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# Serum C - reactive protein in normal pregnancy and preeclampsia- a comparative study

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**Abstract**
The aim and objective of the study to find out association of C – reactive protein with pre-eclampsia, to find out CRP level in pre-eclampsia and to compare CRP level of pre-eclampsia with normal patients.as well as to study the level of C - reactive protein in relation to the severity of the preeclampsia and its pregnancy outcome. A Hospital based prospective comparative study was performed on 80 pregnant women in third trimester of pregnancy include 40 preeclamptic (20 mild and 20 severe) patients and 40 normotensive pregnant women as controls were selected for the study in the department of Obstetrics & Gynaecology, SMS Medical College & attached hospital, Jaipur from April, 2017 to October, 2018 for a period of one year After initial assessment of every patient, blood sample was collected in a sterile empty vial. Serum CRP levels were measured by high CRP sensitivity kit using Particle Enhanced Turbimetric Immunoassay (PETIA) Technique. Clinical outcome were evaluated. Statistical analysis was done using Student's t-test. The mean level of serum CRP in preeclamptic patients was 15.4± 2.37 mg/dl and that in normotensive pregnant women was 2.68 ± 0.9 mg/dl (p-value < 0.0001). And mean level of serum CRP in mild preeclamptic patients was 13.22 ± 0.88 mg/dl and severe pre eclamptic patients was 17.58 ± 0.9 mg/dl ($p$<0.001). Our Study results showed that serum CRP levels were higher in pre-eclampsia patients than normotensive patients. CRP level was raised more in severe pre-eclampsia as compared to mild pre-eclampsia. CRP levels positively correlated with the severity of pre-eclampsia. Therefore, serum CRP level can be used as a utility parameter for the assessment of pre-eclampsia. These women can be monitored carefully as high risk cases thereby helping in early diagnosis and management of pre-eclampsia.

**Keywords:** Preeclampsia, normal pregnancy, C - reactive protein, hypertensive disorders of pregnancy

## Introduction
Hypertensive disorder complicates pregnancy and form one aspect of the deadly triad along with hemorrhage and infection and results in significant maternal morbidity and mortality. Hypertension is the most common medical problem encountered during pregnancy. About 5-10% pregnancies are affected by hypertension [1].

Pre-eclampsia is associated with generalised endothelial dysfunction. The etiology of endothelial dysfunction in preeclampsia is not known, but it has been postulated to be part of an exaggerated maternal inflammatory response to pregnancy [3]. Activated circulating leukocytes [4]; reactive oxygen species [5] and inflammatory cytokines, such as Tumor necrosis factor α (TNF α) and Interleukin-6(IL-6) [6, 7], as well as abnormal activation of the clotting system [8] found more in women with pre-eclampsia compared with normotensive women, supports this hypothesis.

C - reactive protein (CRP) is an objective and sensitive index of overall inflammatory activity in the body [9]. Plasma CRP levels rise in cases of acute infection, malignancy & inflammatory diseases. CRP activates complement through the classical pathway and participates in opsonization of particulate antigens and bacteria. CRP can bind to chromatin, released from apoptotic or necrotic cells, and to small nuclear ribonucleoprotein particles. It has been proposed that CRP acts as a scavenger and is responsible for the clearance of membranes and nuclear antigens [10]. It has been suggested that CRP, in accordance with its proposed function, may play a role in eliciting the inflammatory response characteristics of preeclampsia [3]. Recently, it has been demonstrated that CRP enhanced opsonisation, and phagocytosis of apoptotic cells. Once cells have become necrotic, the effect of CRP is lacking [11]. The present study is carried out with the aim to find out the correlation between C - reactive protein in normal pregnancy with that of preeclampsia as well as to study the level of C - reactive protein in relation to the severity

of the preeclampsia and its pregnancy outcome.

**Materials and methods**

A comparative study to assess value of c- reactive protein in pre-eclampsia and normotensive women among patients attending antenatal clinic was carried out in the Department of Obstetrics and Gynecology, SMS Medical College Jaipur, for a period from April, 2017 to October, 2018. Based on inclusion and exclusion criteria a total of 80 pregnant women were selected for the study. The study included two groups, group A – 40 cases and group B – 40 controls. The Group A comprised 40 preeclampsia patients in third trimester of pregnancy (20 mild preeclampsia and 20 severe preeclampsia cases). The group B comprised of 40 normotensive pregnant women in third trimester.

**Inclusion Criteria:** Third trimester singleton pregnant women with pre-eclampsia (case) and normotensive pregnant women (control) who give consent for this study.

