Original Article

Association Between C-Reactive Protein Level and Preeclampsia in Pregnant Women with Singleton Pregnancy

Safia Perveen[1], Fariha Muzammil[2], Suleman Azhar[3], Hina Ilyas[4], Fizza Mahmood[5], Asia Hussain[6], Tayyaba Yasin[7]

[1-6]Department of Obstetrics & Gynecology, Sahiwal Medical College Teaching Hospital, Sahiwal District, Punjab
[7]Institute of Molecular Biology and Biotechnology (IMBB), The University of Lahore-Pakistan. KM Defense Road, Lahore

Correspondence: *Tayyaba Yasin*
Institute of Molecular Biology and Biotechnology (IMBB),
The University of Lahore-Pakistan. KM Defense Road, Lahore
Email: tayyabayasin1122@gmail.com

Abstract

Objective: To evaluate the C-reactive protein (CRP) levels in pregnant women with preeclampsia and compare it with those of normal pregnancy.

Methodology: An observational study was conducted at the Department of Obstetrics & Gynecology, Sahiwal Medical College Teaching Hospital, Sahiwal from January 11, 2020, to April 30, 2020. The diagnosis of preeclampsia was based on the Royal College of Obstetricians and Gynaecologists' guidelines. It was done on 250 pregnant women, 150 with preeclampsia, and 100 with normal pregnancy in the third trimester. Women with twin pregnancies, generalised infection, anemia, renal problems, or ruptured membranes were excluded from participating in the study. A 5 ml venous sample was taken under an aseptic technique in a sterile tube and analyzed for the level of CRP by the Enzyme-linked immunosorbent assay method.

Results: Among 150 patients with preeclampsia, 97 (64.7%) were multigravida. There were 109 (72.7%) hypertensives, 19(12.7%) diabetics, 24 (16%) who had a history of drug intake, and 1(0.7%) with cardiac disease. Around 60 (50.8%) were found with 2g urinary protein. Among 100 samples without preeclampsia,73% were multigravida, 9% hypertensives, none with diabetes, 2% with drug intake, 2% with cardiac disease, and 1% with 2 g urinary protein ($p<0.01$). Mean age was 26.87±4.40 and 25.93±4.12 years in women with preeclampsia and those without it respectively, mean gestational age was 34.95±3.91and 35.39±3.87 weeks respectively, mean systolic blood pressure (BP) was 150.47±17.54and 119.60±17.16 mmHg respectively, and mean diastolic BP was 99.07±9.64 and 77.30±11.70 mmHg respectively.Mean serum CRP was 5.30±2.75 and 3.13±1.28 respectively ($p<0.01$).

Conclusions: We conclude that increased CRP levels are subsequently developed preeclampsia. It can prove as a useful marker of preeclampsia and help in its better diagnosis and management.

Keywords: C-reactive protein, Preeclampsia, Singleton pregnancy.

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Introduction

Preeclampsia is a pregnancy disease characterized by high blood pressure and proteinuria, which usually occurs late in the pregnancy.[1] It is the leading cause of fetal-maternal morbidity and mortality.[2] Preeclampsia affects about 2-5% of pregnancies around the world, with the prevalence increasing in developing nations.[3] Aetiology of preeclampsia is still debatable, with previous literature proposing endothelial dysfunction and C-reactive protein (CRP) as the causes.[4]

CRP is a plasma protein that is released by the liver during a period of acute aggravation and is influenced by the body's supplement system. Due to inflammation of

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hepatocytes, the level of CRP is increased by 1000-fold of its normal value.[5–7] Defective placentation was associated with an increase in angiogenesis markers such as solvent endoglin and FMS-like tyrosine kinase 1 (sFLT1 or sVEGFR-1) and cytokines in preeclamptic women, suggesting that CRP plays a role in the intensive stage alongside these markers.[8]

CRP detection in amniotic fluid speaks for its role in this disease. Increased maternal CRP convergences have been useful in detecting contamination in preterm labor and preterm membrane rupture during pregnancy.[9] Various studies shows correlation of systolic and diastolic blood pressure with CRP and its increased concentration with the severity of preeclampsia.[10] Another study examined the relationships between mean blood vessel tension and CRP in preeclampsia patients.[11] However, there is just a little amount of literature available. The current review was prompted to analyze the expanded CRP level as a significant biochemical marker for preeclampsia and contrast it with normal pregnancy in order to distinguish proof of aggravation by estimating expanded CRP level.

