Association of C-reactive Protein in Preeclampsia

Jahanara Akter*, Shamsun Nahar Begum2, Pervin Akter3, Mamata Manjuri4, Zenat Rehana5, Umme Salma6

Abstract
Introduction: Preeclampsia is a multisystemic disorder that complicate about 7-10 percent of human pregnancies. Worldwide this syndrome contributes high maternal and perinatal mortality and morbidity. C-reactive protein, a marker of tissue damage and inflammation, is elevated in serum in overt preeclampsia. It is used as an objective and sensitive index of overall inflammatory activities in the body. Aims and Objectives: To explore the association of C-reactive protein level with the preeclampsia patients. Materials and Methods: The present study was a Case-Control study, conducted in the Department of Obstetrics and Gynaecology in collaboration with the Department of clinical pathology of Sir Salimullah Medical College Hospital, Mitford, Dhaka during the period of January 2013 to December 2013. The study population was pregnant women with preeclampsia and normal term pregnant patients admitted during study period. A total of 66 patients were included in the study. Among them 33 were clinically diagnosed preeclampsia women grouped as Cases and another 33 were age, parity and BMI matched term pregnant women as Controls. Estimation of serum C-reactive protein was done by Nyco Card Reader-II method (Appendix-11). Statisticians analysis was perform by using SPSS. Results: C-reactive protein concentration (mg/L) was found significantly higher (p<0.001) in case group (17.93±10.5) than control group (7.45±1.80). C-reactive protein was ≥6mg/L in 29(87.9%) in case group and 9 (27.3%) in control group and C-reactive protein values showed significant positive correlation with systolic and diastolic blood pressure (p<0.001) in case group. C-reactive protein concentration was found significantly higher (p<0.001) in severe preeclampsia group than mild preeclampsia group. Conclusion: Therefore, it can apparently be concluded from this study that increased maternal serum C-reactive protein level might be a strong risk factor for preeclampsia, although the precise role of C-reactive protein in this regard whether causal or consequential, is yet to be determined. Finding of this study might be helpful for formulating a guideline for management of pregnant women with preeclampsia.

Key Words: C-reactive Protein, Preeclampsia.

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Introduction:
Preeclampsia is one of the most common medical complication during second half of pregnancy. Preeclampsia is defined as, the rise of blood pressure equal to or above 140/90 mm Hg in the presence of proteinuria developed after 20 weeks of gestational age in a previously normotensive and non proteinuric women. Preeclampsia can result in eclampsia when convulsion develops or manifests as hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome. Eclampsia and HELLP syndrome are associated with severe complications such as cerebral hemorrhage, renal insufficiency, lung edema and liver hemorrhage. Incidence of preeclampsia is about 7-10 percent throughout the world. In India, the incidence as recorded from hospital statistics varies widely from 5 to 15% percent. Both the incidence & prevalence of preeclampsia and eclampsia is higher in our country. In Sir Salimullah Medical College Hospital, 290 preeclamatic patients were admitted among 13404 obstetric patients in 2012. A maternal mortality of 15 percent still occurs with modern obstetric services. Women who receive no prenatal care are 12 times as likely to die from preeclamptic complication as women who do receive prenatal care. Preeclampsia accounts for 80-84 percent of low birth weight babies. These low birth weight babies are now the major groups of newborn being cared in the neonatal intensive care units worldwide. Endothelial dysfunction is accompanied by elevated levels of inflammatory markers which have been shown to be much higher in women with preeclampsia than those of normal pregnancy. C-reactive protein, as an acute phase reactant, belongs to the pentraxin family of calcium dependent ligand binding plasma protein. It is produced by hepatocytes in response to injury, inflammation, infections and malignant neoplasia. It has short half life, which is constant under all condition of health and disease. Recent studies have been suggested that increased level of CRP is associated with an abnormal systemic endothelial vascular reactivity. CRP is used mainly as a marker of inflammation. Measuring and charting of CRP values can prove useful in early determining of disease, disease progress or effectiveness of treatments. Since maternal health and pregnancy outcome is drastically affected by hypertensive disorders of pregnancy so early detection and timely intervention to minimize the harm should be to our utmost attention and interest.

