

Original Article

Association between Serum C-reactive Protein and Pre-eclampsia

SK Das¹, S Khanam², RK Roy³, S Alam⁴, TK Roy⁵, SB Joy⁶

Abstract:

Among the common disorders of pregnancy, Pre-eclampsia is important one which causes significant maternal and perinatal morbidity and mortality. Its incidence is still high in the developing countries. The triad of high blood pressure, edema and albuminuria is neither specific nor sensitive enough; therefore, a reliable biochemical marker is needed to solve the problem. C-reactive protein (CRP), a marker of tissue damage and inflammation, is elevated in serum in overt preeclampsia. The present study is aimed to explore the association of high maternal serum C-reactive protein (CRP) level with preeclampsia and correlation with the severity of pre-eclamptic process. A total of 60 pregnant women constituting 30 pre-eclamptic (case) and 30 normal (control) pregnant women in the third trimester were enrolled in this study. Both the groups were matched for their age, parity and other baseline characteristics. More than three quarters (76.70%) of the case group exhibited raised serum CRP, which was 20% in control group ($p=0.001$). CRP was elevated about 13 fold higher than that in the normal pregnant women. The mean systolic and diastolic blood pressure were significantly higher in case group (154 ± 12 mm of Hg) vs (107 ± 7 mm of Hg) in control group ($p\leq 0.001$) and serum level of CRP bears linear relationship with both systolic and diastolic blood pressures. Preeclamptic women with higher serum CRP level were at a significantly ($p<0.001$) lower gestational age than control. Twenty two (73.30%) cases had gestational age <37 weeks ($p=0.302$) and 66.70% control group had gestational age >37 weeks. The hypothesis of the study was supported by the study findings that maternal CRP concentration was higher in women with preeclampsia and was correlated with disease progression as evidenced by the investigative analysis.

Key words: Preeclampsia, C-reactive protein (CRP).

Introduction:

Preeclampsia is a very serious disease and is the second leading cause of maternal mortality, accounting for 16 to 18 percent of all maternal death. Preeclampsia complicates 5-7% of all pregnancies, in Bangladesh it is about 8.22% of pregnancies¹. Perinatal mortality

1. Dr. Sanjoy Kumar Das, MBBS, FCPS (Gynae and Obs), MS (Gynae and Obs), Senior Consultant, Dept. of Gynae and Obs, Faridpur Medical College Hospital.
2. Dr. Shafeya Khanam, MS (Gynae and Obs), FCPS (Gynae and Obs), Associate Professor, Dept. of Gynae and Obs, Faridpur Medical College.
3. Dr. Rajib Kumar Roy, DGO, Registrar, Dept. of Gynae and Obs, Faridpur Medical College Hospital.
4. Dr. Samiya Alam, DGO, FCPS (Gynae and Obs), Assistant Professor, Dept. of Gynae and Obs, Faridpur Medical College.
5. Dr. Tapan Kumar Roy, MS (Gynae and Obs), Asst Prof., Dept. of Gynae and Obs, Sheikh Sayera Khatun Medical College, Gopalganj.
6. Dr. Swapna Biswas Joy, MBBS, MCPS, MS (Gynae and Obs), Medical Officer, Faridpur Medical College Hospital, Faridpur.

Address of correspondence :

Dr. Sanjoy Kumar Das, MBBS, FCPS (Gynae and Obs), MS (Gynae and Obs), Senior Consultant, Dept. of Gynae and Obs, Faridpur Medical College Hospital. Mobile: +880-01712194279, E-mail: dr.royrajib@gmail.com

related to mild preeclampsia ranges from 1-8%, increasing to an overall average of 12% in severe preeclampsia, with a higher incidence found with early onset and lower incidence if the onset develops after 37 weeks of gestation². If the disease progresses into the HELLP syndrome or eclampsia or exists in the presence of preexisting chronic hypertension, perinatal mortality can be as high as 60 percent³. Although the incidence of preeclampsia is decreasing in the developed countries, such cases still pose a great problem in the developing countries. In Bangladesh, the incidence of preeclampsia is still very high and constitutes about 5 percent of total deliveries⁴.