Methodology

This was an observational study carried out at the Department of Obstetrics & Gynecology, Sahiwal Medical College Teaching Hospital, and Sahiwal from 01-11-2020 to 30-04-2020. The study received permission from the institutional ethical review board (Ref:61/DME/SLMC/SWL) dated 10-10-2020. This was conducted to evaluate the level of CRP in pregnant patient's with preeclampsia and women with a normal pregnancy in 3rd trimester of pregnancy admitted in the antenatal ward and labor room. The diagnosis of preeclampsia was based on the Royal College of Obstetricians and Gynaecologists guidelines i.e. 1) Systolic blood pressure of 140 mmHg .2) Diastolic blood pressure of greater than 90mmHg or a rise of 15 mmHg, when blood pressure is measured on two occasions at least six hours apart. 3) Proteinuria of 300mg OR more in 24 hours urine sample.

It was done with 250 pregnant women with a singleton pregnancy, 150 with preeclampsia, and 100 with normal pregnancy in the third trimester of pregnancy. After collecting basic demographic data and brief history, a detailed clinical examination was carried out along with routine investigations. Gestational age was calculated by the last menstrual period and 1st-trimester ultrasound. Special consideration was given to the history of hypertension, diabetes mellitus, cardiac diseases, and medicine intake. Women who have had twin pregnancy generalized infection, anemia, renal problems, or ruptured membranes were excluded from the study. A 5 ml venous sample was taken under an aseptic technique in a sterile tube and analyzed for the level of CRP by the Enzyme-linked immunosorbent assay (ELISA) method.

Data were stored and analyzed using IBM-SPSS version 23.0. For baseline qualitative features of data, counts with percentages were reported, and mean with standard deviation were supplied for quantitative variables. Pearson Chi-Square test was used to check the association of maternal parameters in patients with and without Preeclampsia; and the independent sample t-test was used to compare CRP levels between the two groups. Statistical significance was defined as a P-value of less than 0.05.

Results

As seen in Table I, among preeclampsia samples (n=150), 64.7% were multigravida, 35.3% were primigravida, while 90.7% were singleton pregnancies. There were 72.7% hypertensive, 12.7% diabetics, 16% who had a history of drug intake, and 0.7% with cardiac disease. Around 50.8% were found with 2g urinary protein.

Table I: Baseline Characteristics of Studied Samples (n=250)

		C-reactive protein		p-value
		Yes (n=150)	No (n=100)	
Parity	**Primi-gravida**	53 (35.3)	27(27.0)	0.056
	Multi-gravida	97(64.7)	73(73.0)	
Singleton pregnancy	**Yes**	136(90.7)	90(90.0)	0.086
	No	14(9.3)	10(10.0)	
Hypertension	**Yes**	109(72.7)	9(9.0)	<0.001*
	No	41(27.3)	91(91.0)	
Diabetes Mellitus	**Yes**	19(12.7)	0(0.0)	<0.001*
	No	131(87.3)	100(100.0)	
Drug intake	**Yes**	24(16.0)	2(2.0)	<0.001*
	No	126(84.0)	98(98.0	
Cardiac disease	**Yes**	1(0.7)	2(2.0)	0.034
	No	149(99.3)	98(98.0)	
Urinary protein	**1 gm**	39(33.1)	5(5.0)	<0.001*
	2 gm	60(50.8)	1(1.0)	
	3gm	19(16.1)	0(0.0)	

*p<0.005 was considered statistically significant using the Pearson Chi-Square test

Among samples without preeclampsia, 73% were multigravida, 27% were primigravida, while 90% were

singleton pregnancies. There were 9% hypertensive, none with diabetes, 2% with drug intake, 2% with cardiac disease, and 1% with 2 gm urinary protein.

Pearson Chi-square test showed that there was a significant association of hypertension, diabetes, drug intake, and urinary protein with preeclampsia samples (p<0.001).

Table II shows that among preeclampsia samples, mean age was 26.87±4.40 years, mean gestational age was 34.95±3.91 weeks, mean systolic blood pressure (BP) was 150.47±17.54 mmHg, mean diastolic BP was 99.07±9.64 mmHg, and mean serum CRP was 5.30±2.75. On the other hand, among normal samples, mean age was 25.93±4.12 years, mean gestational age was 35.39±3.87 weeks, mean systolic BP was 119.60±17.16, mean diastolic BP was 77.30±11.70 mmHg, mean serum CRP was 3.13 (SD=±1.28). Independent samples t-test gave a significant mean difference for systolic BP, diastolic BP, and CRP between two groups, (p<0.001).

