ORIGINAL ARTICLE

C-Reactive Protein Levels in Preeclampsia Singleton Pregnant Women and Their Outcomes

UMBREEN FATIMA¹, ABDULLAH SHAMSHAD², HAFIZ MUHAMMAD QAMER³, MARIA DHAHRI⁴, MUHAMMAD FAHEEM SIDDIQUI⁵

¹Programme Director, District Health Development Centre, Sahiwal

²Consultant Medical Specialist, Chaudhry Hospital, Gujranwala

³Medical Officer, THQ Hospital, Daska

⁴Consultant OBGY, Indus Hospital & Health Network (IHHN), District Headquarter Hospital, Badin

⁵Assistant Professor, Department of Biochemistry, Pak Red Crescent Medical & Dental College, Dina Nath

Correspondence to: Umbreen Fatima, Email: ambreentehkaal@gmail.com, Cell: 0321-4117544

ABSTRACT

Background: Preeclampsia is a hypertensive disorder that occurs during pregnancy, typically after 20 weeks of gestation and the relationship between C-reactive protein levels and adverse pregnancy outcomes.

Objective: To analyze the C-reactive protein levels in preeclampsia singleton pregnant women and their outcomes.

Methodology: This case control study was performed at District Health Development Centre, Sahiwal from 1st October 2022 to 31st March 2023. A total of 100 women including 50 preeclampsia and 50 controls were enrolled after the ethical clearance of the study. The inclusion criteria consisted of women having singleton pregnancy and were clinically diagnosed to be suffering from preeclampsia. Participants were assessed clinically, biochemically, and via ultrasonography to confirm a normal pregnancy or diagnose preeclampsia. The association between C-reactive protein levels and preeclampsia was then evaluated. The outcomes of pregnancy with preeclampsia and high C-reactive proteins were followed upto 3 days in women after delivery. Results: The maternal mean age was almost similar within both groups as 24.32±4.1 years and 25.26±5.63 years respectively. There was a higher body mass index trend in preeclampsia women than controls (p<0.05). The mean systolic blood pressure and diastolic blood pressure was much higher than control with a mean value as 115.33±9.39 vs 72±7.74 respectively. There were 72% of the preeclampsia vs 15% controls having previous history of hypertension. While only 16% preeclampsia and 10% control was already presenting a clinical history of diabetes. The mean preeclampsia C-reactive protein levels was 6.25±2.8 mg/L ad that of controls was 3.1±1.3 mg/L with 70% cases in preeclampsia group having higher that 15.5 mg/L CRP level in comparison to only 30% controls. The 35(70%) women having high C-reactive protein level and were preeclampsia; had adverse outcomes of their pregnancy including low birth weight in 77.1 (n=27) cases while preterm birth in 62.85 (n=22) cases. Conclusion: Higher levels of C-reactive proteins were linked with preeclampsia in singleton pregnant women leading to adverse outcomes of pregnancy including delivery complications, low birth weight and preterm births in significant number of

Keywords: C-reactive protein, Preeclampsia, Pregnant women, Outcome

INTRODUCTION

Preeclampsia is a pregnancy-specific hypertensive condition marked by maternal endothelial dysfunction and an amplified inflammatory response. 1-3 It shares key pathophysiological features with cardiovascular disease, suggesting a potential link to increased long-term cardiovascular risk. 4-5 Affecting around 5% of pregnancies, preeclampsia is a major contributor to both maternal and neonatal illness and death. Although its exact mechanisms remain only partially understood, several contributing elements have been identified, including defective placental development, oxidative stress, imbalances in angiogenic factors, and inflammation. 6

C-reactive protein (CRP), first identified in the 1930s as a marker of acute inflammation⁷ has garnered renewed attention over the past decade due to its association with cardiovascular disease risk.⁸ This connection has prompted investigations into CRP's potential role in preeclampsia, both as a predictive biomarker and a possible participant in its underlying pathophysiology. Elevated CRP levels have been consistently observed in patients with manifest preeclampsia.^{9,10} However, findings on its effectiveness in predicting preeclampsia before clinical symptoms arise have been more variable.¹¹

The present study was focused on assessing the significance of C-reactive protein levels in preeclampsia singleton pregnant women and their outcomes. The results of the preset study lead in identifying the medical importance of C-reactive protein during preeclampsia which any further assist in predicting cut off value for negative outcome within preeclampsia singleton pregnant women, consequently, assisting in reducing the negative outcomes of pregnancy.

