DOI: https://doi.org/10.3329/medtoday.v36i2.74789

ORIGINAL ARTICLE OPEN ACCESS

Association of C-reactive Protein in Preeclampsia

Jahanara Akter*[1], Shamsun Nahar Begum[2], Pervin Akter[3], Mamata Manjuri[4], Zenat Rehana[5], Umme Salma[6]

Abstract

Introduction: *Preeclampsia is a multisystemic disorder that complicate about 7-10 percent of human pregnancies. Worldwide this syndrome contributes high maternal and perinatal mortality and morbidity. C-reactive protein, a marker of tissue damage and inflammation, is elevated in seurm in overt preeclampsia. It is used as an objective and sensitive index of overall inflammatory activities in the body.* ***Aims and Objectives:*** *To explore the association of C-reactive protein level with the preeclampsia patients.* ***Materials and Methods:*** *The present study was a Case –Control study, conducted in the Department of Obstetrics and Gynaecology in collaboration with the Department of clinical pathology of Sir Salimullah Medical College Hospital, Mitford, Dhaka during the period of January 2013 to December 2013.The study population was pregnant women with preeclampsia and normal term pregnant patients admitted during study period. A total of 66 patients were included in the study. Among them 33 were clinically diagnosed preeclampsia women grouped as Cases and another 33 were age, parity and BMI matched term pregnant women as Controls. Eastmation of serum C-reactive protein was done by Nyco Card Reader-II method (Appendix-11). Statisticians analysis was perform by using SPSS.* ***Results:*** *C-reactive protein concentration (mg/L) was found significantly higher ($p<0.001$) in case group (17.93±10.5) than control group (7.45±1.80). C-reactive protein was ≥ 6mg/L in 29(87.9%) in case group and 9 (27.3%) in control group and C-reactive protein values showed significant positive correlation with systolic and diastolic blood pressure ($p<0.001$) in case group. C-reactive protein concentration was found significantly higher ($p<0.001$) in severe preeclampsia group than mild preeclampsia group.* ***Conclusion:*** *Therefore, it can apparently be concluded from this study that increased maternal serum C-reactive protein level might be a strong risk factor for preeclampsia, although the precise role of C-reactive protein in this regard whether causal or consequential, is yet to be determined. Finding of this study might be helpful for formulating a guideline for management of pregnant women with preeclampsia.*

Key Words: *C-reactive Protein, Preeclampsia.*

Number of Tables: 09, Number of References: 17, Number of Correspondence: 05.

***1. Corresponding Author:**
Dr. Jahanara Akter
Assistant Professor (Obs & Gynae)
OSD, DGHS
Mohakhali, Dhaka, Bangladesh.
Attached: Department of Obs & Gynae
Institute of Child and Mother Health
Matuail, Dhaka, Bangladesh.
Email: akterjahanara856@gmail.com
Contact: 01711261585

2. Professor Dr. Shamsun Nahar Begum
Ex-Head of the Dept. of Obs & Gynae
SSMC & Mitford Hospital
Dhaka, Bangladesh.

3. Dr. Pervin Akter
Professor & Head
Dept. of Physiology
Bashundhara Addin Medical College
South Keraniganj, Dhaka, Bangladesh.

4. Dr. Mamata Manjuri
Assistant Professor (Obs & Gynae)
OSD, DGHS
Mohakhali, Dhaka, Bangladesh.
Attached: Department of Obs & Gynae
Colonel Malek Medical College
Manikganj, Dhaka, Bangladesh.

5. Dr. Zenat Rehana
Assistant Professor (Obs & Gynae)
OSD, DGHS
Mohakhali, Dhaka.
Attached: Department of Obs & Gynae
Mugda Medical College
Mugda, Dhaka, Bangladesh.

6. Dr. Umme Salma
MD (Nuclear Medicine)
BSMMU
Resident Surgeon
National Institute of Traumatology and Orthopedic Rehabilitation (NITOR)
Sher-e- Bangla nagar, Dhaka, Bangladesh.

