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Serum C reactive Protein in Preeclamptic Women

S SULTANA[a], SR DABEE[b], S AKTER[c], MR KHATUN[d], P AKHTER[e]

Summary:

The incidence of preeclampsia is high in the developing countries. Since this condition is preventable if detected and treated at an early stage, it is essential to diagnose the disease at an early stage, and to institute proper medical care on time. The present study carried out in the Department of Obstetrics and Gynaecology, BIRDEM, and Dhaka Medical College Hospital during January 2009 and June 2010, was aimed to find out concentration of serum C reactive protein (CRP) in preeclamptic women. The study included 60 pregnant women; 30 normal (control) and 30 preeclamptic (case) pregnant women in their third trimester. Estimation of CRP was done by immunoprecipitation assay turbulometry method for both groups. The mean (±SD) age was 23.23±4.58 (control) and 23.90±3.20 (case) years (no significant difference). However, BMI, SBP and DBP were significantly (P<0.001) high in case compared to control group (BMI: 23.37±1.47 and 21.81±1.45 kg/m^2; SBP: 148.33±13.41 and 108.00±7.14 mmHg; DBP: 106.67±6.99 and 69.67±5.56 mmHg). C reactive protein concentration (mg/dl) was significantly higher (P<0.001) in case group (10.57±6.71) compared to control group (0.63±0.49). In control and case group, respectively, CRP was normal (£0.8 mg/dl) in 25 (83.3%) and 2 (6.7%), and raised (>0.8 mg/dl) in 5 (16.7%) and 28 (93.3) (P<0.001). This study shows that maternal CRP concentration tends to be significantly high in women with preeclampsia.

Key words: ***CRP, Preeclampsia***

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Introduction:

Preeclampsia is a very serious disease and is the second leading cause of maternal mortality, accounting for 16 18% of all maternal death[1]. If preeclampsia is treated early and effectively, maternal mortality can be reduced significantly. If the disease is allowed to progress to the HELLP (hemolysis, elevated liver enzyme and low platelet count) syndrome or eclampsia, maternal mortality increases to as high as 24%, and morbidity levels are even higher. The most common causes of mortality or morbidity are related to abruptio placentae, pulmonary edema, stroke, renal or hepatic failure, myocardial infarction, disseminated intravascular coagulation (DIC) and cerebral hemorrhage[2,3]. Women who receive no prenatal care are 12 times as likely to die from preeclamptic complications as women who do receive prenatal care[4]. Women who report high levels of stress and low social support during pregnancy are more likely to have increased immune system activity, which can trigger inflammatory responses and put them at risk for preeclampsia[5].

Hypertension is a sign of an underlying pathology which may be preexisting or appears for the first time during pregnancy[6]. Pregnancy may induce hypertension in women who were normotensive before pregnancy and may aggravate hypertension in those who are hypertensive before pregnancy. The clinical and laboratory characteristics of hypertension associated with pregnancy are difficult to differentiate from those of hypertension independent of pregnancy.

CRP is used mainly as a marker of inflammation. After onset of inflammatory or acute tissue injury, CRP synthesis increases with 4 to 6 hours, doubling every 8 hours and peak at 36 to 50 hours. The peak level is as much as 0.4 g/L within 24 to 48 hours. CRP levels remain elevated with ongoing inflammation and tissue destruction but with resolution they decline rapidly, because of a relatively short half life of 17 hours. A cross sectional study reported that CRP concentrations

a. Dr. Sharmin Sultana, Medical Officer, 200 Bedded Hospital, Narayanganj
b. Dr. Seema Rani Dabee, Junior Consultant, 20 Bedded Hospital, Amin Bazar, Savar
c. Dr. Saida Akter, Private Practice
d. Dr. Mst. Rahima Khatun, Junior Consultant, Sadar Hospital, Satkhira
e. Dr. Parul Akhter, Junior Consultant, 200 Bedded Hospital, Narayanganj

Address of Correspondence: Dr. Sharmin Sultana, Chaya Kabba, Flat No. A/47, Plot No. 745, Hazi Nasiruddin Road, Dania, Dhaka, Phone: 01711236047

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were 66 percent higher in women with preeclampsia as compared with controls. Another prospective nested case control study reported that women with CRP concentration >4.1 mg/L experienced 3.5 fold increased risk of preeclampsia as compared with women whose CRP concentrations were <1.1 mg/L[6 10]. The above evidences have shown that there is significant association of elevated maternal serum C reactive protein concentration in peripheral circulation and increased risk of preeclampsia and are believed to correlate with preeclamptic process severity, preterm delivery and poor neonatal outcome.