**Exclusion Criteria:** Patients with history of chronic renal disease, chronic Hypertension, pre-existing diabetes or gestational diabetes, cardiovascular illness, premature rupture of membranes, urinary tract infection, patient with signs of labor or use of labor induction, smokers.

**Sampling Procedure**

40 Pregnant women having pre-eclampsia as case and 40 normotensive women in third trimester of pregnancy as controls would be included on first cum first basis after beginning the study assuming 20% drop outs. CRP Level Estimation: particle enhanced turbidimetric immunoassay (PETIA), where inert latex particles are used to increase the sensitivity of the reaction.

**Sampling procedure**

2 ml of venous blood were collected in plain vial from each patient for measuring serum CRP level. After clotting of the blood sample the serum was separated from the cells by centrifugation within 1 hour of collection and removed using sterile pipette. Serum CRP levels were assayed by latex turbidimetric immunoassay.

**Principle**

Prieturb CRP- Latex is a particle based immunoassay for quantitative determination of C-reactive protein (CRP) in human serum, when latex particle coated with purified anti CRP allowed to react with samples containing CRP agglutinate forms which is determined by comparing it with a calibrator (standard) of known concentration.

The reference values of CRP in normal population are equal or less than 6mg/L.

**Statistical analysis**

Categorical variables were presented in percentage (%) and number, continuous variables were presented as median and mean ± SD and Kolmogorov-Smirnov test was used to check normality of data. Non parametric test was used if the normality was rejected. Between the two groups Quantitative variables were compared by using Independent T test/Mann-Whitney Test. Chi-Square test/Fisher's exact test was used to correlate qualiative variables. Association of blood pressure and CRP levels were assessded by pearson correlation coefficient. Data were statistically significant if p value <0.05. The data was entered in MS Excel spreadsheet and analysis was done with Statistical Package for Social Sciences (SPSS) version 21.0.

Normal reference value of C – reactive protein: < 0.3 mg/dl. For statistical analysis, student's t-test was applied to assess the statistically significant differences in parameters between the cases and controls. Coefficient of Correlation: to see the correlation between two variables co-efficient of correlation (r) is applied. If r is near +1, it indicates a strong positive correlation. A value in minus side indicates inverse correlation. If r=0, it indicates no correlation. The significance of the correlation coefficient was tested by t-test.

**Results**

The mean age (in years) of preeclamptic patients was 25.65 ± 3 and that in controls was 25.92 ± 3.46 in our study and was statistically not significant. So, this is age matched study.

The Table -1 shows that mean level of serum CRP in group A (cases) was 15.4 ± 2.37mg/dl and that in group B (control) was 2.68 ± 0.9mg/dl. The difference in serum CRP level between preeclamptic patients and normotensive pregnant women were found to be very highly significant (p-value < 0.0001).

From Table-2 it is observed that mean level of serum CRP in mild preeclamptic patients was 13.22 ± 0.88 mg/dl and severe preeclamptic patients was17.58 ± 0.9 mg/dl. The difference in serum CRP level between mild and severe preeclamptic patients was found to be very highly significant ($p < 0.001$).

Table 3 shows a significant positive correlation between serum CRP level and blood pressure (mean, systolic and diastolic) in mild pre-eclamptic patients.

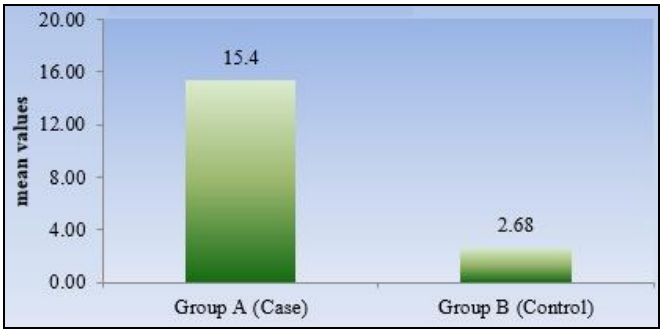
Table 4 shows a significant positive correlation between serum CRP level and blood pressure (mean, systolic and diastolic) in severe pre-eclamptic patients.

