

Levels of C-Reactive Proteins in Pregnant Women and its Relation with Preeclampsia in Singleton Pregnancy

NASREEN AKHTAR¹, ARIFA ZAFAR², QURAT-UL-AIN³, TUBA RASHEED⁴

¹Associate Professor, Department of Obstetrics & Gynaecology, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur Azad Kashmir

²Assistant Professor, Department of Obstetrics & Gynaecology, Pak Red Crescent Medical & Dental College, Lahore

³Senior Registrar, Department of Obstetrics & Gynaecology, Quaid-e-Azam International Hospital, Rawalpindi

⁴4th Year MBBS Student, Bahria University of Health Sciences, Karachi

Correspondence to: Nasreen Akhtar, Email: dr.nasreenak@gmail.com, Cell: 0333-4917188

ABSTRACT

Objective: To find the levels of C-reactive protein pregnant women and its relation with preeclampsia in singleton pregnancy.

Study Design: Case control study.

Place and Duration of Study: Department of Obstetrics & Gynaecology, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur Azad Kashmir from 1st July 2021 to 30th June 2022.

Methodology: One hundred preeclampsia and 50 control women were enrolled. Protein in the urine presenting renal impairment, decrease platelet counts and renal disease were assessed. Cases that had a blood pressure which was chronically high in cases prior to gestation or were chronic renal disease patients were excluded from the study. A biochemical analysis of C-reactive proteins was conducted through ELISA. The results were then interpreted in terms of their association with preeclampsia. Demographic details and clinical parameters as body mass index (kg/m²), familial history, any related comorbidities, clinical signs and symptoms were documented.

Results: The mean age of the preeclampsia women was 31.3±3.2 years while that of pregnant women who were normal controls as 25.8±3.8 years. Primigravida was higher in preeclampsia women while multigravida was higher in normal control pregnant women. Hypertension was prevalent in 73% of the preeclampsia cases than 10% of the normal control pregnant cases. Urinary protein was high as 2 gm in 51% cases of preeclampsia The C-reactive protein value was also significantly higher in preeclampsia cases than normal controlled pregnant women.

Conclusion: There is a direct significant association between preeclampsia and high levels of C-reactive proteins.

Keywords: C-reactive protein, Pre-eclampsia, Pregnancy

INTRODUCTION

Preeclampsia is a condition commonly develops in 4 to 5% of pregnancies. It is clinically featured with high blood pressure as well as proteinuria. It is formed in gestational cases above 20 weeks of gestation. Preeclampsia can cause eclampsia in cases of convulsions or in hemolysis manifestations as well as in cases of increased hepatic enzymes and decreased platelet count syndrome (HELLP). HELLP syndrome and eclampsia are reported as ailments causing severe morbidities including pulmonary edema, cerebral-hemorrhages, hepatic hemorrhage and renal insufficiency.¹

The primary pathogenic cause of preeclampsia is endothelial-cell function disorders.² The disturbances in endothelial function are found to be related with inflammatory biomarkers with a high incidence of these biomarkers in females with preeclampsia. The levels of inflammatory biomarkers are also reported to be escalated in preeclampsia women when compared with normal pregnant women.³

C-reactive protein is a systematic inflammatory biomarker.⁴ Its levels are higher in cases of preeclampsia.⁵ The levels of C-reactive proteins can be analyzed either through the application of labelled antibodies in enzyme linked immune sorbent assay (ELISA) or through the assistance of fluorescent markers.⁶ High sensitivity C-reactive protein value is considered much sensitive than C-reactive proteins. Various attempts to predict preeclampsia value through high sensitivity C-reactive proteins.^{7,8}

There is very less evidence to support that serum high sensitivity c reactive protein values are clinically and biochemically associated with the preeclampsia parameters. However, there is evidential proof for inflammatory markers having association with preeclampsia. This study was conducted to evaluate the association between C-reactive proteins and preeclampsia in singleton deliveries.

MATERIALS AND METHODS

This was a case control study which was carried at Department of Obstetrics & Gynaecology, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur Azad Kashmir from 1st July 2021 to 30th June 2022. A total of 100 preeclampsia and 50 control women

were included and received the informed consent from all participants. The sample size was calculated by available software for sample size calculation using 80% power of test and years and upto 40 years. Only those women who had singleton fetus were included in the study. The age of the women was normal pregnancy was diagnosed on basis of their clinical and biochemical status in addition to their ultrasonography findings. Similarly, the diagnosis of preeclampsia was made through high blood pressure on monitoring post 20 weeks. Protein in the urine presenting renal impairment, decrease platelet counts and renal disease were noted. Cases had a blood pressure which was chronically high in cases prior to gestation or were chronic renal disease patients were excluded from the study. A biochemical analysis of C-reactive proteins was conducted through ELISA. A 3 cc blood was withdrawn for the purpose from each patient/participant and serum was separated through centrifugation at 3000 rpm. The serum was then kept at -20 degree Celsius until analysis was performed. The results were then interpreted in terms of their association with preeclampsia. Demographic details and clinical parameters as BMI in terms of kg/m², familial history, any related comorbidities, clinical signs and symptoms were documented on a well-structured questionnaire. Data was analyzed using SPSS version 25.0 where Chi square test was used for analyzing the values. P value <0.05 was taken significant.

