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Associations between Serum CRP Concentration, Maternal Hypertension, and Fetal Outcome: A Comparative Analysis in Pregnant Women

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Abstract

Introduction*:** Pre-eclampsia is a complex disorder characterized by hypertension and proteinuria after 20 weeks of gestation, posing risks to maternal and fetal health. It is linked to adverse outcomes worldwide, with varying incidence rates across regions. Risk factors include history, maternal age, and socioeconomics. The pathophysiology involves issues with spiral artery adaptation. The study aimed to analyze the associations between serum CRP concentration, maternal hypertension, and fetal outcomes in pregnant women. ***Methods: This cross- sectional analytical study was conducted at the Department of Obstetrics and Gynecology 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. Ethical guidelines were followed, including IRB approval and participant consent. Data were analyzed using SPSS software, version, 22.0. Chi-Square, t-test, and ANOVA test were performed to determine associations among the study variables of the groups, where $p<0.05$ considered as the level of significance. ***Results*:** The study enrolled 120 participants divided into Groups A, B, and C. The majority fell within the 18-25 age range. The mean ages were 24.23±4.52 (Group A), 24.73±4.01 (Group B), and 24.26±3.07 (Group C). BMI was significantly higher in Groups A and B compared to Group C ($p < 0.05$). Gestational age was lower in mild and severe preeclampsia compared to normal pregnancies ($p < 0.05$). Cesarean section delivery was significantly more frequent in preeclamptic mothers ($p < 0.001$). CRP levels varied, with means of 3.07 (Group A), 9.67 (Group B), and 13.15 (Group C), showing significant differences ($p < 0.05$). Fetal birth weight was lowest in Group C (2.61) and highest in Group A (2.95). Severe preeclampsia patients had elevated CRP levels, with 93.3% exhibiting this trend ($p < 0.05$). Adverse neonatal outcomes were more common in preeclampsia cases, including prematurity, LBW, and neonatal complications ($p < 0.05$). Increased CRP levels were associated with low birth weight ($p < 0.001$) and lower APGAR scores ($p < 0.01$). **Conclusion:** Pre- eclampsia shows raised serum CRP levels, particularly pronounced in severe cases, with about 83% of patients affected. This heightened CRP connects to adverse fetal outcomes.

Keywords*:* Pre-eclampsia, Serum CRP, Maternal Hypertension, pregnancy.

INTRODUCTION

Pre-eclampsia, a complex disorder characterized by hypertension and proteinuria after 20 weeks of gestation, poses significant risks to both maternal and fetal health. It is associated with increased maternal and perinatal morbidity and mortality worldwide, as well as neurological disorders, liver disease, and abnormal renal function [1]. The incidence of pre-eclampsia varies across different regions, with South-East Asia and North African regions reporting rates of 1.51% and 1.56%, respectively [2]. In South