Pageitad on 20.05 2022

Received on 20-05-2023 Accepted on 05-10-2023

MATERIALS AND METHODS

This case control study was performed at District Health Development Centre, Sahiwal from 1st October 2022 to 31st March 2023. A total of 100 women including 50 preeclampsia and 50 control were enrolled after the ethical clearance of the study. The sample size was determined using standard software for sample size calculation, with a statistical power of 80%. The inclusion criteria consisted of women having singleton pregnancy and were clinically diagnosed to be suffering from preeclampsia. Participants were assessed clinically, biochemically, and via ultrasonography to confirm a normal pregnancy or diagnose preeclampsia. Preeclampsia was identified by the onset of hypertension after 20 weeks of gestation, accompanied by proteinuria, renal impairment, reduced platelet count, or other signs of organ dysfunction. Women with chronic hypertension prior to pregnancy or a history of chronic kidney disease were excluded from the study. C-reactive protein (CRP) levels were measured using the ELISA method. For this purpose, 3 cc of venous blood was collected from each participant. Serum was separated by centrifugation at 3000 rpm and stored at -20°C until analysis. The association between CRP levels and preeclampsia was then evaluated. A well-designed questionnaire was used for documenting the demographic and clinical information of the patients including body mass index (BMI in kg/m²), family history, comorbid conditions, and relevant signs and symptoms. The outcome of pregnancy with preeclampsia and high C-reactive proteins was followed upto 3 days in women after delivery and recorded. Data were analyzed using SPSS version 25.0. The Chisquare and Odds Ratio test was employed to assess statistical associations, with a p-value of <0.001 considered statistically significant.

RESULTS

The maternal mean age was almost similar within both groups as 24.32±4.1 years and 25.26±5.63 years respectively. There was a higher body mass index trend in preeclampsia women than controls (<0.05). The mean systolic blood pressure and diastolic blood pressure was much higher than control with a mean value as 115.33±9.39 vs 72±7.74 respectively (Table 1). There was 72% of the preeclampsia vs 16% control having previous history of hypertension. While only 16% preeclampsia and 10% control was already presenting a clinical history of diabetes (Fig. 1).

Within the other clinical history variables, the urinary protein was reported highest as 3grams within 18% of the preeclampsia women than 0% of controls in same group. The kidney disease was also prevalent in 46% of the preeclampsia pregnant women

compare to 6% control pregnant women (Table 2). The mean preeclampsia CRP levels was 6.25±2.8 mg/L and that of controls was 3.1±1.3 mg/L with 70% cases in preeclampsia group having higher that 15.5 mg/L CRP level in comparison to only 30% controls. Statistically the difference was significant (P<0.001) [Fig. 2]

The odds Ration comparison of preeclampsia and control pregnant women Baseline CRP levels data in mg/L interpreted around 1.0 Confidence of interval while change in CRP showed 0.997 CI (Table 3). Thirty five (70%) women having high C-reactive protein level and were preeclampsia; had adverse outcomes of their pregnancy including low birth weight (LBW) in 77.1% (n=27) cases while preterm birth in 62.85% (n=22) cases (Fig. 3).

Table 1: Comparison of the maternal, gestational age and hypertension values of enrolled patients

Variable	Preeclampsia (n=50)	Control (n=50)	P value
Maternal age (years)	24.32±4.1	25.26±5.63	0.523
Gestational age (weeks)	33.50±3.98	36.00±3.18	0.325
Body mass index (kg/m ²)	29.25±1.86	25.40±1.72	0.051
Systolic blood pressure (mmHg)	177.2±17.12	116.00±12.98	< 0.001
Diastolic blood pressure (mmHg)	115.335±0.39	72.00±7.74	< 0.001