Received: *09 February 2024* ***Accepted revised version:*** *12 May 2024*

Introduction:

Preeclampsia is one of the most common medical complication during second half of pregnancy[1]. Preeclamsia is defined as, the rise of blood pressure equal to or above 140/90mm Hg in the presence of proteinuria developed after 20 weeks of gestational age in a previously normotensive and non proteinuric women[2]. Preeclamsia can result in eclampsia when convulsion develops or manifests as hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome. Eclampsia and HELLP syndrome are associated with severe complications such as cerebral hemorrhage, renal insufficiency, lung oedema and liver hemorrhage[3]. Incidence of preeclaempsia is about 7-10 percent throughout the world[4]. In India, the incidence as recorded from hospital statistics varies widely from 5 to 15% percent[2]. Both the incidence & prevalence of preeclampsia and eclampsia is higher in our country. In Sir Salimullah Medical College Hospital, 290 preeclamtic patients were admitted among 13404 obstetric patients in 2012. A maternal mortality of 15 percent still occurs with modern obstetric services[5]. Women who receive no prenatal care are 12 times as likely to die from preeclamptic complication as women who do receive prenatal care[6]. Preeclamsia accounts for 80-84 percent of low birth weight babies. These low birth weight babies are now the major groups of newborn being cared in the neonatal intensive care units worldwide. Endothelial dysfunction is accompanied by elevated levels of inflammatory markers which have ben shown to be much higher in women with preeclampsia than those of normal pregnancy[1]. C-reactive protein, as an acute phase reactant, belongs to the pentraxin family of calcium dependent ligand binding plasma protein. It is produced by hepatocytes in response to injury, inflammation, infections and malignant neoplasia It has short half life, which is constant under all condition of health and disease[7]. Recent studies have been suggested that increased level of CRP is associated with an abnormal systemic endothelial vascular reactivity[8]. CRP is used mainly as a marker of inflammation. Measuring and charting of CRP values can prove useful in early determining of disease, disease progress or effectiveness of treatments[9]. Since maternal health and pregnancy outcome is drastically affected by hypertensive disorders of pregnancy so early detection and timely intervention to minimize the harm should be to our utmost attention and interest.

Materials & Methods:

This case control study was conducted in the Department of Obstetrics and Gynaecology in collaboration with the Department of clinical pathology of Sir Salimullah Medical College Hospital, Mitford, Dhaka during the period of January 2013 to December 2013. The study population were pregnant women with preeclampsia and normal term pregnant patients admitted during study period. A total of 66 patients were included in the study. Among them 33 were clinically diagnosed preeclampsia women grouped as Cases and another 33 were age, parity and BMI matched term pregnant women as Controls, taking by consecutive sampling. The patients were enrolled following inclusion & exclusion criteria. **Inclusion criteria are age** - 24-35 years, gestational age - 28-40 weeks and term pregnant patients as matched controls. **Exclusion criteria are** patients with preexisting hypertension, renal diseases –such as glomerulonephritis, nephrotic syndrome, diabetes mellitus, thyroid dysfunction and pyrexia. The research protocol was approved by the institutional ethical review committee. Keeping compliance with Helsinki Declaration for medical research involving human subject 1964, patient was informed verbally about the study, the underlying hypothesis and right for the participant to withdraw from the project at any time, any reason. Written consent was obtained from each patient. It was assured that all recordsional approach would be kept confidential and procedure will be helpful for both the physician and patient in making rational approach regarding management of the cases. Provisional diagnosis of preeclampsia was done by careful history taking and clinical examination. Enrolled patients were asked to take part in an hour-long face to face interview. For recording purpose a predesigned data collection sheet was used, to elicit information regarding maternal socio-demoghraphic characteristics, medical history & family history. A detailed past obstetric history and investigations results were included in the data collection sheet. Gestational age was calculated from the LMP and with the early date ultrasongram records. Physical examination and anthropometric measurement (height, weight) of each study subject was taken and recorded. With full aseptic precaution two ml of venous blood was drawn from each of the study subjects. Then blood was transferred into a clean test tube and trmsported to the clinical pathology laboratory. Random urine sample was collected in a clean test tube and analyzed for presence of protein by dipstick reagent strip. Eastmation of serum C-reactive protein was done by NycoCard Reader-II method (Appendix-11). The data were screened and checked for any missing value and discrepancy and compiled. All data were recorded in tabulated form and the result was expressed as mean ± SD SPSS software was used to analyze the data. Unpaired t" test, chi-square test and r test were used to see the level of significance. 95% confidence limit ($p < 0.05$) was taken as level of significance.

Results:

C-reactive protein concentration (mg/L) was found significantly higher ($p<0.001$) in case group (17.93±10.5) than control group (7.45±1.80). C-reactive protein was ≥ 6mg/L in 29(87.9%) in case group and 9 (27.3%) in control group and C-reactive protein values showed significant positive correlation with systolic and diastolic

blood pressure (p<0.001) in case group. C-reactive protein concentration was found significantly higher (p<0.001) in severe preeclampsia group than mild preeclampsia group. The findings of the study obtained from data analysis are documented below.

