

C Reactive Protein levels are elevated in the Third Trimester in Preeclamptic pregnant Women

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ABSTRACT

Aim: To evaluate the levels of C Reactive protein, an inflammatory marker in preeclamptic and normotensive pregnant women.

Methods: It was a cross sectional analytical study. The participants included 60 cases with preeclampsia and 60 normotensive pregnant women, all in their third trimester. All the participants were in the age group of 20-40 years and a BMI of 18-25. HsCRP levels were measured by Enzyme Link Immunosorbent Assay.

Results: In the preeclamptic group the HsCRP levels were significantly higher as compared to normotensive group.

Conclusion: Presence of elevated C Reactive Protein levels in the preeclamptic pregnant women leads to the conclusion that preeclampsia is characterized by exaggerated maternal systemic inflammatory response.

Keywords: Preeclampsia, C reactive protein, pregnancy, third trimester.

INTRODUCTION

Pregnancy is a complex process which leads to a number of systemic changes. During normal pregnancy all these changes are very well regulated¹. Preeclampsia is a very common disorder of pregnancy and is characterized by hypertension and proteinuria that begins at more than 20 weeks of gestation^{2,3}. Poor placentation with inadequate cytotrophoblast invasion results in widespread maternal endothelial dysfunction^{4,5,6}. There is increasing evidence that preeclampsia is accompanied by exaggerated maternal systemic inflammatory response to this poor placentation⁷.

Abnormal placentation leads to hypoxia with resultant oxidative stress and release of toxic substances⁸. These toxic substances are the cause of widespread endothelial injury. Levels of various cytokines and chemokines are found to be increased in preeclampsia^{9,10}. Widespread endothelial injury results in increased vascular permeability and vascular sensitivity to vasopressin substances¹¹. It also causes activation of neutrophils and coagulation¹².

C Reactive Protein is a highly sensitive but non specific marker of inflammation. Because of the role of CRP in inflammation, it has been proposed that it may contribute to the inflammatory response seen in

preeclampsia and researchers have checked its levels to determine its predictive value in the development of preeclampsia^{13,14}.

METHODS AND MATERIALS

It was a cross sectional analytical study, conducted in the department of physiology, Federal Post-graduate Medical Institute, Shaikh Zayed Medical Complex, Lahore in collaboration with Jinnah Hospital, Lahore. Study population consisted of 60 normotensive and 60 preeclamptic pregnant women in the third trimester of pregnancy. Age for both groups was 20-40 years. Both groups were matched for BMI and all were in the range of 18-25. Women with history of smoking, diabetes, renal disease, arthritis, inflammatory bowel disease, chronic hypertension, other cardiovascular illness (e.g., ischemic heart disease) and symptomatic infectious diseases (bacterial and viral) were excluded. Criteria to rule out infection was temperature of >38°C, leukocyte count >12,000/cu, mm. Women on antibiotic therapy were also excluded. None of the participants had ruptured membranes and were not in labour¹⁶.

After approval from the Ethical Review Board, all the participants were briefed about the nature of the study and an informed consent was taken. Blood pressure of the subjects was recorded using sphygmomanometer. 3cc blood sample for C Reactive Protein was collected using aseptic technique and sterilized disposable syringes. Serum separator tubes were used and samples were allowed to clot for 30 minutes before centrifugation

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for 15 minutes. Serum was separated, aliquoted and kept frozen at -20°C. Standard commercial ELISA-based kits (manufactured by Bio check Inc. Foster city) were used for estimation of C reactive protein. The procedure was done in NHRC, FPGMI. Data was entered and analyzed by using SPSS version 15.0.

