CORRELATION OF C-REACTIVE PROTEIN WITH SEVERITY OF PRE ECLAMPSIA

Gulnaz Begum, Nayyar Zaman, Radhia Khan, Habeel Dar

ABSTRACT

Objective: The objective of this study is to correlate the level of C - reactive protein with severity of pre eclampsia in pregnant women and compare it with normotensive pregnant women.

Study design: Cross sectional analytical.

Methodology: This study was conducted in Gynae/obs department of Hayatabad Medical Complex, Peshawar, from June 2015 to December 2015. In this study 100 pre eclamptic pregnant women were compared with 100 normotensive pregnant women of the same gestational age and parity for determination of C-Reactive protein (CRP). 5mL of venous blood was taken under aseptic techniques in sterile tube, followed by centrifugation for the separation of serum. Serum samples were stored at -4°C for biochemical analysis. CRP levels were measured by ELISA (Enzyme linked immune adsorbent assay) method.

Results: Mean and standard deviation for CRP, systolic and diastolic blood pressure, were highly significant ($p<0.000$) in preeclamptic women as compare to control group. Mean and standard deviation of CRP (10.52 ± 10.24) in preeclamptic women was highly significant $P < 0.000$ when compared with control (5.10 ± 6.20).

Conclusion: CRP shows significant correlation with systolic and diastolic blood pressure and is a better predictor of PE and eclampsia.

Key Words: Preeclampsia, C-Reactive Protein, Eclampsia.

INTRODUCTION

Preeclampsia (PE) is one of pregnancy complications and is an important cause of fetal and maternal mortality and morbidity.[1] This disease merge for the first time after 20th week of gestation and presenting symptoms are hypertension, proteinuria and different levels of ischemic damage to different organs. It is also associated with hemolysis, increase in liver enzymes and decrease in platelet count.[2]

PE is defined as blood pressure ≥ 140 / 90 mmHg at interval of 6 hrs on two different occasions and emerging for the first time in pregnancy, or a single recording of a diastolic blood pressure of 110 mmHg along with proteinuria on dipsticks testing ≥ 2+, after 20 weeks of gestation in pregnant women who previously has normal blood pressure. Severe PE is defined as diastolic blood pressure ≥ 110 mm Hg, systolic blood pressure ≥160 mm Hg, proteinuria 2.0 g/24hr or 3+ dipstick, persistent headache, visual disturbances, persistent epigastric or upper abdominal pain, oliguria (urine output <30 mL/hr), convulsion (eclampsia).[3]

Department of Biochemistry, Khyber Girls Medical College, Peshawar

Address for correspondence:
Dr. Gulnaz Begum
Department of Biochemistry, Khyber Girls Medical College, Peshawar
Cell: 0306-8366772
Email: drgulnaz75@gmail.com

Globally, PE complicates 5-10% of pregnancies while in Pakistan maternal mortality due to PE is about 30%.[4] Maternal deaths due to preeclampsia are mostly due to abruption of placenta, due to pulmonary edema, acute renal failure and rupture of liver. The disease is progressive and become worse with time, and delivery is the only solution.[5] PE is disorder which involves multiple organ systems, associated with damage of endothelium of organs and dysfunction of organ systems through the maternal circulation. Intrauterine growth retardation , premature deliveries, low birth weight, fetal and neonatal mortality are the common complications of PE.[6]

C-reactive protein (CRP) is a sensitive marker of tissue damage and potential marker of inflammatory response characteristic of preeclampsia.[7] The level of CRP is raised with severity of pre-eclampsia. CRP is present in amniotic fluid and also in urine of fetus, and poor pregnancy outcome is noted due to its increased amount.[8]

Previous studies suggest that the high level of CRP is a risk factor for pre-eclampsia. The raised level of plasma CRP in early pregnancy may contribute to subsequent development of pre-eclampsia and can be used for determination of severity of PE and ultimately eclampsia.[9] High level of CRP in third trimester in pre-eclamptic women is associated with complications like HELLP syndrome in mother and IUGR in fetus.[10] The role of CRP for prediction of preeclampsia in pregnant women is contro-versial.[11] The aim of this study is to correlate the level of CRP with severity of preeclampsia.

MATERIAL AND METHODS

This cross sectional comparative study was done to determine the CRP level in preeclamptic pregnant women during the time period of June 2015-December 2015, at Department of Gynecology and Obstetrics, Hayatabad Medical Complex, Peshawar, Khyber Pakhtunkhwa, Pakistan.

The study includes 100 preeclamptic pregnant women and 100 normal pregnant women of the same gestational age and parity. Gestational age was measured by last menstrual period and Ist trimester ultrasound.[12] Women having twin pregnancies, molar pregnancy, diabetes mellitus, chronic hypertension, renal disease, or any other infectious or inflammatory disease or on medication for the said diseases were excluded. 5mL of venous blood was taken under aseptic techniques in sterile tube, followed by centrifugation for the separation of serum. Serum samples were stored at -4°C for biochemical analysis. CRP level was determined by immune absorbent method.[13] Blood pressure was taken by mercury sphygmomanometer twice after interval of rest of about 15 min.[14]

SPSS 16 was used for data processing. For continuous data Mean and Standard Deviations were calculated. Categorical variables like age and parity was presented in term of frequency and percentages. Student t-test was applied for the determination of difference between the groups for continuous biochemical parameters. Similarly simple correlation analysis (Pearson's correlation co-efficient) was carried out to determine relationship between different variable of interest, where statistical significant was accepted at $P < 0.05$.