Materials & Methods:
This case control study was conducted in the Department of Obstetrics and Gynaecology in collaboration with the Department of clinical pathology of Sir Salimullah Medical College Hospital, Mitford, Dhaka during the period of January 2013 to December 2013. The study population were pregnant women with preeclampsia and normal term pregnant patients admitted during study period. A total of 66 patients were included in the study. Among them 33 were clinically diagnosed preeclampsia women grouped as Cases and another 33 were age, parity and BMI matched term pregnant women as Controls, taking by consecutive sampling. The patients were enrolled following inclusion & exclusion criteria. **Inclusion criteria are age - 24-35 years, gestational age - 28-40 weeks and term pregnant patients as matched controls.** **Exclusion criteria are** patients with preexisting hypertension, renal diseases –such as glomerulonephritis, nephrotic syndrome, diabetes mellitus, thyroid dysfunction and pyrexia. The research protocol was approved by the institutional ethical review committee. Keeping compliance with Helsinki Declaration for medical research involving human subject 1964, patient was informed verbally about the study, the underlying hypothesis and right for the participant to withdraw from the project at any time, any reason. Written consent was obtained from each patient. It was assured that all recordsonal approach would be kept confidential and procedure will be helpful for both the physician and patient in making rational approach regarding management of the cases. Provisional diagnosis of preeclampsia was done by careful history taking and clinical examination. Enrolled patients were asked to take part in an hour-long face to face interview. For recording purpose a predesigned data collection sheet was used, to elicit information regarding maternal socio-demographic characteristics, medical history & family history. A detailed past obstetric history and investigations results were included in the data collection sheet. Gestational age was calculated from the LMP and with the early date ultrasonogram records. Physical examination and anthropometric measurement (height, weight) of each study subject was taken and recorded. With full aseptic precaution two ml of venous blood was drawn from each of the study subjects. Then blood was transferred into a clean test tube and transported to the clinical pathology laboratory. Random urine sample was collected in a clean test tube and analyzed for presence of protein by dipstick reagent strip. Eastmann of serum C-reactive protein was done by NycoCard Reader-II method (Appendix-11). The data were screened and checked for any missing value and discrepancy and compiled. All data were recorded in tabulated form and the result was expressed as mean ± SD SPSS software was used to analyze the data. Unpaired t” test, chi-square test and r test were used to see the level of significance. 95% confidence limit (p <0.05) was taken as level of significance.

Results:
C-reactive protein concentration (mg/L) was found significantly higher (p<0.001) in case group (17.93±10.5) than control group (7.45±1.80). C-reactive protein was ≥ 6mg/L in 29(87.9%) in case group and 9 (27.3%) in control group and C-reactive protein values showed significant positive correlation with systolic and diastolic
blood pressure (p<0.001) in case group. C-reactive protein concentration was found significantly higher (p<0.001) in severe preeclampsia group than mild preeclampsia group. The findings of the study obtained from data analysis are documented below.

Table I shows no significant difference between mean age of case and control group but highly significant difference between mean gestational age in both groups.

### Table I: Comparison of age and gestational age of the study subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case (n=33)</th>
<th>Control (n=33)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean ± SD (Range)</td>
<td>Mean ± SD (Range)</td>
<td>0.876</td>
</tr>
<tr>
<td></td>
<td>26.76±3.37 (24-35)</td>
<td>26.70±2.85 (24-35)</td>
<td></td>
</tr>
<tr>
<td>Gestational age</td>
<td>Mean ± SD (Range)</td>
<td>Mean ± SD (Range)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>37.36±2.57 (28-40)</td>
<td>39.12±0.93 (37-40)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data were analysed using Unpaired t-Test and were presented as mean±SD. p<0.05 is statistically significant.

Table II shows that the case and control groups were almost identical regarding their gravidity.

### Table II: Distribution of gravidity in the study subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case (n=33)</th>
<th>Control (n=33)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gravida</td>
<td>Total no. Percentage</td>
<td>Total no. Percentage</td>
<td>0.319</td>
</tr>
<tr>
<td>Primi</td>
<td>16 (48.5)</td>
<td>12 (36.4)</td>
<td></td>
</tr>
<tr>
<td>Multi</td>
<td>17 (51.5)</td>
<td>21 (63.6)</td>
<td></td>
</tr>
</tbody>
</table>

Data were analysed using chi-square test. p<0.05 is statistically significant.

Table III shows no significant difference between the case and control groups regarding their antenatal care.