Africa, the prevalence ranges from 1.8% to 7.1% [3], while developing countries have reported rates between 1.8% and 16.7% [4]. Bangladesh, a developing country, lacks specific data on the incidence of pre-eclampsia. However, it contributes to 20.0% of maternal deaths, along with eclampsia [5]. According to the extrapolated annual estimate from the US Census Bureau International Data Base in 2004, the incidence of pre-eclampsia in Bangladesh is approximately 76,032 cases [6]. Several risk factors have been identified that influence the development of pre-eclampsia. These include a history of the disorder, extremes of maternal age, race, socioeconomic factors, change of paternity, twin pregnancy, nulliparity, increased birth interval, increased body mass index (BMI), increased blood pressure in early pregnancy, increased rate of weight gain during pregnancy, and the presence of gestational diabetes [7]. High altitude has also been associated with an increased incidence of pre-eclampsia, attributed to factors such as placental hypoxia, smaller uterine artery diameter, and lower uterine artery blood flow [8]. The pathophysiological mechanism of pre-eclampsia involves the failure of the trophoblastic invasion of spiral arteries, leading to maladaptation of maternal spiral arterioles. This maladaptation is associated with increased resistance in the uterine artery and decreased placental perfusion [9]. Clinical studies have shown a relationship between the aggravation of hypertension complications and changes in the concentration of various chemicals in the mother's serum [10]. Some studies have suggested that alterations in blood trace element levels may implicate the pathogenesis of pre-eclampsia, while others have failed to establish a clear association [11- 13]. Pre-eclampsia and eclampsia are associated with unfavorable outcomes for both the mother and the fetus. Maternal complications include placental abruption, preterm birth, and HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets). Fetal complications include stillbirth, low birth weight, and small for gestational age [14]. Furthermore, pre-eclampsia has been linked to an increased prevalence of cardiovascular diseases risk factors, such as metabolic syndrome, impaired insulin metabolism, microalbuminuria, endothelial dysfunction, inflammatory factors, and oxidative stress [15, 16]. Preeclampsia and eclampsia contribute significantly to maternal mortality, particularly in developing countries, where approximately 40,000 women die each year due to these conditions. Preeclampsia alone accounts for 40% to 60% of maternal deaths in developing countries [17]. C-reactive protein (CRP) is an acute-phase protein that serves as a sensitive and specific marker of overall inflammatory activity in the body [18]. Elevated CRP levels have been observed in pregnant women, although to a lesser extent than in those with pre-eclampsia [19]. CRP production is stimulated by proinflammatory cytokines, such as interleukin-1, interleukin-6, and tumor necrosis factor-alpha. Elevated CRP levels during gestation have been associated with adverse pregnancy outcomes, including pre-eclampsia and intrauterine growth restriction [21]. Additionally, elevated serum CRP levels have been linked to an increased risk of preterm delivery [22]. This study aims to evaluate the association between maternal serum CRP levels in pre-eclampsia and its impact on fetal outcomes in singleton pregnant women. By examining the relationship between CRP concentration, maternal hypertension, and fetal outcomes, this research seeks to contribute to a better understanding of the pathophysiology and potential predictive markers of pre- eclampsia. Pre-eclampsia is a significant health concern globally, with varying incidence rates across different regions. Several risk factors have been identified, and the pathophysiological mechanisms involve the failure of trophoblastic invasion and maladaptation of maternal spiral arterioles. Pre-eclampsia is associated with adverse maternal and fetal outcomes, and it contributes significantly to maternal mortality, particularly in developing countries. CRP, as an inflammatory marker, has shown potential as a predictor of adverse pregnancy outcomes. This study aimed to explore the associations between serum CRP concentration, maternal hypertension, and fetal outcomes, providing valuable insights into the management and prediction of pre-eclampsia.

METHODS

This cross-sectional analytical study was conducted at the Department of Obstetrics and Gynecology 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.
- Primi and multi-para with a 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 1: Distribution of participants by their demographic profile (n=120)

Variables	Group A n=60	Group B n=30	Group C n=30	p-value
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	0.830
BMI				
Underweight (<18.5)	1(1.7)	0	0	0.039
Normal (18.5-24.9)	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)	

p value determined by the Chi-square test and one-way ANOVA.
Group A: Normal pregnancy Group B: Mild preeclampsia Group C: Severe preeclampsia

The majority of the patients from all groups were aged between 18-25 years (73.3,63.3 and 75 % respectively of groups A, B, and C). The mean age of group A, B an C participants were respectively 24.23±4.52 years, 24.73±4.01 years, and 24.26±3.07 years. The distribution was similar across groups (p>0.05). BMI was significantly higher in group A and group B patients than in group C participants.

Table 2: 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	

The distribution of parity was also similar across groups. Gestational age was significantly lower in mild and sever preeclampsia in comparison to normal pregnant mothers (p <0.05).

Table 3: Mode of delivery among the study population (n=120)

Mode of Delivery	Group A (n=60)	Group B (n=30)	Group C (n=30)	p-value
Normal Vaginal Delivery	47(78.3)	11(36.7)	6(20.0)	<0.001
Caesarian Section	9(15.0)	17(56.7)	24(80.0)	
Assisted Vaginal Delivery	4(6.7)	2(6.7)	0	

CS delivery was significantly more common among preeclamptic mothers than that of normal and assisted vaginal delivery (p<0.001)

Table 4: Comparison of serum CRP level & 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±0.48	2.68±0.49	2.61±.40	<0.05

The average CRP level of group A, group B and group C participants were respectively 9.67±5.49,13.15±4.10 and 3.07±1.15 mg/dl. ANOVA and independent samples t test shows that CRP level significantly different from each other.