Table 2: Comparison of clinical history of cardiac disease and urinary protein in enrolled patients

Variables	Pre-eclampsia (n = 50)	Control (n = 50)			
Drug intake	4%	-			
Cardiac disease	2%	1%			
Urinary protein (gm)					
1	32%	4%			
2	50%	2%			
3	18%	-			
Kidney disease	46%	6%			

Table 3: Odds ratio comparison of preeclampsia and control pregnant women

Variable	Preeclampsia	Controls	OR (95% CI)	Adjusted OR
	Median (range)	Median (range)		(95% CI)
Baseline CRP (mg/L)	11.8 (0.9, 57.4)	10.00 (0.1, 49.7)	1.000 (1.000, 1.000)	1.0 (1.000, 1.000
CRP closest to delivery (mg/L)	29 (0.6, 31)	42 (0.1, 46.5)		
Change in CRP (mg/L)	-0.1 (-2.1, 3.1)	-0.3 (-4.0, 0.4)	0.997 (0.993, 1.001)	0.994 (0.981, 1.000)#

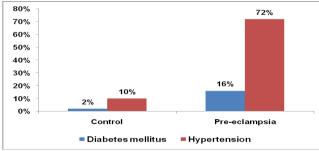


Fig. 1: Frequency of preeclampsia within enrolled patients

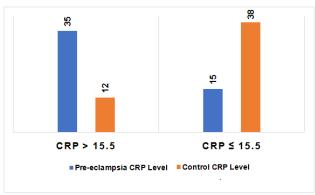


Fig. 2: Comparison of the preeclampsia and control pregnant women CRP levels

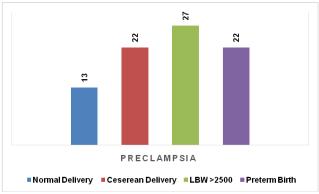


Fig. 3: The frequency of adverse outcomes in preeclampsia pregnant women with high CRP levels $\,$

DISCUSSION

The principal finding of the present study indicates that C-reactive protein (CRP) serves as a significant predictive biomarker for preeclampsia. The data clearly demonstrate markedly elevated CRP levels in pregnant women diagnosed with preeclampsia compared to those in the healthy control group. These results are consistent with prior research, which has similarly reported a positive correlation between elevated CRP concentrations and the occurrence of preeclampsia. 12-15

Although the current investigation did not include longitudinal follow-up, comparable findings have been reported by Meena et al¹⁶, who observed that elevated CRP levels were associated with preterm births among women with preeclampsia. Likewise,

scientist highlighted that women exhibiting elevated CRP levels were at increased risk for both preeclampsia and preterm delivery. Similar associations were also reported elsewhere ad in the current research.17

The presence of systemic inflammation appears to contribute to physiological alterations in pregnant women, including elevated CRP levels and increased blood pressure. Furthermore, this study underscores a greater prevalence of cardiac and metabolic syndrome/disease complications, renal impairment, and obesity in affected patients. Proteinuria was also commonly observed among preeclamptic cases, aligning with findings from earlier studies. 18,19

CONCLUSION

Higher levels of CRP proteins were linked with preeclampsia in singleton pregnant women. The C-reactive proteins may be high due to metabolic syndromes or heart diseases. The result of this high C-reactive proteins leads to delivery complications, low birth weight and preterm births in significant number of cases.

REFERENCES

- Gestational hypertension and preeclampsia: ACOG practice bulletin, number 222. Obstet Gynecol 2020;135(6):e237-60.
- Das S, Das R, Bajracharya R, Baral G, Jabegu B, Odland JØ, et al. Incidence and risk factors of pre-eclampsia in the Paropakar Maternity and Women's Hospital, Nepal: a retrospective study. Int J Environ Res Public Health 2019;16(19):3571.
- World Health Organization. WHO Recommendations for Prevention and Treatment of Pre-eclampsia and Eclampsia. Geneva: World Health Organization; 2011. Available https://www.who.int/publications/i/item/9789241548335
- Benschop L. Duvekot JJ. Versmissen J. van Broekhoven V. Steegers EAP, Roeters van Lennep JE. Blood pressure profile 1 year after severe preeclampsia. Hypertens (Dallas, Tex 1979) 2018;71(3):491-
- Amaral LM, Wallace K, Owens M, LaMarca B. Pathophysiology and current clinical management of preeclampsia. Curr Hypertens Rep 2017:19(8):61.
- 6 Adejumo OA, Okaka EI, Okwuonu CG, Iyawe IO, Odujoko OO. Serum C-reactive protein levels in pre-dialysis chronic kidney disease patientsin southern Nigeria. Ghana Med J 2016;50(1):31-8.