### Table III: Status of antenatal care in the study subjects

<table>
<thead>
<tr>
<th>Antenatal care</th>
<th>Case (n=33)</th>
<th>Control (n=33)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>Total no. Percentage</td>
<td>Total no. Percentage</td>
<td>0.115</td>
</tr>
<tr>
<td></td>
<td>14 (42.4)</td>
<td>17 (51.5)</td>
<td></td>
</tr>
<tr>
<td>Irregular</td>
<td>19 (57.6)</td>
<td>16 (48.5)</td>
<td></td>
</tr>
</tbody>
</table>

chi-square test was done to analyse the data. p<0.05 is statistically significant.

Table IV shows that over 52.9% of the case group had history of preeclampsia in previous pregnancy as compared to only 4.7% of the control group.

### Table IV: Distribution of the study subjects according to history of preeclampsia in previous pregnancy

<table>
<thead>
<tr>
<th>History of preeclampsia</th>
<th>Case (n=37)</th>
<th>Control (n=21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>Total no. Percentage</td>
<td>Total no. Percentage</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>9 (52.9)</td>
<td>1 (4.7)</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>8 (47.0)</td>
<td>20 (95.2)</td>
<td></td>
</tr>
</tbody>
</table>

chi-square test was done to analyse the data. p<0.05 is statistically significant.

Table V shows significant difference between the case and control groups regarding BMI, Systolic blood pressure and Diastolic blood pressure respectively.

### Table V: Comparison of physical examination findings in the study subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case (n=33)</th>
<th>Control (n=33)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>Mean ± SD (Range)</td>
<td>Mean ± SD (Range)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>23.37±1.47 (20-26)</td>
<td>21.81±1.45 (18-24)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>(140-170)</td>
<td>(140-170)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>(100-120)</td>
<td>(100-120)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Data were analysed using Unpaired t-Test and were presented as mean±SD. p<0.05 is statistically significant.

Table IV shows that Serum C-reactive protein level was found >6mg/L in 29 (87.9%) women in case group and only 9 (27.3%) women in the control group respectively. Serum C-reactive protein level was found <6 mg/L in majority (72.7%) of the control group.

### Table VI: Serum C-reactive protein status in the study subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Case (n=33)</th>
<th>Control (n=33)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP status</td>
<td>Total no. Percentage</td>
<td>Total no. Percentage</td>
<td></td>
</tr>
<tr>
<td>(&gt;6 mg/L)</td>
<td>29 (87.9)</td>
<td>9 (27.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(&lt;6 mg/L)</td>
<td>4 (12.1)</td>
<td>24 (72.7)</td>
<td></td>
</tr>
</tbody>
</table>

chi-square test was done to analyse the data. p<0.05 is statistically significant.

Table VII shows that Serum C-reactive protein level was found <6mg/L in 29 (72.7%) of control group. Majority of cases and control group were within the range of 6-15mg/L. Only case group were found within the range of 16-25 mg/L and ≥ 26mg/L of Serum C-reactive protein concentration.

### Table VII: Distribution of serum C-reactive protein level in the study subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Case (n=33)</th>
<th>Control (n=33)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP level (mg/L)</td>
<td>Total no. Percentage</td>
<td>Total no. Percentage</td>
<td></td>
</tr>
<tr>
<td>&lt;6</td>
<td>4 (12.1)</td>
<td>24 (72.7)</td>
<td></td>
</tr>
<tr>
<td>6-15</td>
<td>15 (45.4)</td>
<td>9 (27.3)</td>
<td></td>
</tr>
<tr>
<td>16-25</td>
<td>9 (27.2)</td>
<td>0 (0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥ 26</td>
<td>5 (15.1)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

chi-square test was done to analyse the data. p<0.05 is statistically significant.

Table VIII shows the mean serum C-reactive protein concentrations with its range in the study subjects when concentrations were >26mg/L, which in case & control were 17.93±10.05 (6-48) mg/L and 7.45±1.80 mg/L (6-15) respectively and serum C-reactive protein concentrations were higher in case group than control group.
Preeclampsia is defined as the rise of blood pressure equal to or insufficiency, lung oedema and liver hemorrhage severe complications such as cerebral hemorrhage, renal complication during second half of pregnancy. An abnormal systemic endothelial vascular reactivity to injury, inflammation, infections and malignant pentraxin family of calcium dependent ligand binding and eclampsia is higher in our country. In Sir Salimullah population were pregnant women with preeclampsia and of Obstetrics and Gynaecology in collaboration with the attention and interest.