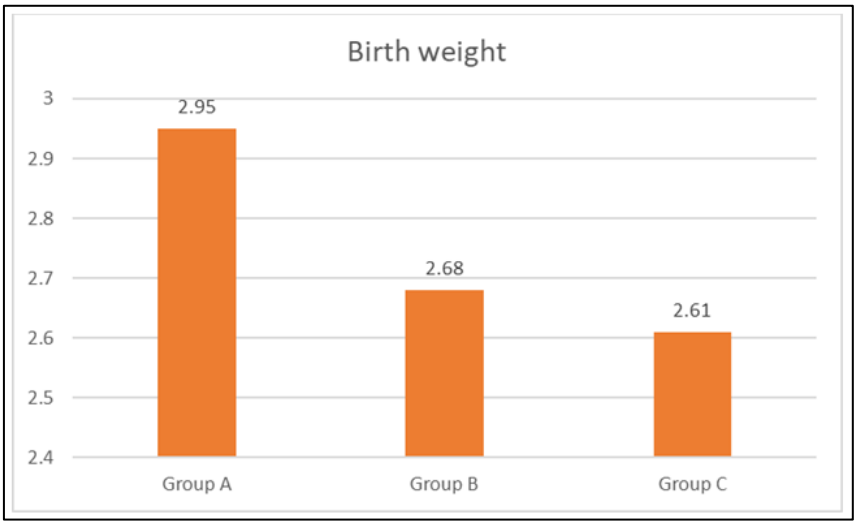

Figure 1: Simple Bar diagram showing mean fetal birth weight among different groups of the study population

In the figure provided, 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.

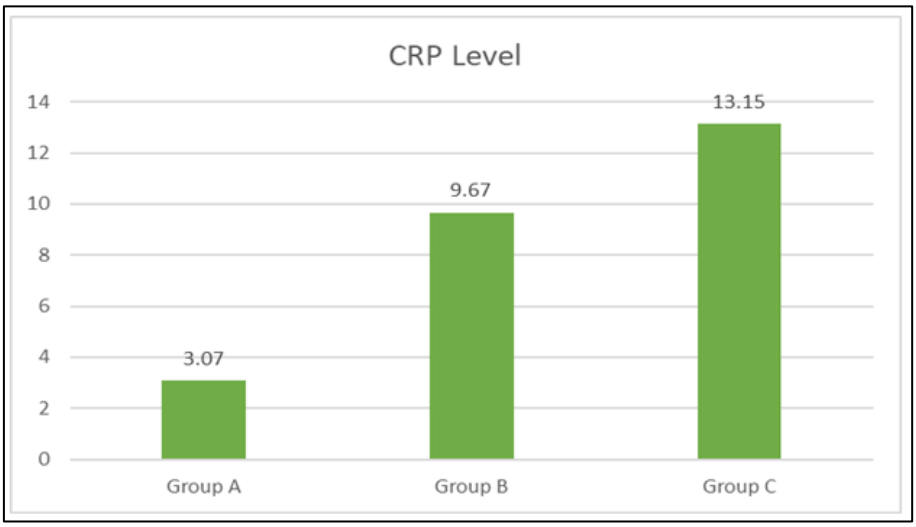

Figure 2: Simple Bar diagram showing mean serum CRP level among different groups of the study population

Group A had the lowest mean CRP level at 3.07, while Group B exhibits a higher mean CRP level of 9.67. Group C shows the highest mean CRP level among the three groups, measuring 13.15.

Table 5: 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)	<0.001
Raised (>5mg/dl)	4(6.7%)	22(73.3)	28(93.3)	

Among 30 patients with severe preeclampsia, 93.3% had raised CRP and 6.7% had normal CRP level. Respectively 73.3, 93.3 and 6.7% 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).

