Original Article

Comparison of the Level of C-reactive Protein in Pre-eclampsia and Normal Pregnancy

Fozia Shaikh, Feriha Fatima Khidri, Mubeena Laghari, Farhana Shaikh, Sania Feroz Daudpota

ABSTRACT

OBJECTIVES: To measure the serum C-reactive protein levels in women with pre-eclampsia and compare its level in the normal pregnant women.

METHODOLOGY: This comparative cross-sectional study was conducted in the biochemistry department, Liaquat University of medical and health sciences (LUMHS), Jamshoro from January to June 2017. A total of 80 subjects were recruited and grouped into n=40 women with normal pregnancy (control) and n=40 women with pre-eclampsia (cases) by non-probability consecutive sampling technique. The serum concentrations of C-reactive protein were determined by immunoturbidimetric assay. The variables were analyzed on SPSS software version 16 and p≤0.05 was considered as significant.

RESULTS: There was no significant difference in the age (p-value = 0.52) and gestational age (p-value = 0.09) between women with pre-eclampsia and normal pregnancy. Mean serum C-reactive protein concentration was significantly raised (p-value < 0.001) in women with pre-eclampsia (2.80±1.3 mg/dl) in comparison to normal pregnant women (0.63±0.39 mg/dl).

CONCLUSION: The findings of this study indicated the increased C-reactive protein levels in women with preeclampsia as compare to normal pregnant women. The level of C-reactive protein can be utilized as inflammatory and biochemical marker in the pre-eclampsia. Furthermore, screening of pregnant women for C-reactive protein levels during early antenatal period in high risk obstetrical cases may be helpful in diagnosis of pre-eclampsia, which may reduce the feto-maternal morbidity and mortality.

KEYWORDS: C-reactive protein, Preeclampsia, Pregnancy.

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INTRODUCTION

Pre-eclampsia is the disorder of pregnancy specified by hypertension and proteinuria ensuing later in pregnancy[1]. It is one of the prime contributors of raising feto-maternal morbidity and mortality[2]. It complicates 2–5% of the pregnancies worldwide; whereas the prevalence is higher in the underdeveloped countries[3-5]. The exact etiology of the pre-eclampsia is still debatable and various factors are considered to have a role in the pathogenesis, such as genetical and immunological factors, increased insulin resistance and oxidative stress, nutritional deficiencies and prostaglandin imbalance[6-10]. The inflammation and anti-angiogenesis mechanisms have demonstrated the vital components in its pathogenesis[8]. Previous literature has proposed the endothelial dysfunctions as the possible key factor in the pre-eclampsia and emphasized the function of C-reactive protein[11]. C-reactive protein is the plasma protein released during the acute phase of inflammation in early phase by the liver and contributes by interacting with complement system. C-reactive protein increases in earlier phases of inflammation by more than 1000-fold, marking its increased synthesis by hepatocytes[12-14].

Defective placentation in pre-eclampsia along with the involvement of markers of angiogenesis consisting of soluble endoglin and fms-like tyrosine kinase 1 (sFlt1or sVEGFR-1) and cytokines were observed at higher levels in women with pre-eclampsia suggesting the C-reactive protein role in the acute phase along with the increment of these markers[15-17].

The C-reactive protein detection in amniotic fluid suggests its role in preeclampsia. Furthermore, it has also been linked to increased cardiovascular disorder risks exhibiting its association with pre-eclampsia[18], which may show C-reactive protein as a possible predictor and contributor in the pathogenesis of preeclampsia. Increased maternal concentrations of C -reactive protein have been valuable in diagnosing

subclinical infection in pregnancy with preterm labour and premature rupture of membranes. Previously, elevated levels of C-reactive protein during gestation have been associated with adverse pregnancy outcomes showing the presence of intrauterine infection[19].

Various other studies have also exhibited the correlation of systolic and diastolic BP with levels of C-reactive protein and found increased concentrations with severity of pre-eclampsia[20-21]. Another study reported the correlation between mean arterial pressure and C-reactive protein in women with preeclampsia[22], however, limited literature is available in our setting. Early identification of the inflammation by detecting increased C-reactive protein levels may assist to prevent pre-eclampsia; thus current study was conducted to estimate the increased C-reactive protein level as the important biochemical marker for pre-eclampsia.

The objectives of the present study were to measure the serum C-reactive protein in women with pre-eclampsia and compare its level with normal pregnant women.