Discussion:
In this Case-Control study, the serum C-reactive protein concentration have measured in preeclamptic women (case) and normotensive term pregnant women (control) to evaluate the association of C-reactive protein level in preeclampsic women. In this study mean age of case group was 26.76±3.37 years. Most subjects in both groups were within range of 24-29 years of age and Muslims. This was nearly consistent with several other study. The present study has revealed the mean serum C-reactive protein concentration was 7.45 ± 1.80 mg/L (range of 6-15 mg/L) in control group. Mean serum C-reactive protein concentration found in case group was 17.93±0.05mg/L (range of 6.48 mg/L). This study has shown mean serum C-reactive protein concentration in preeclampsia cases significantly high in comparison to control (P < 0.001). Same phenomenon observed in many other studies around the world. Considering preeclampsia sub types of this study, serum C-reactive protein concentration in severe preeclampsia group found significantly higher (P < 0.001) than that of mild preeclampsia. This is harmonious with some other studies done abroad. In this study, it was found that C-reactive protein levels were significantly higher (P < 0.001) in preeclampsic women and positively correlated to the degree of blood pressure elevation. Same phenomenon observed in many other studies. In present study, serum C-reactive protein was found within the range of 6-15 mg/L in 45.4% of cases and 27.2% of controls. About 72.7% control and only 12.1% of cases are found <6mg/L. Serum C-reactive protein concentration was found to be maximum in severe preeclampsia group (48 mg/L) and lowest in control group (03mg/L). The results of present study are not in agreement with those of other study who reported in their cross sectional study, that maternal serum C-reactive protein is not elevated with preeclamptic women when compared with normal term pregnant women but increased when compared to non pregnant women. Probable explanation of disagreement may be attribute to several factors such as variable demographic characteristics of patients under study, wide variability of serum C-reactive protein in infection, inflammation, tissue damage and malignant neoplasia in general poulotion & variation in prevalence of subclinical infections of women under studies etc. In fact, the path physiology of preeclampsia is still unknown and precise role of C-reactive protein in this regard is still cloudy. One school of thought proposes that overt or occult inflammation as the cause of preeclampsia and raised serum C-reactive protein to be simply the marker of inflammation as a component of acute phase reactant, which expected to help in promising the diagnostic and prognostic potentials.

Conclusion:
The study concludes that serum C-reactive protein level was found to be significantly higher in preeclamptic patients. It signifies strong association of C-reactive protein with preeclampsia in our Bangladeshi women. Higher the severity of preeclampsia, serum C-reactive protein tends to be higher.

Conflict of Interest: None.

Acknowledgement:
I would like to express my gratitude to all my teachers and supervisor who guide me and all my patients who inspire of their sorrows and sufferings helped me in getting all my clinical information. Last of all I like to acknowledge the sacrifice and support of my family members.

References:
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20. https://doi.org/10.1111/j.1471-0528.2002.01130.x

Table VIII: Serum C-reactive protein status in the study subjects when concentration were ≥6mg/L.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Case (n=24) Mean ± SD (Range)</th>
<th>Control (n=9) Mean ± SD (Range)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum C-reactive protein level</td>
<td>17.93 ± 10.05 (6-48)</td>
<td>7.45 ± 1.80 (6-15)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table IX: Serum C-reactive protein status in mild and severe preeclampsia patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild preeclampsia</th>
<th>Severe preeclampsia</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP status</td>
<td>n=24</td>
<td>n=9</td>
<td></td>
</tr>
<tr>
<td>(≥6 mg/L)</td>
<td>20 (83.4)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>(&lt;6 mg/L)</td>
<td>4 (16.7)</td>
<td>0 (0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>12.92 ± 5.7</td>
<td>27.8 ± 17.3</td>
<td></td>
</tr>
<tr>
<td>Range (mg/L)</td>
<td>(3-25)</td>
<td>(6-48)</td>
<td></td>
</tr>
</tbody>
</table>

Table IX shows that mean serum C-reactive protein concentrations level were higher in the severe preeclampsia group than those in the mild preeclampsia group.

Data were analysed using Unpaired t-Test and were presented as mean±SD. p<0.05 is statistically significant.
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Akter, et al.


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PMid:16054955


PMid:20722986


PMid:19390201