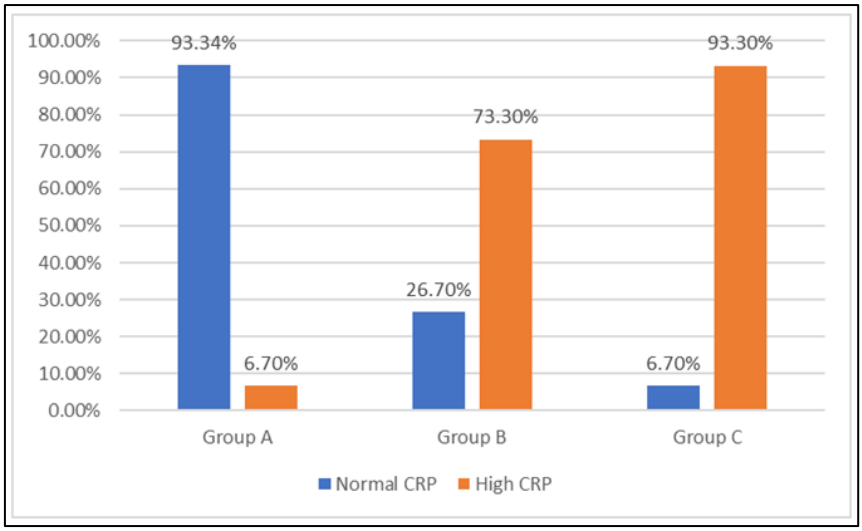

Figure 3: Multiple Bar diagram showing the distribution of CRP status in different groups of the study population

In Group A, the majority of individuals (93.34%) have a normal CRP status, while a small percentage (6.7%) have a high CRP status. In Group B, a significantly lower proportion (26.7%) have a normal CRP status, with the majority (73.3%) falling into the high CRP category. Group C exhibits the highest percentage of individuals with a high CRP status (93.3%), with only a small fraction (6.7%) having a normal CRP status.

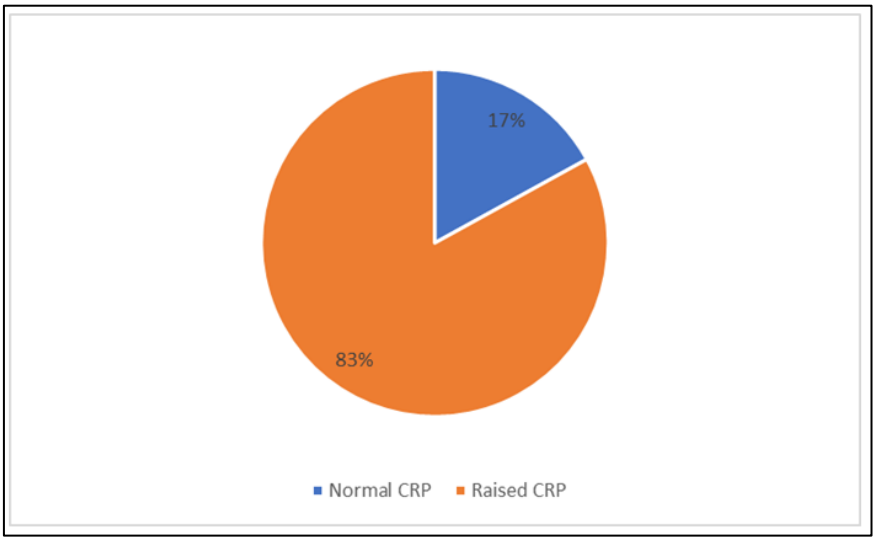

Figure 4: Pie chart showing the proportion of CRP status among the pre-eclamptic patients (n=60)

The pie chart 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%) exhibit a raised CRP level.

Table 6: Association of neonatal outcome with pre-eclampsia in the study population (n=120)

Fetal outcome	Normal Pregnancy (n=60)	Mild pre-eclampsia (n=30)	Severe pre-eclampsia (n=30)	P-value
prematurity				
No prematurity	55(91.7)	17(56.7)	22(73.3)	
Prematurity	5(8.3)	13(43.3)	8(26.7)	<0.001
Birth Weight				
Normal	57(95)	25(83.3)	23(76.7)	
Low	3(5.0)	5(16.7)	7(23.3)	<0.001
IUGR				

Fetal outcome	Normal Pregnancy (n=60)	Mild pre-eclampsia (n=30)	Severe pre-eclampsia (n=30)	P-value
Normal	59(98.3)	24(80.0)	23(76.7)	
Retarded	1(1.7)	6(20.0)	7(23.3)	<0.01
APGAR Score				
≥7	59(98.3)	23(79.3)	22(75.9)	
3-6	1(1.7)	4(13.8)	4(13.8)	<0.05
≤3	0	2(6.9)	3(10.3)	
Neonatal condition				
live birth	60(100)	29(96.7)	29(96.7)	
Stillbirth	0	11(3.3)	1(3.3)	0.362
Neonatal Complication				
No neonatal Asphyxia	58(96.6%)	25(83.3%)	25(83.3%)	
Neonatal Asphyxia	2(3.4%)	5(16.7%)	5(16.7%)	<.05