In Bangladesh, the incidence of preeclampsia is high, about 8.22%[7]. Most case of preeclampsia are mild, and 90% occur after 34 weeks of gestation. Earlier cases of preeclampsia tend to be more severe, although severe disease may develop at term. It is about 5 15 % of pregnancies after 20 weeks of gestation, responsible for 16% of maternal deaths, 28% of perinatal mortality.

This study was intended to determine the elevated maternal CRP with risk of preeclampsia.

Materials and Methods:

This was a case control study carried out in the Department of Obstetrics and Gynaecology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), and Dhaka Medical College Hospital (DMCH) during July 2009 and June 2010. The study included consecutively selected 60 women at third trimester (30 normotensive and 30 preeclamptic).

Inclusion Criteria:

The selection criteria for control subjects was normal blood pressure throughout pregnancy and no proteinuria, and cases were (a) blood pressure [3]140/90 mmHg taken on two occasions, 6 hours apart after the gestational age of 20 weeks, and (b) urinary protein 0.3 g/L or more.

Exclusion Criteria:

Exclusion criteria for both control and case were (a) history of hypertension and/or proteinuria prior to conception or before 20 weeks of gestation, (b) renal disease, (c) diabetes mellitus, (d) thyroid disease, and (e) any infection.

Ethical Consideration:

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.

Clinical Assessment

Two ml of venous blood was drawn from each of the study subjects taking full aseptic precautions. The blood was transferred into a clean, dry test tube and taken to laboratory. 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 2000 rpm for 5 minutes. The separated serum was carefully drawn by micropipette and was stored in a microcentrifuged tube at 70^{o}C until the analysis was done. Random urine sample was collected in a clean test tube and analyzed for presence of protein by dipstick reagent strip. Estimation of serum C reactive protein concentrations was done by liquid phase immunoprecipitation assay and turbulometry at DMCH from January 2009 to June 2010.

Data processing:

The data obtained from each individual study subject was included in a predesigned data collection sheet, and the collected data was compiled, and appropriate analyses were done using SPSS.

Results:

Table I shows characteristics of the study subjects. Mean (±SD) age showed no significant difference between control (23.23±4.58 years) and case (23.90±3.80 years). Mean (±SD) BMI was significantly high (P<0.001) case group (23.37±1.47 kg/m^2) compared to control (21.81±1.45 kg/m^2), likewise, SBP (control 108.00±7.14, case 148.33±13.141 mmHg) and DBP (control 69.67±5.56, case 106.67±6.99 100.00 120.00 mmHg) both were significantly high (P<0.001) in case group. Similarly, mean (±SD) gestational age was also significantly high (P<0.001) in case group (36.27±0.91 weeks) compared to control (38.47±0.97 weeks).

Table II shows status of serum CRP. Mean (±SD) CRP was significantly (P<0.001) high in case group (10.57±6.71 mg/dl) compared to control (0.63±0.49 mg/dl). In control CRP was normal (£0.8 mg/dl) in 25 (83.3%) and raised (>0.8 mg/dl) in 5 (16.7%) subjects; however, in case group 2 (6.7%) had normal and 28 (93.3%) raised CRP (P<0.001).

Table I

Characteristics of the study subjects

Variables	Control (n=30)	Case (n=30)	P value
Age (years)			
Mean±SD	23.23±4.58	23.90±3.80	0.542^{ns}
Range	17.00 32.00	18.00 32.00	
Body mass index (kg/m^2)			
Mean±SD	21.81±1.45	23.37±1.47	0.0001***
Range	18.75 24.46	20.45 26.40	
Systolic blood pressure (mmHg)			
Mean±SD	108.00±7.14	148.33±13.41	0.0001***
Range	100.00 120.00	130.00 180.00	
Diastolic blood pressure (mmHg)			
Mean±SD	69.67±5.56	106.67±6.99	0.0001***
Range	60.00 80.00	100.00 120.00	

Unpaired Student's 't' test, ns = not significant, *** = significant (P<0.001)

Table-II

C reactive protein level in the study subjects

CRP (mg/dl)	Control (n=30) No. (%)	Case (n=30) No. (%)	P value
Normal (£0.8)	25 (83.3)	2 (6.7)	0.0001***
Raised (>0.8)	5 (16.7)	28 (93.3)	
Mean±SD	0.63±0.49	10.57±6.71	0.0001***
Range	0.02 1.60	0.08 25.60	

Chi square test/Unpaired Student's 't' test, *** = significant (P<0.001)

Discussion:

One of the major complications of preeclampsia is eclampsia which occurs in 0.2 0.5% of all deliveries in the developed countries[8]. It arises without any obvious symptoms in 15 20% cases. Fifty percent cases occur before labor, 25% during labor and 25% in the postpartum period. Postpartum eclampsia usually occurs within the first 48 hours but may occur up to 2 3 weeks later[9].

