)	<0.001

Group A: Normal pregnancy Group B: Mild preeclampsia Group C: Severe preeclampsia

The **Table V** shows the distribution of CRP among different groups. Among 30 patients with severe preeclampsia, 93.3% had raised CRP and 6.7% had normal CRP levels. Respectively 73.3, 93.3 and 6.7% of participants with mild pre-eclampsia, severe preeclampsia and normal blood pressure had raised CRP. The differences among and between groups were statistically significant ($p<0.05$).

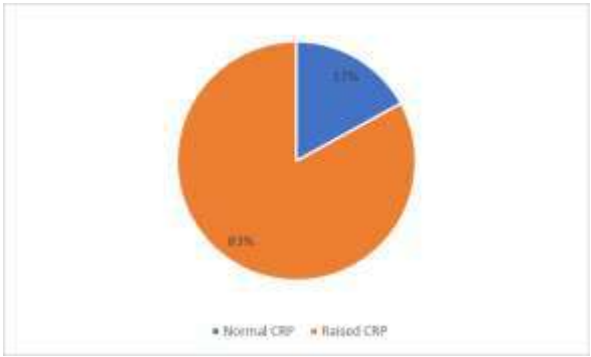

Figure 3: Pie chart showing the proportion of CRP status among the pre-eclamptic patients (n=60)

The pie chart in **Figure 3** represents the proportion of C-reactive protein (CRP)

status among pre-eclamptic patients, with a total sample size of 60 individuals. The majority of pre-eclamptic patients (83%) have a normal CRP status, while a smaller proportion (17%) exhibits a raised CRP level.

Table VI: Comparison of fetal birth weight in between different groups (n=120)

Birth weight of baby(kg)	Group A n=60(%)	Group B n=30(%)	Group C n=30(%)	p-value
Normal	57(95.0)	25(83.3)	23(76.7)	0.034
Low	3(5.0)	5(16.7	7(23.3	

The findings in **Table VI** show that fetal birth weight was low in 23.3% of severe preeclampsia patients, in 16.7% of mild preeclampsia patients and 5.0% of normal pregnancies. The difference was statistically significant

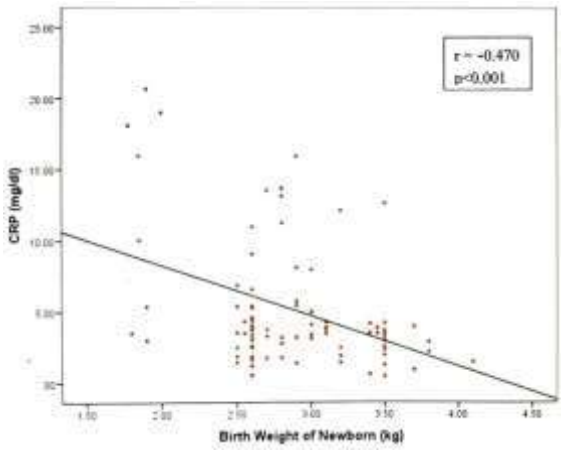

Figure 4: Correlation between CRP level of mother and birth weight of the newborn.

The **Figure 4** shows a Scatter Plot. The correlation coefficient (r = -0.470) suggests a significant negative relationship between maternal CRP levels and newborn birth weights ($p < 0.001$). As maternal CRP levels decrease, there is a tendency for newborn birth weights to increase.

Table VII: Association of serum CRP status with newborn baby outcome (n=120)

Variable	Serum CRP status		P value
	Normal	Raised	
Low Birth Weight			
Normal	64(61.0)	41(39.0)	<0.001
Low	2(13.3)	13(86.7)	
IUGR			
Absent	65(58.6)	46(41.4)	<0.01
Present	1(11.1)	8(88.9)	
APGAR Score			
>7	64(61.5)	40(38.5)	<0.01
3-6	1(11.1)	8(88.9)	
<3	1(20.0)	4(80.0)	
Neonatal condition			
Live birth	66(55.9)	52(44.1)	0.200
Stillbirth	0	2(100.0)	

Table VII shows the association between serum CRP status with newborn baby

outcome. Among mothers of low-birth-weight babies, 86.7% had increased CRP; among mothers of normal birth-weight babies, 39% had raised CRP. The difference was statistically significant ($p < 0.001$). Of mothers of babies with IUGR, 88.9% had increased CRP; among mothers of normal babies, 41.4% had raised CRP. The difference was statistically significant ($p < 0.01$). Mothers of babies with higher APGAR scores had a lower proportion of raised serum CRP levels. The difference was statistically significant ($p<0.01$). The difference in CRP levels in neonatal conditions was not statistically significant.