P-value determined by Chi-square test. Two data missing due to still birth

Prematurity, low birth weight baby, retarded intra-uterine growth, low APGAR score and neonatal complications were significantly more common in preeclampsia patients (both mild and severe) (p<0.05). Mothers with severe preeclampsia had more cases of LBW baby, low APGAR score baby and neonatal complications than mild preeclampsia patients.

Table 7: Association of serum CRP status with birth weight of newborn (n=120)

Serum CRP Status	Low Birth Weight		p-value
	Normal (n=15)	Low (n=105)	
Normal	64(61.0)	2(13.3)	<0.001
Raised	41(39.0)	13(86.7)	

P value determined by Chi-squared test

Among mothers of low-birth-weight babies, 86.7% had increased CRP and among mothers of normal birth-weight babies, 39% had raised CRP. The difference was statistically significant (p <0.001).

Table 8: Association of serum CRP status with APGAR Score of newborns (n=120)

Serum CRP Status	APGAR Score			p-value
	≥7 (n=104)	3-6 (n=9)	<3 (n=5)	
Normal	64(61.5)	1(11.1)	1(20.0)	<0.01
Raised	40(38.5)	8(88.9)	4(80.0)	

P value determined by the Chi-squared test

Mothers of babies with higher APGAR scores had a lower proportion of raised serum CRP levels. The difference was statistically significant (p<0.01).

DISCUSSION

Hypertensive disorders complicate 5% of all pregnancies [22]. Preeclampsia is a serious hypertensive disorder of pregnancy that may lead to maternal and fetal morbidity and mortality. 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. Group A, B, and C consisted of respectively 60 normal pregnant women, 30 mild preeclamptic, and 30 severe preeclamptic patients. mild preeclamptic, 30 severe preeclamptic. The mean age of the three groups was respectively 24.26±3.07, 24.23±4.52, and 24.73±4.01 years. Another similar study found an average age of 24.58±4.05 years among preeclamptic and 23.92±3.72 years among normal pregnancy controls [23]. In another study conducted in a tertiary care setting of Bangladesh involving only preeclamptic mothers an average age of 24.06±3.71 years was reported which is endorses the finding of his study [24]. 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 [25]. 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 [26]. 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 [23]. 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. 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 levels in comparison to mild preeclampsia and normal pregnancies ($p<0.05$). This is concordant with the 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 ($p<0.001$) [26]. 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 ($p<0.05$) [23]. 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 [27]. Preeclamptic pregnant mothers as well as mother with increased level of CRP has had significantly more cases of low birth weight, premature and IUGR babies than that control($p<0.05$). Even among preeclamptic patients those who had raised had all the fetal complications. This indicates that raised CRP was associated with poor fetal outcomes. This is explainable. Because CRP is an inflammatory marker that represents systemic inflammation and early onset, severe maternal preeclampsia is often associated with fetal intrauterine growth restriction [28]. Whereas CRP levels in preeclampsia are believed to correlate with preeclamptic process severity [25]. 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) [23-25], in their studies. The main finding of this study is that maternal serum levels of CRP during pregnancy represent a useful predictor of fetal complications. Moreover, a positive association between maternal CRP levels and the composite endpoint including both maternal and neonatal adverse outcomes has been demonstrated. These results are in accordance with prior studies exploring the association between CRP and pregnancy adverse outcomes. [29, 30] As CRP is an inflammatory marker when compared to previous investigations, the findings of the present stud are likely to highlight that even a little increase in the degree of systemic inflammation during pregnancy can represent an additional risk for the development of pregnancy complications, both for mother and baby.

LIMITATION OF THE STUDY: The limited sample size from a single center, compounded by budget constraints, hinders the generalizability of the findings.