Materials and Methods:

This study was carried out in the Dept of Obstetrics and Gynaecology Dhaka medical college hospital during the period from January 2011 to December 2011. The study included consecutively selected 60 third trimester pregnant women, among them 30 normotensive and 30 preeclamptic. Women with normal blood pressure throughout pregnancy and no proteinuria were selected as control group and patients with blood pressure $\geq 140/90$ mmHg taken on two occasions, 6 hours apart after the gestational age 20 weeks, urinary protein 0.3 g/L or more were included as cases.

Those had history of hypertension and or proteinuria prior to conception or before 20 weeks of gestation, renal disease, diabetes mellitus, any infection, and thyroid disease were excluded. All the third trimester pregnant women enrolled in the study were explained about the nature and purpose of the study, and only those who gave well-informed and written consents were included in the study. Two ml. of venous blood was drawn from each of the study subjects taking full aseptic precautions. Blood was allowed to stand still for about 30 minutes to clot. Clot was then separated from the test tube by wooden stick and was centrifuged within one hour of collection at 2000rpm for minutes. The separated serum was carefully drawn by micropipette and was stored in a micro centrifuged tube at -70°C until the analysis was done. Random urine sample was collected in a test tube and analyzed for presence of protein by dipstick reagent strip. Serum C-reactive protein was done by liquid phase immunoprecipitation assay and turbulometry. Data was recorded in predesigned sheet and analysis was done using computer based software, Statistical Package for Social Science (SPSS, version 11.5).

Result:

Regarding age distribution, a higher proportion of patient in both case and control groups were >30 years old (73.3% and 66.7% respectively). About 17% of cases was 20 or <20 years and 10% between 20-30 years old. The mean age was almost comparable between case and control groups (255.2±4.1 VS 24.1±4.5 years, p=0.344). (Table-I)

Table I: Comparison of age between case and controls

Age (yrs)	Group		p-value
	Case(n=30)	Control (n=30)	
20	5(16.7)	7(23.3)	0.344
20-30	3(10.0)	3(10.0)	
>30	22 (73.3)	20(66.7)	
Mean±SD	25.2±4.1	24.1±4.5	

Body mass index of the patients demonstrates that majority of the patients in both cases (83.3%) and control group (70%) were overweight or obese. (Table-

Table II: Comparison of BMI between groups

BMI (kg/m ²)	Group		p-value
	Case(n=30)	Control (n=30)	
Normal (18.9 -24.9 kg/m ²)	5(16.7)	9(30)	0.071
Overweight & obese (>25 kg/m ²)	25(83.3)	21(70.0)	
Mean±SD	28.0±3.2	26.4±3.2	

Table III shows that the mean systolic and diastolic blood pressures were significantly higher in case group than those in control group (154±12 vs 107±7 mmHg, p<0.001 and 101±11 vs 74±6 mmHg, p<0.001 respectively).

Table III. Comparison of mean systolic and diastolic blood pressure between groups.

Blood pressure (mmHg)	Group		p-value
	Case(n=30)	Control (n=30)	
Systolic BP	154±12	107±7	<0.001
Diastolic BP	101±11	74±6	<0.001

Table IV shows that 73.3% of the cases and 66.7% of the controls had gestational age below 37 weeks (p=0.002). Over half (56.7%) of the cases and 46.7% of the controls were nullipara (p=0.497). The prevalence of primigravid was although higher in the case group than that in the control group the difference did not reach the level of significance (p=0.438).

Table IV: Comparison of obstetric profile between groups

Obstetric profile	Group		p-value
	Case(n=30)	Control (n=30)	
Gestational age (weeks) <37 (preterm)	22(73.3)	20 (66.7)	0.302
37 (term)	8 (26.7)	10 (33.3)	
Gravida	16 (53.3)	13 (43.3)	0.438
Primigravida			
Multigravida	14 (46.7)	17 (56.7)	

Table V shows more than three-quarters (76.7%) of the case group exhibited raised serum CRP (>6 mg/L) as opposed to 20% of the control group (p=0.001). The likelihood of having elevated CRP in women with preeclampsia was estimated to be 13 fold (95% CI = 3.8 - 45.0) higher than that in the normal pregnant

Table V: Association between serum level of CRP and Preeclampsia

Serum level of CRP (mg/L)	Group		OR (95% CI)	p-value
	Case (n=30)	Control (n=30)		
>5	23(26.7)	6 (20.0)	13.1 (3.8-45.0)	<0.001
5	7(23.3)	24 (80.0)		