METHODOLOGY

It was a comparative cross-sectional study, conducted in the Biochemistry department, with the cooperation of departments of Gynecology/Obstetrics and pathology and diagnostic/research laboratory, Liaquat University of medical and health sciences (LUMHS), Jamshoro from January to June 2017, after obtaining the approval from the ethics committee. The sample size was calculated in OpenEpi, software available online by taking pre-eclampsia prevalence as 5% in Pakistan[23] and 95% confidential interval (CI). The calculated sample size n=80 grouped into n=40 women with normal pregnancy (control) and n=40 women with pre-eclampsia (cases). The subjects were recruited by non-probability consecutive sampling technique. The inclusion criteria for controls and cases were pregnant women with normal pregnancy and diagnosed pre-eclampsia, respectively and between 16-45 years of age in their second or third trimester of pregnancies. Those women with preeclampsia that were diagnosed to have essential hypertension, chronic kidney disease, cardiac diseases, connective tissue disease, autoimmune disorders and tuberculosis were excluded. Pre-eclampsia for the present study was defined as blood pressure (BP) ≥ 140/90 mmHg and proteinuria ≥ 0.3g/24h after completion of 20th weeks of pregnancy in the women with normal BP, previously[24]. The normal level of C-reactive protein is 1-3 mg/L and > 3.0 mg/L was labeled as positive[25.]

The venous blood (5ml) was collected from subjects by standard protocol after written informed consent. After allowing the blood to clot in a test tube, the supernatant serum was obtained after centrifugation and sample stored at -20^{o}C for afterward analysis[26]. The levels of C-reactive protein in serum were determined by immunoturbidimetric assay on Roche/ Hitachi Cobas C system according to the protocol provided by manufacturer's kit[27].

The categorical and continuous variables were analysed on SPSS software version 16[28]. The mean and standard deviation (SD) were computed and comparison of means was analysed by Student t-test. For the present study, p value ≤ 0.05 was considered as significant.

RESULTS

No significant difference was found in the mean age (p-value = 0.52) and gestational age (p-value = 0.09) between both groups in the present study; however, as expected the significant differences in mean systolic and diastolic BP were observed between both groups (p-value <0.001). Women with preeclampsia significantly exhibited positive family history of preeclampsia, whereas family history of essential hypertension was not significantly different, showed in **Table I.**

Mean serum C-reactive protein was significantly raised in women with preeclampsia in comparison to normal pregnant women (p-value < 0.001), showed in **Table II.**

TABLE I: COMPARISON OF VARIABLES BETWEEN CASES AND CONTROLS

Variables	Controls	Cases	P-value
Age (years)	27.2±4.4	27.9±4.3	0.52
Gestational age (weeks)	31.4±4.0	32.8±3.4	0.09
Systolic BP (mmHg)	108.6±9.4	148.0±10.8	<0.001
Diastolic BP (mmHg)	75.2±5.6	100.6±5.3	<0.001
Family history of essential hypertension	07 (17.5%)	10 (25%)	0.59
Family history of pre-eclampsia	-	06 (15%)	0.0255

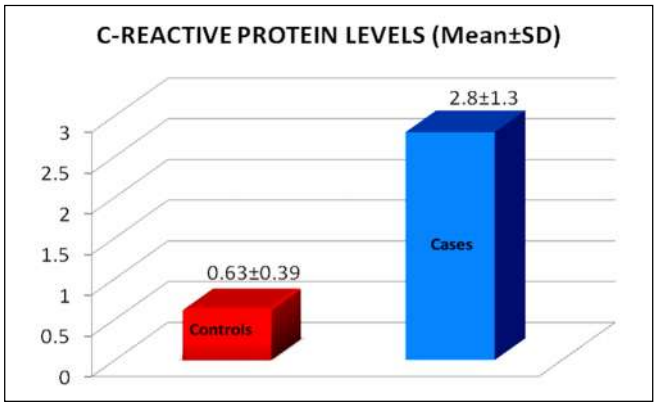
BP: Blood pressure
Bold fonts indicate significant P-value

TABLE II: COMPARISON OF C-REACTIVE PROTEIN LEVELS BETWEEN CASES AND CONTROLS

C-reactive protein levels	Controls	Cases	P-value
Mean	0.63±0.39 mg/dl	2.80±1.3 mg/dl	<0.001
Minimum	0.7 mg/dl	0.8 mg/dl	
Maximum	1.50 mg/dl	5.36 mg/dl	

Bold fonts indicate significant P-value

FIGURE I: LEVELS OF C-REACTIVE PROTEIN IN CASES AND CONTROLS



DISCUSSION

Pre-eclampsia is the systemic inflammatory disease correlated with endothelial cell dysfunction[29]. Previous studies have exhibited the contribution of factors related to endothelial activation or inflammation, including the role of C-reactive protein, as a sensitive indicator of tissue inflammation and impairment in the pre-eclampsia[13].