RESULTS

The study consisted of two groups. The data was deviating from normality so Mann Whitney U test was applied for comparison between the two groups. Group1 consisted of 60 preeclamptic women and group 2 of 60 normotensive pregnant women. Mean±SD age of group one was 27.6±4.6 years and for the group two was 25.7±4.7 years with almost similar distribution among various age groups (Table 1) The C-reactive protein (CRP) levels were also distributed differently among the two groups. The CRP levels were distributed from less than 3mg/L to > 24mg/L in the preeclamptic cases, while among the normotensive controls the maximum value was found to be 9.8mg/L (Table.2). The mean±SD for CRP levels were 10.83±7.32 and 5.13±3.07 in preeclamptic and normotensive women respectively and were significantly different with p-value <0.001. (table.3)

Table 1: Age distribution of females in both groups (n=60)

Age	Preeclamptic	Normal
<= 20	1(1.7%)	6(10%)
21 – 25	23(38.3%)	26(43.3%)
26 – 30	23(38.3%)	20(33.3%)
31 – 35	10(16.7%)	6(10%)
36+	3(5%)	2(3.3%)
Mean ± SD	27.6 ± 4.6	25.7 ± 4.7
Median	26.0	24.5
Q1	25	22
Q3	30	29

Table 2: Distribution of cases according to C-reactive protein levels for both groups

CRP level(mg/l)	Preeclamptic	Normal
≤ 3.0	8(13.3%)	18(30%)
3.01 - 6.0	12(20%)	20(33.3%)
6.01 - 9.0	12(20%)	12(20%)
9.01 - 12.0	5(8.3%)	10(16.7%)
12.01 - 15.0	5(8.3%)	0
15.01 - 18.0	5(8.3%)	0
18.01 - 21.0	5(8.3%)	0
21.01 - 24.0	5(8.3%)	0
> 24.0	3(5%)	0
Mean ± SD (Range)	10.83 ± 7.32 (0.3 - 25.5)	5.13 ± 3.07 (0.24 - 9.8)
Median	8.8	5.4
Q1	4.5	2.6
Q3	16.5	7.7

Table 3: Comparison of C Reactive Protein Levels between the two groups.

Variables	CPR
Preeclamptic	
Mean rank	74.3
Sum of ranks	4460
Normal	
Mean rank	46.7
Sum of ranks	2800
Mann Whitney U	970
P value	<0.001

DISCUSSION

This study is the first research in Pakistan regarding levels of CRP, an inflammatory marker, in preeclamptic and normotensive pregnant women. We noted that levels of serum C reactive protein were significantly high in third trimester in the preeclamptic cases as compared to normotensive controls.

Our results are similar to the results of a number of studies, who have proposed that persistent and exaggerated systemic inflammation during pregnancy leads to endothelial dysfunction and preeclampsia.^{10, 15, 16}

C reactive protein is an acute phase reactant produced by the liver in response to placental pro inflammatory cytokines, especially IL-6 and TNF-α. Serum levels of CRP are higher in healthy pregnant women as compared to non pregnant women because even normal pregnancy is accompanied by mild systemic inflammatory response.¹⁷ Hwang HS and colleagues in 2007 measured serum CRP levels in preeclamptic and normal pregnant women and found similar results. They reported that the levels of hsCRP were significantly high in the preeclamptic group and correlated with severity of the disease.¹³ In 2010, Ertas IE et al measured serum hsCRP levels by immunoturbidimetric method. They formed groups according to severity of the disease as mild and severe preeclampsics and concluded that elevated CRP level is useful parameter in severity of preeclampsia¹⁸.

Our results are in contrast to the studies who found no significant difference in the levels of hsCRP in pregnancies complicated by preeclampsia as compared to normotensive pregnant women.^{19, 20, 21} These studies differ from ours in view of sample size¹⁹ and collection of sample before the onset of disease.²¹

CONCLUSION

We found significantly high levels of C reactive protein in third trimester in pregnancies complicated by preeclampsia as compared to normotensive pregnant women. We conclude that exaggerated systemic inflammation is characteristic of

preeclampsia and C reactive protein as an marker of inflammation is increased in preeclampsia.

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