DISCUSSION

Preeclampsia remains a significant health concern during pregnancy, affecting both maternal and fetal health. This study investigates the relationship between C-reactive protein (CRP) levels in pre-eclamptic women and fetal outcomes, comparing these findings with existing literature. A total of 120 pregnant mothers were included in the study. Among them 60 had preeclampsia and another 60 had normal pregnancy. They were grouped into three categories. Groups A, B, and C consisted of 60 normal pregnant women, 30 mild preeclamptic, and 30 severe preeclamptic patients. mild preeclamptic, 30 severe preeclamptic. The mean ages of the three groups were respectively 24.26±3.07, 24.23±4.52 and 24.73±4.01 years. This is similar to the findings of Sharmin and colleagues. They found an average age of 24.58±4.05 years among preeclamptic and 23.92±3.72 years among normal pregnancy controls [10]. In another study conducted in a tertiary care setting in Bangladesh involving only preeclamptic mothers an average age of 24.06±3.71 years was reported which endorses the findings of his study [10]. In this study, the majority of mothers from all groups completed primary education. Among preeclamptic mothers 18.3% from group A and 30% from group B were illiterate and 20% of normal pregnant mothers were illiterate. In comparison, Ramesh and his colleagues found respectively 22 and 20% illiterate among preeclamptic and normal pregnancies in their study [12]. Although the difference in education among groups was not significant, it goes along with the findings of Opitasari and Andayasari who reported an increased risk of preeclampsia among mothers with lower levels of education [13]. Housewives constituted respectively 71.7, 73.3. and 76.7% of group A, B, and C mothers. This is concordant with the findings of Yeasmin and Uddin (2017) who found 80% of housewives in their preeclamptic study population [11]. In this study, the majority of preeclamptic patients (60%) and normal pregnancies (50%) came from lower socioeconomic classes. The distribution of socioeconomic status was similar across groups which is concordant with the findings of Saxena et al (2014) [14]. Most of the preeclamptic cases and controls (40% of group A, 56.7% of group B and 50% of group C were nulliparas in the present study. In a similar study, Paternoster and his team found respectively 51 and 43% nulliparity among preeclamptic and normal pregnancy groups [15]. The mean gestational age of the fetus at delivery was lower in preeclamptic women than in healthy pregnancies. The average gestational age among mild preeclamptic, severe preeclamptic and normal pregnancies were respectively 36.33±2.36, 36.10±2.80 and 37.30±2.80 weeks. This reiterates the findings of Gharib et al (2016) [16]. They

found an average gestational age of respectively 33.40±3.60, 33.60±4.18 and 36.00±3.18 weeks for mild preeclamptic, severe preeclamptic and normal pregnancies. Sharmin et al found a significantly higher gestational age for healthy mothers in comparison to preeclamptic mothers [10]. The average CRP level of group A, group B and group C participants were respectively 3.07±1.15 mg/dl. 9.67±5.49 and 13.15±4.10. The mean CRP level was significantly higher among patients with mild preeclampsia in comparison to normal pregnancies($p<0.05$). Also, severe preeclampsia patients had significantly higher mean CRP level in comparison mild preeclampsia and normal pregnancies ($p<0.05$). This is concordant with findings of Gharib et al. who reported an average CRP level of 15, 43.1 and 1.8 mg/dl respectively in mild preeclamptic, severe preeclamptic and healthy pregnancies ($p<0.001$) [16]. In this study, 6.67% of the normal pregnancies had raised CRP while 83.3% of preeclamptic pregnancies had raised CRP which is significant ($p<0.001$). Similarly, Sharmin et al found 68% preeclamptic cases and 2% healthy controls of raised CRP with the difference being significant ($p<0.05$) [10]. In addition, among preeclamptic women, those with severe eclampsia had a significantly higher proportion of elevated CRP than mild preeclampsia patients ($p<0.05$). Fetal birth weight was found significantly lower in preeclamptic patients in the present study, which is concordant with the findings of Teran and colleagues [17]. Preeclamptic pregnant mothers as well as mother with an increased level of CRP has had significantly more cases of low birth weight, and premature and IUGR babies than that control($p<0.05$). Even among preeclamptic patients those who had raised CRP had all the fetal complications. This indicates that raised CRP was associated with poor fetal outcomes. This is explainable. Because CRP being an inflammatory marker represents systemic inflammation and early onset, severe maternal preeclampsia is often associated with fetal intrauterine growth restriction [18]. Whereas CRP levels in preeclampsia are believed to correlate with preeclamptic process severity [15]. An important finding was a significant negative correlation between CRP level with neonatal birth weight which was also elicited by Paternoster et al (2006) and Sharmin et al (2016) in their studies [15,10].

LIMITATIONS OF THE STUDY

The study was conducted in a single center with a small sample size. So, the results may not represent the whole community.

CONCLUSION

This study highlights a significant link between elevated CRP levels in preeclamptic women and adverse fetal outcomes, including lower birth weights, prematurity, and IUGR. It underscores the importance of CRP monitoring during pregnancy, especially in cases of preeclampsia, for early intervention and improved fetal health.

RECOMMENDATION

It is advisable to include CRP measurements in routine prenatal care for at-risk or diagnosed preeclamptic women, aiding in early identification of those at higher risk for adverse fetal outcomes and guiding appropriate management. Additionally, further research should delve into the mechanisms behind elevated CRP

levels and poor fetal outcomes in preeclampsia to inform targeted interventions. Lastly, public health efforts should prioritize improving the overall health and socioeconomic status of pregnant women to reduce preeclampsia incidence and related complications, benefiting both maternal and fetal health.

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CONFLICT OF INTEREST:
None declared

ETHICAL APPROVAL:
The study was approved by the Institutional Ethics Committee

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