**Table 1:** Comparison of mean Serum C-reactive protein level between Group A (Case) and Group B (Control)

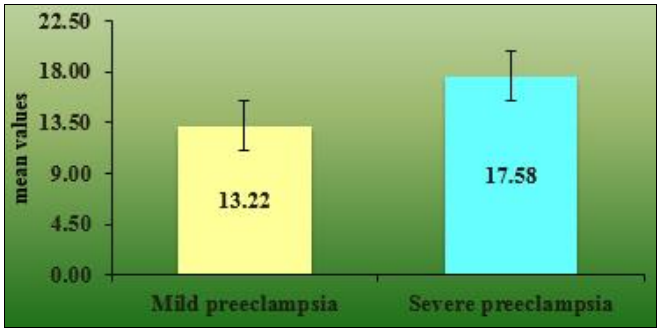
| CRP Level (mg/dl) | Group A (Case) | Group B (Control) |
|---|---|---|
| Sample size | 40 | 40 |
| Mean ± SD | 15.4 ± 2.37 | 2.68 ± 0.9 |

**Table 2:** Relation between mean serum C - reactive protein level and severity of pre-eclampsia

| CRP Level (mg/dl) | Mild preeclampsia | Severe Pre-eclampsia |
|---|---|---|
| Sample size | 20 | 20 |
| Mean ± SD | 13.22 ± 0.88 | 17.58 ± 0.9 |



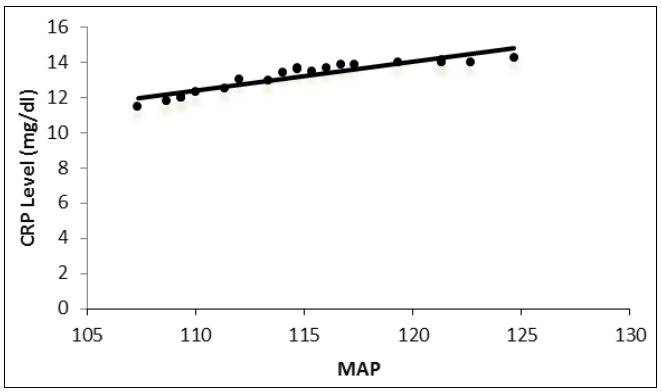

CRP Level (mg/dl)



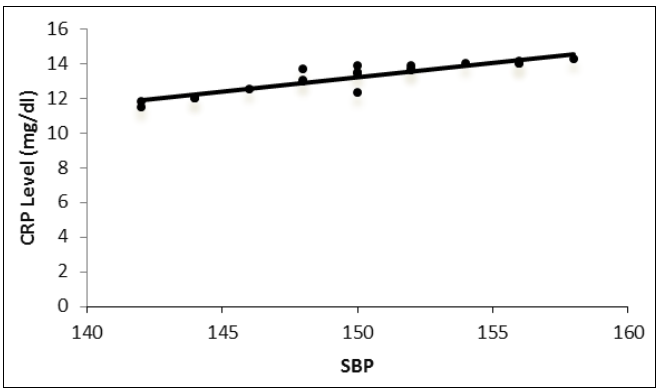

CRP Level (mg/dl)

**Table 3:** Correlation between serum C - reactive protein levels (mg/dl) with mean arterial pressure, systolic blood pressure & diastolic blood pressure in mild pre-eclampsia

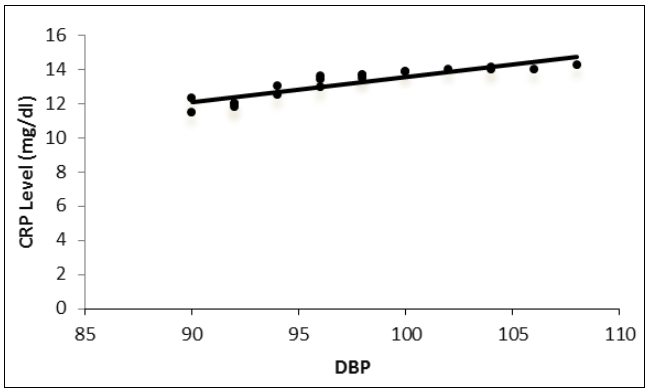
| Parameter | CRP (mg/dl) | |
|---|---|---|
| | R | P |
| Mean blood pressure (MAP) | 0.92 | <0.0001 |
| Systolic blood pressure (SBP) | 0.90 | <0.0001 |
| Diastolic blood pressure (DBP) | 0.89 | <0.0001 |




Correlation bw MAP and CRP level (mg/dl)



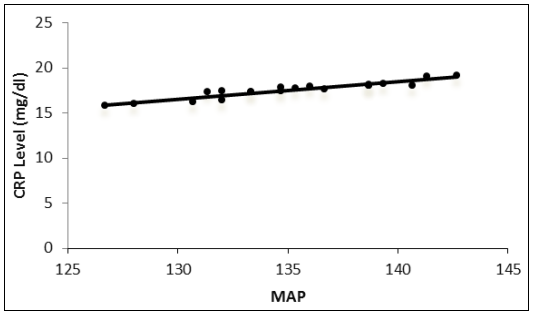

Correlation bw SBP and CRP level (mg/dl)