Table I shows no significant difference between mean age of case and control group but highly significant difference between mean gestational age in both groups.

Table I: Comparison of age and gestational age of the study subjects

Variable	Case (n=33)	Control (n=33)	p-value
	Mean ± SD (Range)	Mean ± SD (Range)	
Age (years)	26.76±3.37 (24-35)	26.70±2.85 (24-35)	0.876
Gestational age (weeks)	37.36±2.57 (28-40)	39.12±0.93 (37-40)	<0.001

Data were analysed using Unpaired t-Test and were presented as mean±SD. p<0.05 is statistically significant.

Table II shows that the case and control groups were almost identical regarding their gravidity.

Table II: Distribution of gravidity in the study subjects

Variable	Case (n=33)		Control (n=33)		p-value
Gravida	Total no.	Percentage	Total no.	Percentage	0.319
Primi	16	(48.5)	12	(36.4)	
Multi	17	(51.5)	21	(63.6)	

Data were analysed using chi-square test.

p<0.05 is statistically significant

Table III shows no significant difference between the case and control groups regarding their antenatal care.

Table III: **Status of Antenatal care in the study subjects.**

Variable	Case (n=33)		Control (n=33)		p-value
Antenatal care	Total no.	Percentage	Total no.	Percentage	
Regular	14	(42.4)	17	(51.5)	0.115
Irregular	19	(57.6)	16	(48.5)	

chi-square test was done to analyse the data.

p<0.05 is statistically significant.

Table IV shows that over 52.9% of the case group had history of preeclampsia in previous pregnancy as compared to only 4.7% of the control group.

Table IV: Distribution of the study subjects according to history of preeclampsia in previous pregnancy.

Variable	Case (n=17)		Control (n=21)		p-value
History of preeclampsia	Total no.	Percentage	Total no.	Percentage	
Present	9	(52.9)	1	(4.7)	0.006
Absent	8	(47.0)	20	(95.2)	

chi-square test was done to analyse the data.

p<0.05 is statistically significant.

Table V shows significant difference between the case and control groups regarding BMI, Systolic blood pressure and Diastolic blood pressure respectively.

Table V: Comparison of physical examination findings in the study subjects

Variable	Case (n=33)	Control (n=33)	p-value
	Mean ± SD (Range)	Mean ± SD (Range)	
BMI (kg/m^2)	23.37±1.47 (20-26)	21.81±1.45 (18-24)	<0.001
Systolic blood pressure (mmHg)	148.33±13.41 (140-170)	108±7.14 (100-120)	<0.001
Diastolic blood pressure (mmHg)	106.67±6.99 (100-120)	69.67±5.56 (60-80)	<0.001

Data were analysed using Unpaired t-Test and were presented as mean±SD.

p<0.05 is statistically significant.

Table IV shows that Serum C-reactive protein level was found ≥6mg/L in 29 (87.9%) women in case group and only 9 (27.3%) women in the control group respectively. Serum C-reactive protein level was found <6 mg/L in majority (72.7%) of the control group.

Table VI: Serum C-reactive protein status in the study subjects.

Parameter	Case (n=33)		Control (n=33)		p-value
CRP status	Total no.	Percentage	Total no.	Percentage	
(≥6 mg/L)	29	(87.9)	9	(27.3)	<0.001
(<6 mg/L)	4	(12.1)	24	(72.7)	

chi-square test was done to analyse the data.

p<0.05 is statistically significant.

Table VII shows that Serum C-reactive protein level was found <6mg/L in 72.7% of control group. Majority of cases and control group were within the range of 6-15mg/L. Only case group were found within the range of 16-25 mg/L and ≥ 26mg/L of Serum C-reactive protein concentration.

Table VII: Distribution of serum C-reactive protein level in the study subjects.

Parameter	Case (n=33)		Control (n=33)		p-value
CRP level (mg/L)	Total no.	Percentage	Total no.	Percentage	
<6	4	(12.1)	24	(72.7)	
6-15	15	(45.4)	9	(27.2)	
16-25	9	(27.2)	0	(0)	<0.001
≥ 26	5	(15.1)	0	(0)	

chi-square test was done to analyse the data.

p<0.05 is statistically significant.