RESULTS

The mean age of the preeclampsia women was 31.3±3.2 years while that of pregnant women who were normal controls as 25.8±3.8 years. Primigravida was higher in preeclampsia women while multigravida was higher in normal control pregnant women. Only one woman from control group had twin delivery while rest all women had singleton (Table 1).

The variables as hypertension, diabetes as well as cardiac and kidney disease had a higher prevalence in preeclampsia cases than normal control pregnant. Hypertension was prevalent in 73% of the preeclampsia cases than 10% of the normal control pregnant cases. Urinary protein was high as 2 gm in 51% cases of preeclampsia and 16% in 3 gm of preeclampsia cases while it was

only 4% and 2% in 1 gm and 2gm cases with nil cases for 3 gms (Table 2).

The present study was having a mean gestational age was almost similar in both groups with no significant variance. The systolic blood pressure of preeclampsia was 150.5±17.55 while of control pregnant women were 120±17.2. The diastolic blood pressure was also very high in preeclampsia cases than control pregnant women. The C-reactive protein value was also significantly higher in preeclampsia cases than normal controlled pregnant women (Table 3).

Table 1: Demographic comparison of pre-eclampsia and controls

Variables	Pre-eclampsia (n=100)	Control (n=50)	P-Value
Age (years)	31.3±3.2	25.8±3.8	0.042
Parity			
Primigravida	35 (35%)	13 (26%)	0.057
Multigravida	65 (65%)	37 (74%)	
Singleton Pregnancy			
Yes	100 (100%)	49 (98%)	0.188
No	-	1 (2%)	

Table 2: Comorbidities, drug intake and urea protein level in study cases and controls

Variables	Pre-eclampsia (n=100)	Control (n=50)	P-Value
Hypertension			
Yes	73 (73%)	5 (10%)	<0.001
No	27 (27%)	45 (90%)	
Diabetes mellitus			
Yes	13 (13%)	-	<0.001
No	87 (87%)	50 (100%)	
Drug intake			
Yes	16 (16%)	1 (2%)	<0.001
No	84 (84%)	49 (98%)	
Cardiac disease			
Yes	1 (1%)	1 (2%)	0.035
No	99 (99%)	49 (98%)	
Urinary protein			
1gm	33 (33%)	2 (4%)	<0.001
2gm	51 (51%)	1 (2%)	
3gm	16 (16%)	-	
Kidney disease			
Yes	54 (54%)	1 (2%)	<0.001
No	46 (46%)	49 (98%)	

Table 3: Comparison of gestational age and blood pressure within pregnant cases and controls

Variables	Pre-eclampsia (n=100)	Control (n=50)	P-Value
Body mass index	28.9±4.0	24.0±3.01	0.01
Gestational age (weeks)	35±3.90	35.4±3.9	0.14
Systolic blood pressure (mmHg)	150.5±17.55	120.0±17.2	<0.001
Diastolic blood pressure (mmHg)	99.10±9.6	77.0±12.0	<0.001
Serum C-reactive protein mg/L	5.25±2.8	3.1±1.3	<0.001

DISCUSSION

The major finding of present study elaborates that c reactive protein is directly associated predictor for preeclampsia cases. The results of the present study evidently proved higher significant values of C-reactive proteins in pregnant preeclampsia women in comparison to normal control pregnant women. The previous studies also facilitate the main findings of current research where a positive association was identified between both variables.¹²⁻¹⁷

Although this study was not a follow-up but results from a study by Sorokin and his colleagues described that high C-reactive protein levels were associated with preterm deliveries in preeclampsia women.¹⁴ Pitiphat and colleagues¹² elaborate that women having a higher C-reactive protein value are at higher risk

of preterm deliveries and preeclampsia. Ertas et al¹¹ also demonstrated the similar findings through their research. The increased risk of systematic-inflammation results in the formation of modification in body system including high C-reactive proteins, increased blood pressure.

This research additionally highlights the fact that cases where preeclampsia is presented have higher morbidities including cardio vascular events, hepatic related issues as well as kidney disease and obesity. Protein urea is also commonly noticed in cases of preeclampsia. Similar results have been elaborated by various previous researchers.¹⁸⁻²⁰

CONCLUSION

There is a direct significant association between preeclampsia and high levels of C-reactive proteins. C-reactive protein can act like a biomarker for identification of preeclampsia and comorbidities related with it.