During pregnancy increased C-reactive protein levels have been associated with obstetrical complications including premature birth, pre-eclampsia, small for gestational age and low birth weight of newborns; and its levels in mid pregnancy may help in the prediction of late gestational complications until delivery. It is also an important biomarker to evaluate and monitor the treatment response and prediction of outcome in inflammatory disorders[30,31].

In the present study, C-reactive protein levels were measured in women with pre-eclampsia and compared with levels in the normal pregnant women. The mean age of women with normal pregnancy and pre-eclampsia was 27.2±4.4 and 27.9±4.3 years, respectively in the present research. This age range is with the agreement of the findings of the study of Gammill HS, et al[31]. Sharmin S, et al[32] study results were also consistent with the present study, exhibiting no significant difference of age between both groups. In our study, no significant differences in mean gestational age between both groups were present. These findings are supported by the previous studies, however, in contrast to the gestational weeks range in our study, Gammill HS, et al[31] reported the mean gestational age of women with pre-eclampsia to be 18.6±4.5 weeks and normal pregnant women to be 19.3±4.3 weeks. The gestational age in their study corresponds to the second trimester, whereas mean gestational age in our study corresponds to the third trimester.

In this study, C-reactive protein levels were found increased in women with pre-eclampsia as contrast to normal pregnant women (p-value< 0.001); where, mean C-reactive protein levels were 2.80±1.3 mg/dl in women with preeclampsia and 0.63+0.39 mg/dl in normal pregnant women. Similar results were observed in Mohammadi B 2010[33] study, depicting a significant relationship between C-reactive protein levels with pre-eclampsia. Another study performed by Begum G 2017[20] found that the serum C-reactive protein concentration was higher in women with pre-eclampsia with contrast to normal pregnant women with a mean serum level of C-reactive protein as 10.52±10 in women with preeclampsia and 5.10±6.2 in women with normal pregnancy. Das KK 2015[34] also found a significant association of serum C -reactive protein level with hypertension in both severe and mild pre-eclamptic patients (p-value < 0.0001).

Teran E 2005[35], found C- reactive protein levels in normal pregnant women in range of 2.9 to 3.6 mg/l, whereas in women with preeclampsia it ranged from 2.6 to 5.9 mg/l; whereas in our study C- reactive protein in normal pregnant women were found in range of 0.7 to 1.5 mg/l and in women with preeclampsia as 0.8 to 5.36 mg/l. In another study by Jannesari R 2017[36], researchers found 5.44 ng/ml levels in normal pregnancy where levels increased to 7.71 ng/ml in pregnancies complicated with preeclampsia.

Similarly, in agreement with the findings of our study Ali Z, et al[37] found increased concentration of C-reactive protein as inflammatory marker, after second trimester in women with pre-eclampsia. Previously, researchers have observed correlation of C-reactive protein levels with the severity of pre-eclampsia; further more its levels are also found valuable in prediction of peri-neonatal mortality in early onset severe preeclampsia[38].

In contrast to the findings of the present study, few studies showed contradictory results and did not show a significant association of C-reactive protein levels in preeclampsia[39,40]. The differences in the findings may be due to different sample size, inclusion criteria, sample collection time and different techniques to detect C-reactive protein levels[41].

Normal pregnancy is related to a systemic

inflammatory response which further exacerbates in preeclampsia. Several possible factors released from placenta may evoke the inflammatory responses[41]. Therefore, the increased C-reactive protein levels in preeclampsia may serve as inflammatory marker and reflect severity of disorder in patients delivering earlier as compared to women with preeclampsia with less severity and delivering later in pregnancy[38].

CONCLUSION

The findings of this study indicated the increased C-reactive protein levels in women with preeclampsia as compare to normal pregnant women possibly explaining the exaggerated inflammation in pre-eclampsia. Our study findings suggest that C-reactive protein levels can be utilized as an inflammatory and biochemical marker in pre-eclampsia.

RECOMMENDATIONS

We recommend screening of pregnant women for C-reactive protein levels during early antenatal period in high risk obstetrical cases suspecting pre-eclampsia in order to reduce the feto-maternal morbidity and mortality. Further, large scale studies are required with increased sample size to support and strengthen our findings.

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