Table VIII shows the mean serum C-reactive protein concentrations with its range in the study subjects when concentrations were ≥6mg/L; which in case & control were 17.93±10.05 (6-48) mg/L and 7.45±1.80 mg/L (6-15) respectively and serum C-reactive protein concentrations were higher in case group than control group.

Table VIII : Serum C-reactive protin status in the study subjects when concentration were ≥6mg/L.

Variable	Case (n=24)	Control (n=9)	p-value
Serum C-reactive protein level	Mean ± SD (Range)	Mean ± SD (Range)	
(≥6mg/L)	17.93+10.05 (6-48)	7.45+1.80 (6-15)	<0.001

Data were analysed using Unpaired t-Test and were presented as mean±SD.

p<0.05 is statistically significant.

Table IX shows that mean serum C-reactive protein concentrations level were higher in the severe preeclampsia group than those in the mild preeclampsia group.

Table IX : Serum C-reactive protein status in mild and severe preeclampsia patients

Parameter	Mild preeclampsia (n=24)		Severe preeclampsia (n=9)	p-value
CRP status	Total no	percentage	percentage	
(≥6 mg/L)	20	(83.4)	(0)	
(<6 mg/L)	4	(16.7)	(0)	<0.001
Mean ± SD	12.92±5.7		27.78 ±17.37	
Range (mg/L)	(3 – 25)		(6 – 48)	

Data were analysed using Unpaired t-Test and were presented as mean±SD.

p<0.05 is statistically significant.

Discussion:

In this Case-Control study, the serum C-reactive protein concentration have measured in preeclamptic women (case) and normotensive term pregnant women (control) to evaluate the association of C-reactive protein level in preeclamptic women. In this study mean age of case group was 26.76±3.37 years. Most subjects in both groups were within range of 24-29 years of age and Muslims. This was nearly consistent with several other study[8,10,11]. The present study has revealed the mean serum C-reactive protein concentration was 7.45 ± 1.80 mg/L (range of 6-15 mg/L) in control group. Mean serum C-reactive protein concentration found in case group was 17.93±10.05mg/L (range of 6-48 mg/L). This study has shown mean serum C-reactive protein concentration in preeclampsia cases significantly high in comparison to control (P < 0.001). Same phenomenon observed in many other studies around the world[3,12,13,14,15]. Considering preeclampsia sub types of this study, serum C-reactive protein concentration in severe preeclampsia group found significantly higher (P < 0.001) than that of mild preeclampsia. This is harmonious with some other studies done abroad[4,12,15,16]. In this study, it was found that C-reactive protein levels were significantly higher (P < 0.001) in preeclampsia women and positively correlated to the degree of blood pressure elevation. Same phenomenon observed in many other studies[3,13,15]. In Present study, serum C-reactive protein was found within the range of 6-15 mg/L in 45.4% of cases and 27.2% of controls. About 72.7% control and only 12.1% of cases are found <6mg/L. Serum C-reactive protein concentration was found to be maximum in severe preeclampsia group (48 mg/L) and lowest in control group (03mg/L). The results of present study are not in agreement with those of other study[17] who reported in their cross sectional study, that maternal serum C-reactive protein is not elevated with preeclamptic women when compared with normal term pregnant women but increased when compared to non pregnant women. Probable explanation of disagreement may be attribute to several factors such as variable demographic characteristics of patients under study, wide variability of serum C-reactive protein in infection, inflammation, tissue damage and malignant neoplasia in general poulation & variation in prevalence of subclinical infections of women under studies etc. In fact, the path physiology of preeclampsia is still unknown and precise role of C-reactive protein in this regard is still cloudy. One school of thought proposes that overt or occult inflammation as the cause of preeclampsia and raised serum C-reactive protein to be simply the marker of inflammation as a component of acute phase reactant, which expected to help in promising the diagnostic and prognostic potentials.

Conclusion:

The study concludes that serum C-reactive protein level was found to be significantly higher in preeclamptic patients. It signifies strong association of C-reactive protein with preeclampsia in our Bangladeshi women. Higher the severity of preeclampsia, serum C-reactive protein tends to be higher.

Conflict of Interest: None.

Acknowledgement:

I would like to express my gratitude to all my teachers and supervisor who guide me and all my patients who inspite of their sorrows and sufferings helped me in getting all my clinical information. Last of all I like to acknowledge the sacrifice and support of my family members.

