

Research Article**Serum C - reactive protein in Normal Pregnancy and Preeclampsia- a Comparative Study****Dr. Karuna Kanta Das¹, Prof. Kailash Bhattacharyya², Dr. Mun Konwar³**¹Associate Professor, ³Post Graduate Student, Department of Obstetrics and Gynaecology, Assam Medical College & Hospital (AMCH), Dibrugarh, Assam²Professor & Head, Department of Biochemistry, Assam Medical College & Hospital (AMCH), Dibrugarh, Assam***Corresponding author**

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Abstract: The aim and objective of the study is to find out the correlation between C - reactive protein (CRP) 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. A Hospital based prospective comparative study was performed on 100 singleton pregnant women after 20 weeks of gestation include 50 preeclamptic (25 mild and 25 severe) patients and 50 normotensive pregnant women as controls were selected for the study in the department of Obstetrics & Gynaecology, Assam Medical College and Hospital 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 2.1 ± 1.36 mg/dl and that in normotensive pregnant women was 0.39 ± 0.09 mg/dl (p-value < 0.0001). And mean level of serum CRP in mild preeclamptic patients was 1.08 ± 0.53 mg/dl and severe preeclamptic patients was 3.12 ± 1.16 mg/dl (p < 0.001). We therefore conclude that CRP level is raised in preeclampsia than normal pregnancy and also these results suggests that CRP levels are increased more in severe preeclampsia than mild preeclampsia. Thus, CRP can be used as a useful parameter for the assessment of preeclampsia.**Keywords:** Preeclampsia, normal pregnancy, C - reactive protein

INTRODUCTION

Pregnancy is a physiological state associated with many alterations in metabolic, biochemical, physiological, hematological and immunological process and all these changes are reversible following a few days to a few months after delivery [1]. Hypertensive disorders of pregnancy especially preeclampsia and eclampsia and their complications are one of the major cause of maternal mortality and morbidity in the world after obstetric hemorrhage, sepsis and unsafe abortions [2]. In addition, it is strongly associated with fetal growth retardation and prematurity and also it contributes largely to perinatal mortality and morbidity. Several studies have been carried out till date to understand the patho-physiological basis of this disease but exact patho-physiology is not fully understood till now.

Preeclampsia is a disease of pregnancy associated with endothelial cell damage. There are increasing evidences that preeclampsia is a systemic inflammatory

disease. C - reactive protein (CRP) is classical marker for systemic inflammation and tissue injury as an acute phase reactant [3]. CRP activates complement through the classical pathway and participates in opsonization of particulate antigens and bacteria. It interacts with nuclear antigens including chromatin and small nuclear ribonucleoproteins (snRNPs). CRP interacts with the nuclear antigens, released from apoptotic or necrotic cells and this interaction could militate against deposition of these antigens in tissue and autoimmune reactivity [4]. It has been suggested that CRP, in accordance with its proposed function, may play a role in eliciting the inflammatory response characteristics of pre-eclampsia [5]. The endothelial cell dysfunction and inflammatory process have been implication in the pathogenesis of preeclampsia. However, little is known about their correlation with the severity of the disease.

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

The present study entitled "Serum C-reactive protein in normal pregnancy and preeclampsia – A Comparative Study" was carried out in the Department of Obstetrics and Gynecology, Assam Medical College and Hospital (AMCH), Dibrugarh, for a period of one year from 1st July, 2013 to 31st June, 2014.

Based on inclusion and exclusion criteria a total of 100 subjects were selected for the study. The study included two groups: Group A – 50 cases and Group B – 50 controls. The Group A comprised 50 preeclampsia patients above 20 weeks of gestation (25 mild preeclampsia and 25 severe preeclampsia cases). The group B comprised of 50 age matched normotensive pregnant women above 20 weeks gestation.

Inclusion criteria – Primigravida above 20 weeks of gestation, Diagnosis of preeclampsia was made according to the criteria mentioned by American College of Obstetrics and Gynecology [6].