REFERENCES

- Chavan AR, Griffith OW, Wagner GP. The inflammation paradox of mammalian pregnancy: turning a foe into a friend. *Curr Opin Genet Develop* 2017; 47:24-32.
- Erlebacher A. Immunology of the maternal-fetal interface. *Annual Rev Immunol* 2013; 31: 387-411.
- Romero R, Espinoza J, Gonçalves LF, Kusanovic JP, Friel LA, Nien JK. Inflammation in preterm and term labour and delivery. *Seminars Fetal Neonat Med* 2006; 11(5): 317-26.
- Ferreira LMR, Meissner TB, Tilburgs T, Strominger JL. HLA-G: at the interface of maternal-fetal tolerance. *Trends Immunol* 2017; 38(4): 272-86.
- Ginsberg Y, Khatib N, Weiner Z, Beloosesky R. Maternal inflammation, fetal brain implications and suggested neuroprotection: a summary of 10 years of research in animal models. *Rambam Maimonides Med J* 2017; 8(2): e0028.
- Boyle AK, Rinaldi SF, Norman JE, Stock SJ. Preterm birth: Inflammation, fetal injury and treatment strategies. *J Reprod Immunol* 2017; 119: 62-6.
- Mihu D, Razvan C, Malutan A, Mihaela C. Evaluation of maternal systemic inflammatory response in preeclampsia. *Taiwanese J Obstet Gynecol* 2015; 54(2): 160-66.
- Udenze I, Amadi C, Awolola N, Makwe CC. The role of cytokines as inflammatory mediators in preeclampsia. *Pan African Med J* 2015; 20: 219.
- Musilova I, Kacerovsky M, Stepan M, et al. Maternal serum C-reactive protein concentration and intra-amniotic inflammation in women with preterm prelabor rupture of membranes. *PLoS ONE* 2017; 12(8): e0182731.
- Rewatkar M, Jain S, Jain M, Mohod K. C-reactive protein and white blood cell count as predictors of maternal and neonatal infections in prelabour rupture of membranes between 34 and 41 weeks of gestation. *J Obstet Gynaecol* 2018; 1-7.
- Ertas IE, Kahyaoglu S, Yilmaz B, et al. Association of maternal serum high sensitive C-reactive protein level with body mass index and severity of preeclampsia at third trimester. *J Obstet Gynaecol Res* 2010; 36(5): 970-77.
- Pitiphat W, Gillman MW, Joshipura KJ, Williams PL, Douglass CW, Rich-Edwards JW. Plasma C-reactive protein in early pregnancy and preterm delivery. *Am J Epidemiol* 2005; 162(11): 1108-13.
- Sorokin Y, Romero R, Mele L, et al. Maternal serum interleukin-6, C-reactive protein, and matrix metalloproteinase-9 concentrations as risk factors for preterm birth <32 weeks and adverse neonatal outcomes. *Am J Perinatol* 2010; 27(8): 631-40.
- Tjoa ML, Van Vugt JMG, Go ATJJ, Blankenstein MA, Oudejans CBM, Van Wijk IJ. Elevated C-reactive protein levels during first trimester of pregnancy are indicative of preeclampsia and intrauterine growth restriction. *J Reprod Immunol* 2003; 59(1): 29-37.
- Hwang HS, Kwon JY, Kim MA, Park YW, Kim YH. Maternal serum highly sensitive C-reactive protein in normal pregnancy and pre-eclampsia. *Int J Gynecol Obstet* 2007; 98(2): 105-9.
- Sacks GP, Seyani L, Lavery S, Trew G. Maternal C-reactive protein levels are raised at 4 weeks gestation. *Human Reprod* 2004; 19(4): 1025-30.
- Mor G, Cardenas I, Abrahams V, Guller S. Inflammation and pregnancy: the role of the immune system at the implantation site. *Ann NY Acad Sci* 2011; 1221(1): 80-87.
- Silverberg O, Park AL, Cohen E, Fell DB, Ray JG. Premature cardiac disease and death in women whose infant was preterm and small for gestational age. *JAMA Cardiol* 2018; 3(3): 247-51.
- Schummers L, Hutcheon JA, Hacker MR, et al. Absolute risks of obstetric outcomes risks by maternal age at first birth. *Epidemiology* 2018; 29(3): 379-87.
- Leaños-Miranda A, Méndez-Aguilar F, Ramírez-Valenzuela KL, et al. Circulating angiogenic factors are related to the severity of gestational hypertension and preeclampsia, and their adverse outcomes. *Medicine* 2017; 96(4): e6005.