- Alamolhoda SH, Yazdkhasti M, Namdari M, Zakariayi SJ, Mirabi P. Association between C-reactive protein and gestational diabetes: a prospective study. J Obstet Gynaecol 2020;40(3):349-53.
- Mou AD, Barman Z, Hasan M, Miah R, Hafsa JM, Das Trisha A, et al. Prevalence of preeclampsia and the associated risk factors among pregnant women in Bangladesh. Sci Rep 2021;11(1):21339
- Trost SL, Beauregard JL, Smoots AN, Ko JY, Haight SC, Moore Simas TA, et al. Preventing pregnancy-related mental health deaths: insights from 14 US maternal mortality review committees, 2008-17. Health Aff (Millwood) 2021;40(10):1551-9.
- Kristensen K, Wide-Swensson D, Lindstrom V, Schmidt C, Grubb A, Strevens H. Serum amyloid a protein and C-reactive protein in normal pregnancy and preeclampsia. Gynecol Obstet Invest 2009;67(4):275-
- Perveen S, Muzammil F, Azhar S, Ilyas H, Mahmood F, Hussain A. 11. Association between C-reactive protein level and preeclampsia in pregnant women with singleton pregnancy. J Soc Obstet Gynaecol Pak 2022:11(4):238-41.
- Cunningham FG, Leveno KJ, Bloom SL, Dashe JS, Hoffman BL, Casey BM, et al. No title. In Williams Obstetrics, 25e [Internet]. New NY: McGraw-Hill Education, 2018. Available http://obgyn.mhmedical.com/content.aspx?aid=1151896101
- Phipps E, Prasanna D, Brima W, Jim B. Preeclampsia: updates in pathogenesis, definitions, and guidelines. Clin J Am Soc Nephrol 2016;11(6):1102-13.
- Gandevani SB, Banaem LM, Mohamadi B, Moghadam B, Asghari M. Association of high-sensitivity C-reactive protein serum levels in early pregnancy with the severity of preeclampsia and fetal birth weight. J Perinat Med 2012;40(6):601-5.
- Dangal MM, Giri A, Subedi RK, Karki A, Karki A. Maternal and fetal outcomes in pre-eclampsia in a tertiary care hospital in Eastern Nepal: a retrospective study. Int J Res Med Sci 2020;8(4):1368–73.
- Meena ML. Meena K. Meena BS. Gidwani C. Serum C-reactive protein in normal pregnancy and preeclampsia-a comparative study. Int J Clin Obstet Gynaecol 2019;3(2):141-5.
- Lopez-Jaramillo P, Barajas J, Rueda-Quijano SM, Lopez-Lopez C, Felix C. Obesity and Preeclampsia: Common Pathophysiological Mechanisms. Front Physiol 2018;9:1838.
- Peres GM, Mariana M, Cairrão E. Pre-eclampsia and eclampsia: an update on the pharmacological treatment applied in Portugal. J Cardiovasc Dev Dis 2018 Jan;5(1):3.
- Gencheva DG, Nikolov FP, Uchikova EH, Mihaylov RD, Pencheva BG, Ivanova KI. High-sensitivity CRP levels in women with gestational hypertension, preeclampsia and in normotensive pregnant women and its correlations. Folia Med (Plovdiv) 2021;63(4):511-8.

The article may be cited as: Fatima U, Shamshad A, Qamer HM, Dhahri M, Siddiqui MF: A C-Reactive Protein Levels in Preeclampsia Singleton Pregnant Women and Their Outcomes. Pak J Med Health Sci, 2023;17(11):261-263.