CONCLUSION

In pre-eclampsia, there is an elevation in serum CRP concentration, with more pronounced increases observed in cases of severe pre-eclampsia compared to milder forms. Approximately 83% of individuals with pre-eclampsia exhibit elevated CRP levels. This heightened CRP level is additionally linked to unfavorable fetal outcomes.

RECOMMENDATION

Additional population-based studies are required to extend these findings to the broader populace. It is essential to provide counseling to individuals with pre-eclampsia and elevated CRP levels regarding the heightened risk of adverse fetal outcomes, emphasizing the need for appropriate readiness measures. Incorporating CRP estimation as a predictive tool for pre-eclampsia would be advisable**.**

REFERENCES

1. Kiondo, P., Wamuyu-Maina, G., Wandabwa, J., Bimenya, G. S., Tumwesigye, N. M., & Okong, P. (2014). The effects of vitamin C supplementation on pre-eclampsia in Mulago Hospital, Kampala, Uganda: a randomized placebo controlled clinical trial. *BMC pregnancy and Childbirth*, *14*, 1-10.
2. Abalos, E., Cuesta, C., Carroli, G., Qureshi, Z., Widmer, M., Vogel, J. P., ... & WHO Multicountry Survey on Maternal and Newborn Health Research Network. (2014). Pre-eclampsia, eclampsia and adverse maternal and perinatal outcomes: a secondary analysis of the W orld H ealth O rganization Multicountry S urvey on M aternal and N ewborn H ealth. *BJOG: An International Journal of Obstetrics & Gynaecology*, *121*, 14-24.
3. Osungbade, K. O., & Ige, O. K. (2011). Public health perspectives of preeclampsia in developing countries: implication for health system strengthening. *Journal of pregnancy*, *2011*.
4. Lakew, Y., Reda, A. A., Tamene, H., Benedict, S., & Deribe, K. (2013). Geographical variation and factors influencing modern contraceptive use among married women in Ethiopia: evidence from a national population based survey. *Reproductive health*, *10*, 1-10.
5. Yeasmin, S., & Uddin, M. J. (2017). Determination of Risk Factors for Pre–Eclampsia in aTertiary Hospital of Bangladesh. *Chattagram Maa-O-Shishu Hospital Medical College Journal*, *16*(1), 29-32.
6. Jesmin, S., Jahan, S., Khan, M., Sultana, N., Jerin, J., Habib, S., & Paul, D. (2012). The Incidence, Predisposing Factors, Complications and Outcome of Preeclampsia in Diabetic Pregnancy',*BIRDEM Medical Journal*, *1*, (1), 10-14.