Table VI shows that staggeringly higher level of serum CRP was observed in patients with severe preeclampsia (38.7 mg/L) than that in patients with mild preeclampsia (10.6 mg/L) (p=0.006)

Table VI: Relationship between severity of preeclampsia and CRP

Severity of preeclampsia	CRP (mg/L)		p-value
	Mean(n=21)	SD (n=9)	
Mild	10.6	2.5	0.006
Severe	38.7	10.9	

Discussion:

A higher proportion of patients in both case and control groups were >30 years old (73.3% and 66.7% respectively). About 17% of cases were 20 or <20 years and 10% between 20-30 years old. The mean age was almost comparable between case and control groups (25.2±4.1 vs 24.1±4. years, P=0.344). This result is consistent with the findings of paternoster⁵. They found that both the groups matched in regard to age, and there was no statistically significant difference in age. Assessing 253 patients in their study, they obtained the age in case (n=63) group as 32±7 years and in control (n=190)31±5 years. In a case control study, Teran reported mean age in case group as 24.5±1.6 years and control group as 24.4±1.3 years⁶. Their finding is almost similar to us. An article in the American Journal of hypertension reported a study in which CRP, a clinical marker of systemic inflammation, was measured in maternal serum collected at 13 weeks of gestation on average, to determine whether elevations precede the clinical manifestation of preeclampsia. Using a prospective, nested case-control study design, CRP concentrations were measured using competitive immunoassays in 60 women who developed preeclampsia and in 506 women who remained normotensive throughout pregnancy. Logistic regression procedures were used to calculate odds ratio (OR) and 95% confidence interval (CI). The aim of a study by Ustun was to determine the level of CRP in preeclampsia and their association with the severity of the disease⁷. CRP level was investigated in 26 normal pregnant women, 26 mild preclampsia and 26 severe preeclampsia in the third trimester of pregnancy. Mean arterial pressure (MAP) was used as an indicator of the severity of the disease. Analysis of variance with the Kruskal-Wallis test was used when three groups were compared. For correlations, Spearman's rank correlation tests were used. Plasma CRP and fibrinogen levels in mild and severe preeclampsia patients were markedly higher than that of control third trimester pregnant women. There were significant correlations between MAP and CRP (r=0.51, p<0.001) in pregnancies complicated with preeclampsia.

The present study was carried out to assess whether CRP level is raised in preeclampsia and to reflect its relation with disease progression. In the present study, more than three-quarters (76.7%) of the case group exhibited raised serum CRP (>5mg/L) as opposed to 20% of the control group (p=0.001). The likelihood of having elevated CRP in women with preeclampsia was estimated to be 13-fold (95% CI=3.8-45.0) higher than that in the normal pregnant women (Table VII). Statistically the difference was significant (p<0.001). Significant difference (p<0.001) in CRP between severe and mild preeclampsia was also observed. Tjoa ML showed maternal serum CRP levels were higher preeclampsia group than in the control group (p<0.001)⁸. Their study result was similar to our findings.

In a prospective case control study by Wolf showed that first trimester CRP levels were significantly higher among women who subsequently developed preeclampsia compared with control (4.6 vs 2.3 mg/L, p<0.05)⁹.

Teran showed similar results in high-risk Andean population⁶. They observed that concentration of CRP was significantly higher in preeclampsia women (2.49±0.37 mg/dl; p<0.001) and nonpregnant control (1.33±0.15 mg/dl; p<0.001). The difference between normal pregnancy and control was also significant (p<0.01).

Ustun in a case-control study done in the third trimester of pregnancy showed plasma CRP levels in mild and severe preeclampsia were significantly higher than that of the normal third trimester pregnant women (r=0.515, p<0.01)⁷. These findings are consistent with the present study.

In the present study, CRP level showed significant positive correlation with SBP, DBP and also with MAP (<0.001), which was consistent with the study done by Paternoster⁵. They found similar strong positive correlation of CRP level with SBP and DBP. Recent studies demonstrated increased levels of CRP in women with preeclampsia^{5-7,9}.

Conclusion :

Persisting high CRP level is an area of concern, where obstetricians can focus their attention, and in this respect, CRP level may be clinically useful to monitor disease activity and response to treatment in preeclampsia patients. By this study it will also help to assess its severity and to take necessary steps to prevent further complications. In this way we can take part to provide a healthy mother with a healthy child to build a healthy nation.

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