Exclusion criteria – Patients with other medical disorders, multiple pregnancy, premature rupture of membranes, chorio-amnionitis, patient in labour, patients with history of inflammatory diseases and patients under treatment of corticosteroids.

Collection of blood sample – Blood samples were collected in a sterile empty vial (SEV). The collected blood sample was allowed to stand for sometime till formation of clot and was then subjected to centrifugation in a clinical centrifuge machine at 3000 rpm to separate the serum. The separate serum was used to estimate CRP concentration by Dimension RxL Max autoanalyzer, Siemens. In pre-eclampsia group, blood samples were collected when the patient presented for evaluation and before initiation of medical therapy.

Estimation of serum CRP – Serum CRP levels were measured by high CRP sensitivity kit using Particle Enhanced Turbimetric Immunoassay (PETIA) Technique (By Dimension RxL Max autoanalyzer, Siemens) [7, 8, 9, 10].

Principle: Synthetic particles coated with antibody to C - reactive protein (AbPR) aggregate in the presence of C - reactive protein in the sample. The increase in turbidity which accompanies aggregation is proportional to the C - reactive protein concentration.

CRP + AbPR Aggregate (absorbs at 340 nm), 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. Co-efficient 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 AND OBSERVATIONS

Most of the patients (62%) were in the age group of 21 -25 years in both preeclamptic and normotensive pregnant group and minimum number of patients (6%) in the age group of more than 30 years in both the groups. The mean age (in years) of preeclamptic patients was 24.34 ± 4.36 and that in controls was 24.4 ± 3.79 in our study and was statistically not significant. So, this is age matched study.

Table-1 shows distribution of systolic and diastolic blood pressure in normotensive pregnant women and preeclamptic women which is statistically significant.

Table-2 shows that the differences in systolic as well as diastolic blood pressure between mild and severe preeclamptic patients were very highly significant (p-value < 0.0001).

The Table -3 shows that mean level of serum CRP in preeclamptic patients was 2.1 ± 1.36 mg/dl and that in normotensive pregnant patients was 0.39 ± 0.09 mg/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-4, it is observed that mean level of serum CRP in mild preeclamptic patients was 1.08 ± 0.53 mg/dl and severe preeclamptic patients was 3.12 ± 1.16 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-5 shows a significant positive correlation between serum CRP level and blood pressure (systolic and diastolic) in both mild and severe preeclamptic patients.

The Table-6 shows that the Controls group had higher rate of vaginal delivery (78%), where as higher rate of caesarean section was found in the preeclampsia group (36%) in our study.

Indications of caesarean section in the preeclampsia group were mainly fetal distress and IUGR and in the controls group, main indication was only fetal distress. The incidence of maternal

complications was mostly seen in the preeclamptic group.

Table – 7 shows that the birth weight of 48% of newborn of preeclamptic mothers and 26% newborn of normotensive pregnant mothers were less than 2.5 Kg while the birth weight of 52% newborn of preeclamptic mothers and 74% newborn of normotensive pregnant

mothers were more than 2.5 Kg. P-value is <0.0001 which is statistically significant.

The neonatal complications such as respiratory distress syndrome, neonatal jaundice and admission to NICU were found in both preeclamptic as well as controls group.

Table-1: Mean Level of Blood Pressure in Cases and Controls

Blood Pressure	Normotensive (Controls) mean±SD	Preeclampsia (Cases) mean±SD	P - value
Systolic (mm Hg)	116.08 ± 8.73	163.10 ± 22.80	< 0.0001
Diastolic (mm Hg)	76.0 ± 5.87	103.52 ± 10.13	<0.0001

Table-2: Mean Level of Blood Pressure among Mild and Severe Preeclamptic Patients

Blood Pressure	Mean Level (Mean ± S.D)		P - value
	Mild Preeclamptic Patients	Severe Preeclamptic Patients	
Systolic (mm Hg)	146.36 ± 17.39	179.84 ± 13.25	< 0.0001
Diastolic (mm Hg)	94.08 ± 3.29	112.96 ± 3.61	<0.0001

Table 3: Mean Level Of Serum CRP Among Preeclamptic Patients And Normal Pregnant Women