After onset of inflammatory or acute tissue injury, CRP synthesis increases with 4 6 hours, doubling every 8 hours and peak at 36 50 hours[10,11]. The peak level is as much as 0.4 g/L within 24 48 hours. CRP levels remain elevated with ongoing inflammation and tissue destruction but with resolution they decline rapidly, because of a relatively short half life of 17 hours[12].

A cross sectional study reported that CRP concentrations were 66% higher in women with preeclampsia as compared with controls[13]. Another prospective nested case control study reported that women with CRP concentration >4.1 mg/L experienced 3.5 fold increased risk of preeclampsia as compared with women whose CRP concentrations were <1.1 mg/L[14]. The above evidences have shown that there is significant association of elevated maternal serum C reactive protein concentration in peripheral circulation and increased risk of preeclampsia and are believed to correlate with preeclamptic process severity, preterm delivery and poor neonatal outcome.

Mean age of control group was 23.23±4.58 years and case group was 23.90±3.80 years. Most of the women were between 17 32 years age group, which is consistent with the findings of Paternoster *et al*[15]. In a case control study, Teran *et al*. reported mean age in control group as 24.4±1.3 years and case group as 24.5±1.6 years[13]. Their finding is almost similar to our finding. BMI in control and case groups were mean (±SD) 21.81±1.45 and 23.37±1.47 kg/m^2, respectively.

In this study, in control and case groups, respectively, mean (SD) SBP was 108.00±7.14 (range 100.00 120.00) and 148.33±13.31 (range 130.00 180.00) mmHg, and DBP was 69.67±5.56 (range 60.00 80.00) and 106.67±6.99 (range 100.00 120.00) mmHg were significantly (P<0.001) high in case group.

We found that CRP level was normal (£0.8 mg/dl) in 25 (83.3%) control and 2 (6.7%) case subjects, while it was raised (>0.8 mg/dl) in 5 (16.7%) and 28 (93.3%) subjects, respectively. Mean (±SD) serum CRP was significantly (P<0.001) high in case group (10.57±6.71 mg/dl) compared to control (0.63±0.49 mg/dl). Paternoster *et al*. also showed maternal serum CRP levels were higher (P<0.001) in preeclampsia group than in the control group[15]. Batashki *et al*. also observed a significant difference (P<0.01) in plasma concentration of CRP between case and control group at their third trimester[16]. They concluded that CRP values would be higher in women with preeclampsia compared to normal pregnancy, which is similar to the present study.

Wolf *et al*. in a prospective case control study 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)[14]. Teran *et al*. showed similar results in high risk Andean population where concentration of CRP was significantly higher in preeclamptic women (4.11±0.37 mg/dl); P<0.001) compared to normal pregnant women (2.49±0.37 mg/dl; P<0.01) 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)[13].

Recent studies demonstrated increased level of CRP in women with preeclampsia, which is consistent with the findings of the present study[13 18].

Sufficient data regarding incidence and prevalence of preeclampsia and eclampsia are lacking. In India, the incidence as recorded from hospital statistics varies widely from 5 15%[6]. There is no community based statistics regarding preeclampsia and eclampsia in Bangladesh. Health facilities available in our country are deficit than that of our neighbours. Therefore, both incidence and prevalence of preeclampsia and eclampsia is probably higher in our country. In Dhaka Medical College Hospital in 2009, total 13,606 patients were admitted in the Department of Obstetrics and Gynaecology, of whom 578 (4.25%) were preeclamptic and 535 (3.93%) were eclamptic.

Conclusion:

Preeclampsia is a disease difficult to study because it is present far in advance of the appearance of clinical signs and symptoms, and is multisystemic and without a single biochemical marker. The current research suggest that elevated maternal CRP level is associated with preeclampsia and may be the cause or the effect of preeclampsia. Therefore, identification of raised CRP levels and appropriate measures like intervention, close monitoring, if delivery is not chosen, should be done for maternal and fetal complications, such as IUGR and uteroplacental insufficiency. CRP levels may be clinically useful to monitor disease activity and response to treatment in early onset preeclampsia. Further studies involving larger sample size, in which CRP and other inflammatory markers are assayed at multiple time points in pregnancy and postpartum period are needed to support the findings of the present study.

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