Table II: Comparison of C-reactive protein levels and other studied parameters in Preeclamptic and normal pregnant women

	C-reactive protein				p-value
	Yes (n=150)		No (n=100)		
	Mean	SD	Mean	SD	
Age (years)	26.87	4.40	25.93	4.12	0.009
Gestational age (weeks)	34.95	3.91	35.39	3.87	0. 004
Systolic blood pressure (mmHg)	150.47	17.54	119.60	17.16	<0.001*
Diastolic blood pressure (mmHg)	99.07	9.64	77.30	11.70	<0.001*
Serum C-reactive protein	5.30	2.75	3.13	1.28	<0.001*

*p<0.005 was considered statistically significant using an independent sample t-test

Discussion

Preeclampsia is a medical disorder specific to pregnancy. Inflammation and endothelial cell dysfunction is supposed to have a role in the pathophysiology of preeclampsia. The pathogenesis of it is still unclear in many aspects but there is a lot of improvement in the diagnosis and treatment.[12] Preeclampsia is a serious pregnancy complication. Around 30% of mortality in Pakistan is due to hypertensive disorders and preeclampsia affects 5-14% of all pregnant ladies globally.[13]

CRP is an acute-phase protein, the levels of which rise in response to inflammation. It is also an innate immune mediator, which is observed to rise in the serum of patients with preeclampsia before the onset of symptoms.[14]Keeping in view this characteristic of CRP and its relationship with preeclampsia, our study aims to assess serum CRP levels in pregnant females with preeclampsia and females with normal pregnancy. We evaluated its clinical utility in the diagnosis of preeclampsia and if it can be used as a marker and predictor of preeclampsia.

Our study showed a significant association of hypertension, diabetes, and urinary proteins with preeclampsia samples (p<0.001). This is supported by a multivariate analysis of Shams et al.[15] They found that women having pre-gestational diabetes, mental stress, and a family history of hypertension and diabetes were at a higher risk of preeclampsia. Our findings were also corroborated by a review that showed a link between preeclampsia and a family history of hypertension, cardiovascular illness, and diabetes, but the study found no link between diabetes and preeclampsia.[16]

A study by Mahmoud et al. found a significant correlation between serum CRP, systolic BP (r=0.643, p<0.001), and diastolic BP (r=0.729, p<0.001) in women with preeclampsia.[17] Begum G et al. found that the mean and standard deviation of CRP, systolic, and diastolic BP were highly significant in preeclamptic women as compared to the control group.[10]

Our study showed a significant mean difference between systolic BP (150.47±17.54, p<0.001) and diastolic BP (99.07±9.64, p<0.001) in women with preeclampsia. It was found significantly higher in preeclamptic women when compared with females with normal pregnancy (p<0.01). Our findings were supported by Sharmin et al. showing that the case group of CRPs was raised in 68% of pregnant women with preeclampsia, which was much higher in comparison to females with normal pregnancy (2%).[18]

The positive association between the development of preeclampsia and CRP level was confirmed in 18 studies as shown in a systemic review.[19] In our study, CRP levels were substantially greater in preeclamptic women than in women who were pregnant normally (p<0.001). The same finding was shown in a study conducted by OzKaplan SE et al. They found a significantly high level of CRP, which was 28 mg/L vs 6.2 mg/L between preeclamptic women and women with normal pregnancy.[20] Badehnoosh B et al found a P-

value of <0.001 for CRP when they compared preeclamptic women with healthy control women. The finding exactly matched our study as we got the same p-value for CRP in our study.[21] In our study, the CRP level was 5.30±2.75 in preeclamptic patients. Parmar U conducted a study in 2017 and observed significantly high levels of CRP (3.70±1.58 mg/L) (p<0.001).[22]

The study of Serrano NC et al, which was a large case-control study, nullified the causal association between elevated levels of CRP and the presence of preeclampsia. That was the largest study conducted to date.[23] Also; there were a few studies on the Pakistani population that have been conducted to date. There is a need for more studies with a large number of studied populations to strengthen the correlation between levels of CRP and preeclampsia so that it can be used as a marker and predictor of preeclampsia.

The strengths of our study are genuine data collection and evaluation of the patients by senior consultants. The weaknesses include small sample size and single-center data collection with less variation of ethnicities.

Conclusion

The increased CRP levels are positively correlated with preeclampsia was proven correct. Thus, it can prove as a useful marker of preeclampsia and help in its better diagnosis and management. Multi-centric large studies are invited to study its correlation with the assessment of the severity of preeclampsia and its correlation with feta-maternal outcome.

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