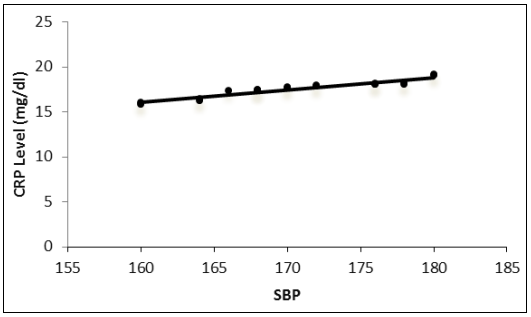

Correlation bw DBP and CRP level (mg/dl)

**Table 4:** Correlation between serum C - reactive protein levels (mg/dl) with mean arterial pressure, systolic blood pressure & diastolic blood pressure in severe pre-eclampsia

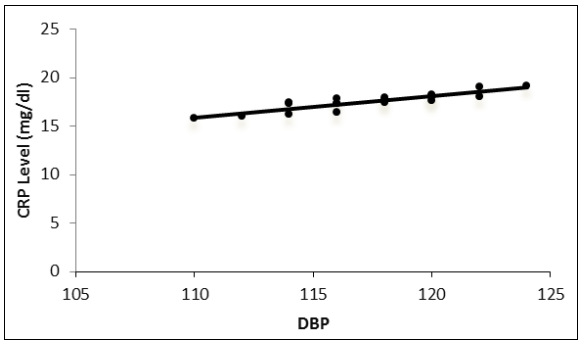
| Parameter | CRP (mg/dl) | |
|---|---|---|
| | R | P |
| Mean blood pressure (MAP) | 0.94 | <0.0001 |
| Systolic blood pressure (SBP) | 0.93 | <0.0001 |
| Diastolic blood pressure (DBP) | 0.89 | <0.0001 |




Correlation bw MAP and CRP level (mg/dl)




Correlation bw SBP and CRP level (mg/dl)




Correlation bw DBP and CRP level (mg/dl)

## Discussion

The present study was undertaken to find out the correlation between serum C-reactive protein level in normotensive pregnant women and patients with preeclampsia, and also to study the CRP level in relation to the severity of preeclampsia and its pregnancy outcome.

In the present study, serum CRP concentration was found to be significantly higher ($p$<0.001) in preeclamptic patients (2.10 + 1.36 mg/dl) than in normal pregnant women (0.39 + 0.09 mg/dl). Among the preeclamptic patients, serum CRP concentration was found to be significantly higher ($P$<0.001) in severe preeclampsia as compared to mild preeclampsia.

K. Omkara Murthy *et al.* found that serum CRP concentration was higher in preeclampsia group as compared to normotensive pregnant group. CRP levels were also significantly elevated in women with severe preeclampsia as compared to those patients with mild preeclampsia. ($p$<0.001)

This observation is comparable to various observation i.e. Gulec UK, Ozgunen FT, Guzel AB, *et al.* [33] (2012). CRP levels were significantly higher in patients with severe pre-eclampsia than mild pre-eclampsia. There were significant positive correlations between serum CRP levels and mean arterial pressure, systolic blood pressure and diastolic blood pressure. Logistic regression analysis using the normotensive and pre-eclampsia group showed that higher CRP (OR, 14.29; 95%-CI, 3.08-66.34) levels were found in pre-eclampsia.

In the present study, a significant positive correlation was found between serum CRP concentration and blood pressure (systolic and diastolic) in both mild and severe preeclamptic patients. Fatemeh Mirzaie., Fatemeh Rahimi *et al.* [28] (2008) also found that serum CRP level in mild and severe PE were markedly higher than of normal third trimester pregnant women and CRP levels positively correlated blood pressure.

## Conclusion

Preeclampsia is a disorder associated with generalized dysfunction of endothelial cells probably as a result of systemic inflammatory maternal reaction. CRP is a positive marker of inflammation higher at overt preeclampsia than normal pregnancy. In our study, CRP levels correlated positively with the severity of the disease. We also found a positive correlation between serum CRP and biochemical and clinical parameters in preeclampsia.

We therefore conclude that CRP level is raised in preeclampsia than normal pregnancy and also CRP level is raised more in severe preeclampsia as compared to mild preeclampsia. Thus, serum CRP level can be used as a utility parameter for the assessment of preeclampsia; however, further cohort studies on a larger sample are needed to substantiate our findings before firm conclusion can be drawn.

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