References:

1. Sibai and Baha. Diagnosis and management of gestational hypertension and pre-eclampsia. Obstet. Gynecol. 2003; 102: 181-192.
https://doi.org/10.1097/00006250-200307000-00033
https://doi.org/10.1016/S0029-7844(03)00475-7
PMid:12850627

2. Dutta DC. Hypertensive Disorder in Pregnancy in Text book of Obstetrics. 7th Edition. Konar Hiralal, Calcatta India. 2011; 219-230.

3. Kumru S, Godekmerdan A, Kutlu S and Ozcan A. Correlation of maternal serum high- sensitive C-reactive protein-levels with biochemical and clinical parameters in preeclampsia. Eur Obstet Gynecol Reprod Biolo. 2006; 35: 230-233.
https://doi.org/10.1016/j.ejogrb.2005.05.007
PMid:16054746

4. Sawsan, K. Correlation maternal C-reactive Protein and Serum fibrinogen with the severity of preeclamipsia. kufaMed. Journal. 2012; 15: 11.

5. Chamberlain, Woloshin S and Schartz LM. Distribution of C-reactive protein values in United States. N Erigl J med. 2005; 352(15): 1611-1613.
https://doi.org/10.1056/NEJM200504143521525
PMid:15829550

6. MacKay A, Berg C. & Atrash H. Pregnancy related mortality from preeclampsia and eclampsia. JAMA. 2001; 282: 356-362.

7. Picklesimer A, Jared H, Moss K, Offenbacher S and Beck J, BK. Racial differences in C-reactive protein level during normal pregnancy. Am J Obstet Gynecol. 2008; 199 (5): 523-526.
https://doi.org/10.1016/j.ajog.2008.04.017
PMid:18539258 PMCid:PMC2665720

8. Makrina D, Savvidou, Chaistoph C, Lees, Mauro Parra and Aroon, D. Levels of C-reactive protein in pregnant women who subsequently develop preeclampsia. BJOG. 2002; 109: 297-301.
https://doi.org/10.1016/S1470-0328(02)01130-8
https://doi.org/10.1111/j.1471-0528.2002.01130.x

PMid:11950185

9. Mark B P. C-reactive protein fifty years on. The Lancet. 1981; 1: 653-656.

https://doi.org/10.1016/S0140-6736(81)91565-8

PMid:6110874

10. Chunfang Q, Luthy DA, Zhang C, Walsh SW, Leisenring WM & Williams MA. Maternal C-reactive protein concentrations and risk of preeclampsia. Am J Hypertens. 2004; 17: 154-160.

https://doi.org/10.1016/j.amjhyper.2003.09.011

PMid:14751658

11. Hilary S, Gammill MD, Robert W and Rebecca G et al. Does C-reactive Protein predict recurrent preeclampsia?. PMC. 2012; 29 (4): 399-409.

https://doi.org/10.3109/10641950903214633

PMid:20701468 PMCid:PMC3339658

12. Bargale A, Jayashree V, Jaanu, Dhiraj J, Trivedi and Nittin Nagane. Serum Hs- CRP and Uric acid as indicator of severity in Preeclampsia. International Journal of Pharma and Bio Sciences. 2011; 2 (3): 340-345.

13. Ustun, Yapral Engin-Ustrn and Mansur Kamaci. Associations of Fibrinogen and C-reactive Protein with severity of preeclampsia. Eur J Obstet Gynecol Reprod Biol. 2005; 121: 154-158.

https://doi.org/10.1016/j.ejogrb.2004.12.009

PMid:16054955

14. Belo E, Serkan K, and Bulent Y. Association of maternal serum high senitive CRP level with body mass index and severity of pre-eclampsis at third trimester. Obstet. Gynecol. 2005; 36 (5): 970-977.

https://doi.org/10.1111/j.1447-0756.2010.01279.x

PMid:20722986

15. Sultana S. Serum C-reactive Protein in preeclampsia. (Thesis) BIRDEM Academy, Dhaka, Library of Dhaka Medical College, Dhaka, Bangladesh. 2010.

16. Nanda K, Sadanand G, Muralidhara, Krishna CS, and Mahadevappa. C-reactive protein as a predictive factor of preeclampsia. Int. Biol Med Res. 2012; 8(1): 1307-1310.

17. Kristen K, Wide-Swensson D, Lindstrom V, Schmidt, C, Grubb A. and Strevens H. Serum amyloid a protein and C-reactive protein in normal pregnancy and preeclampsia. Gynecol Obstet Invest. 2009; 67(4): 275-80.

https://doi.org/10.1159/000214081

PMid:19390201