7. Barton, J. R., & Sibai, B. M. (2008). 'Prediction and prevention of pre-eclampsia', *ObstetGynecol*, *112*, (1), 39-72.
8. Julian, C. G. (2011). High altitude during pregnancy. *Clinics in chest medicine*, *32*(1), 21-31.
9. Ward, K., & Lindheimer, M. D. (2009). 'Chesleyl's Hyperensive Disorders in Pregnancy. Williams OBSTETRICS, Hypertensive disorders of pregnancy. *McGraw - Hill 2009.23 rd Edition'*.
10. Osmanağaoğlu, M. A., Topçuoğlu, K., Özeren, M., & Bozkaya, H. (2005). Coagulation inhibitors in preeclamptic pregnant women. *Archives of gynecology and obstetrics*, *271*, 227-230.
11. Caughey, A. B., Stotland, N. E., Washington, A. E., & Escobar, G. J. (2005). Maternal ethnicity, paternal ethnicity, and parental ethnic discordance: predictors of preeclampsia. *Obstetrics & Gynecology*, *106*(1), 156-161.
12. Bringman, J., Gibbs, C., Ahokas, R., Syamal, B., Ramsey, R., & Egerman, R. (2006). Differences in serum calcium and magnesium between gravidas with severe preeclampsia and normotensive controls. *American Journal of Obstetrics & Gynecology*, *195*(6), S148.
13. James, D. K., Steer, P. J., Weiner, C. P., & Gonik, B. (2010). *High risk pregnancy e-book: Management options-expert consult*. Elsevier Health Sciences.
14. Ward, K., & Lindheimer, M. D. (2009). 'Chesleyl's Hyperensive Disorders in Pregnancy. Williams OBSTETRICS, Hypertensive disorders of pregnancy. *McGraw - Hill 2009.23 rd Edition'*.
15. Aykas, F., Solak, Y., Erden, A., Bulut, K., Dogan, S., Sarli, B., ... & Kanbay, M. (2015). Persistence of cardiovascular risk factors in women with previous preeclampsia: a long-term follow-up study. *Journal of Investigative Medicine*, *63*(4), 641-645.
16. Akiibinu, M. O., Kolawole, T. O., Ekun, O. A., & Akiibinu, S. O. (2013). Metabolic dysfunctions in Nigerian pre-eclamptics. *Archives of gynecology and obstetrics*, *288*, 1021-1026.
17. Lakew, Y., Reda, A. A., Tamene, H., Benedict, S., & Deribe, K. (2013). Geographical variation and factors influencing modern contraceptive use among married women in Ethiopia: evidence from a national population based survey. *Reproductive health*, *10*, 1-10.
18. Qiu, C., Sorensen, T. K., Luthy, D. A., & Williams, M. A. (2004). A prospective study of maternal serum C-reactive protein (CRP) concentrations and risk of gestational diabetes mellitus. *Paediatric and perinatal epidemiology*, *18*(5), 377-384.
19. Ertas, I. E., Kahyaoglu, S., Yilmaz, B., Ozel, M., Sut, N., Guven, M. A., & Danisman, N. (2010). Association of maternal serum high sensitive C-reactive protein level with body mass index and severity of pre-eclampsia at third trimester. *Journal of Obstetrics and Gynaecology Research*, *36*(5), 970-977.
20. Wolf, M., Kettyle, E., Sandler, L., Ecker, J. L., Roberts, J., & Thadhani, R. (2001). Obesity and preeclampsia: the potential role of inflammation. *Obstetrics & Gynecology*, *98*(5), 757-762.
21. Hvilsom, G. B., Thorsen, P., Jeune, B., & Bakketeig, L. S. (2002). C-reactive protein: a serological marker for preterm delivery?. *Acta obstetricia et gynecologica Scandinavica*, *81*(5), 424-424.
22. WHO. (2005). The World Health Report 2005: Make every mother and child count The, World Health Report.
23. Sharmin, S., Chy, S., Alam, D., Banu, N., Rashid, F., & Kabir, S. (2016). Association of Serum C-reactive Protein in Preeclampsia and its Effect on Fetal Birth Weight A Case Control Study. *Bangladesh Journal of Obstetrics & Gynaecology*, *31*(2), 75-80.
24. Yeasmin, S., & Uddin, M. J. (2017). Determination of Risk Factors for Pre–Eclampsia in aTertiary Hospital of Bangladesh. *Chattagram Maa-O-Shishu Hospital Medical College Journal*, *16*(1), 29-32.
25. Paternoster, D. M., Fantinato, S., Stella, A., Nanhornguè, K. N., Milani, M., Plebani, M., ... & Girolami, A. (2006). C-reactive protein in hypertensive disorders in pregnancy. *Clinical and applied thrombosis/hemostasis*, *12*(3), 330-337.
26. Gharib, M. A., Mostafa, M. S., Harira, M. M., & Ali Attia, A. A. (2016). 'Predictive Value of Maternal Serum C-Reactive Protein Levels with Severity of Preclampsia', *ZUMJ*, *22*, (2), 70-81.
27. Teran, E., Escudero, C., & Calle, A. (2005). C-reactive protein during normal pregnancy and preeclampsia. *International journal of gynaecology and obstetrics*, *89*(3), 299-300.
28. Duhig, K., Vandermolen, B., & Shennan, A. (2018). 'Recent advances in the diagnosis and management of pre-eclampsia', *F1000Research*, *7*, 242.
29. Zerbo, O., Traglia, M., Yoshida, C., Heuer, L. S., Ashwood, P., Delorenze, G. N., ... & Croen, L. A. (2016). Maternal mid-pregnancy C-reactive protein and risk of autism spectrum disorders: the early markers for autism study. *Translational psychiatry*, *6*(4), e783-e783.
30. Vecchié, A., Bonaventura, A., Carbone, F., Maggi, D., Ferraiolo, A., Carloni, B., ... & Cordera, R. (2018). C-reactive protein levels at the midpregnancy can predict gestational complications. *BioMed Research International*, *2018*.