Parameter	Preeclamptic Patients		Normal Pregnant Women		p-value
	Range	Mean ± SD	Range	Mean ± SD	
CRP (mg/dl)	0.52 – 5.23	2.1 ± 1.36	0.24 – 0.72	0.39 ± 0.09	< 0.0001

Table-4: Mean Level of Serum CRP among Mild and Severe Preeclamptic Patients

Parameter	Mild Preeclamptic Patients		Severe Preeclamptic Patients		P-value
	Range	Mean ± SD	Range	Mean ± SD	
CRP(mg/dl)	0.5 – 2.76	1.08 ± 0.53	0.54 – 5.23	3.12 ± 1.16	< 0.001

Table-5: Correlation of Serum CRP Level with Blood Pressure in Mild and Severe Preeclamptic Patients

Parameter		CRP (mg/dl)	
		r	p
Mild Preeclampsia	Systolic Blood Pressure (mmHg)	0.49	<0.05
	Diastolic Blood Pressure (mmHg)	0.61	<0.01
Severe Preeclampsia	Systolic Blood Pressure (mmHg)	0.48	<0.05
	Diastolic Blood Pressure (mmHg)	0.77	<0.05

Table-6: Mode of Delivery in Normotensive and Preeclamptic Patients

Mode of Delivery	Normotensive (Controls)		Preeclampsia (Cases)	
	n	%	n	%
Spontaneous Delivery	39	78.00	29	58.00
Forceps delivery	2	4.00	3	6.00
Caesarean Section	9	18.00	18	36.00
Total	50	100.00	50	100.00

Table 7: Neonatal Outcome According To Birth Weight

Birth Weight (Kg)	Normotensive (Controls)		Preeclampsia (Cases)	
	n	%	n	%
< 2.5	13	26.00	24	48.00
>2.5	37	74.00	26	52.00
TOTAL	50	100.00	50	100.00

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.

Similar type of study done by Ghazavi A *et al.*; [11] 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.

Farzadnia M *et al.*; [12] in their cross sectional study for determination of serum highly sensitive (hs)-CRP levels in normotensive women, mild and severe preeclampsia patients in the department of Obstetrics and Gynecology of the Ghaem Academic Hospital in Mshhad University of Medical Sciences, Iran, found that there was significant difference in the mean serum hs-CRP levels between normal pregnant women and mild preeclamptic women ($p < 0.05$). Serum hs-CRP levels were significantly higher in severe preeclampsia ($P < 0.05$) than in normal pregnant women. There was also significant difference in serum hs-CRP levels between mild and severe preeclamptic patients ($P < 0.05$).

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.

Ahmed K *et al.*; [13] also found significant positive correlation between serum CRP levels in both systolic ($P < 0.05$) and diastolic blood pressure ($P < 0.05$) among 30 preeclamptic patients admitted in Aim Shams University Maternity Hospital, Egypt.

Fatemeh M *et al.*; [14] conducted a study in Afzalipour Hospital, Iran consisting of 43 mild and 43 severe preeclamptic patients in their third trimester of pregnancy. They found that in mild to severe preeclampsia groups, there was a positive correlation between serum CRP levels and systolic and diastolic blood pressure.

In the present study, the mean birth weight of preeclamptic patients and normotensive pregnant women were 2.48 ± 0.26 kg and 2.76 ± 0.38 kg respectively which is statistically significant. We also found that the birth weight of mild (2.59 ± 0.25 kg) and severe preeclamptic (2.37 ± 0.22 kg) patients were also statistically significant and is similar to other study conducted by Hossein A *et al* [15] and Mehdi F *et al.*; [16].

Hossein A *et al.*; [15] reported the mean birth weight in mild preeclampsia, 2.3 ± 0.68 kg and severe preeclampsia, 2.1 ± 0.97 kg, and Mehdi F *et al.*; 2013, [16] found the mean birth weight 2.3 ± 0.68 kg and 2.1 ± 0.97 kg in mild and severe preeclampsia group respectively.

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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