RESULTS

In this cross sectional comparative study, the 200 registered women were divided into two groups. Group I including pregnant women with PE and Group II including normal pregnant women, matched for gestational age and parity.

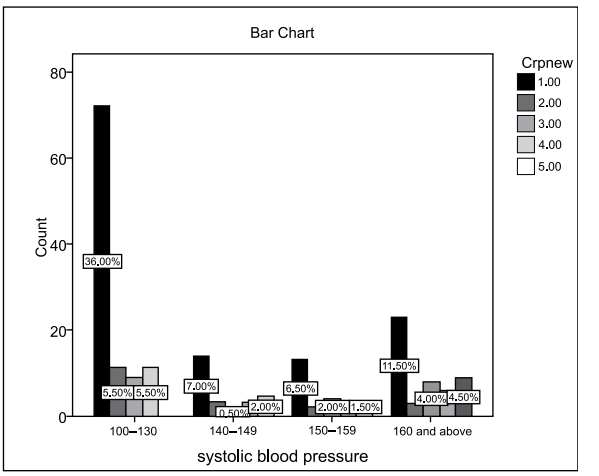
Table 1 show the demographic characteristics of Pre-eclamptic and control individuals. Age, weight, parity and gestational age of both Groups were insignificant at P>0.05. 2 indicates the level of CRP and

Table 1: Demographic Characteristics of PE and Control Subjects

Variables	Patients (n=100)	Controls (n=100)	P-value
Age (years)	28.05±4.74	27.18±4.67	0.193
Weight (Kg)	69.32 ± 4.47	68.71± 4.70	0.348
Gravidity	2.52±1.21	2.46±1.18	0.723
Gestational age (weeks)	33.34±5.26	33.36±5.31	0.979

Table 2: CRP levels of control and hypertensive pregnant women

Parameters	Patients	Controls	P-value
Systolic.BP (mm Hg)	153.59±12.42	114.90±8.70	0.000
Diastolic BP (mm Hg)	101.65±9.72	74.80±7.03	0.000
C-Reactive protein (CRP) μg/mL	10.52±10.24	5.10±6.20	0.000



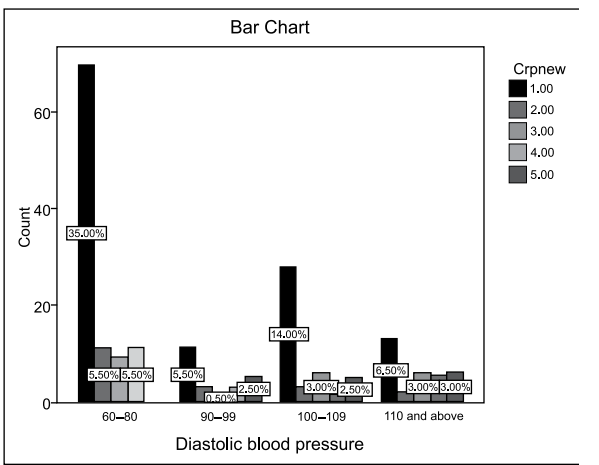


Figure 1 and 2: Shows the significant correlation between CRP and systolic and diastolic blood pressure respectively. As the blood pressure increases the level of CRP also increases which confirms CRP as marker of severity for PE.

systolic and diastolic blood pressure of pre-eclamptic and control groups. The CRP values of Group I (Pre-eclamptic women) were significantly higher at P<0.001 than the control subjects. The mean value of CRP in Group I was 10.52±10.24 μg/mL as compared to 5.10±6.20 μg/mL in Group II. Similarly the systolic

and diastolic blood pressure of Group I was 153.59 ±12.42mm Hg, 101.65 ±9.72 mm Hg as compared to 114.90 ±8.70 mm Hg, 74.80 ±7.03 mm Hg in control group.

DISCUSSION

The main cause of maternal mortality and morbidity in all over the world is hypertension in pregnancy. This also results in still births, neonatal morbidity and neonatal death1. About sixty three thousand women die every year due to different causes during pregnancy, delivery and during puerperium, among which hypertension, pre eclampsia, eclampsia are the major cause of death.[2] Total mortality due to hypertensive disorder in pregnancy in Pakistan is 30%.[4] Worldwide maternal mortality due to hypertension is 10-15% (7-27), of which 16% mortality is due to preeclampsia.[15]

The main causes of mortality and morbidity due to PE in Pakistan are, lack of education and access to prenatal and antenatal care, under equipped hospitals in low resource areas, non availability of trained health professional and diagnostic tools. Because of all the above causes there is delayed medical intervention to reduce the risk of HTN, PE and Eclampsia.[11-12]

The present study was designed to evaluate the cheapest and easily available test for early detection of pre eclampsia, to reduce its mortality and morbidity. Farzana Atighpour 16 studied in 2013 on Iranian population. She selected 200 women, which includes both normal and hypertensive after 20 weeks of gestation. Her data showed that CRP levels in control group were 6.57± 7.5491 and in patient CRP level were 15.106 ± 18.281 ($p < 0.001$).Our findings also shows CRP level in control group 5.1023± 6.202 and in patients CRP level is 10.520 ± 10.243 while $p<0.000$ which is highly significant and thus in agreement with above cited study.

Oncea Mihela 17studied CRP in Romania on 120 pregnant women both hypertensive and normal in first and second trimester. Her data showed pearson coefficient correlation between blood pressure and CRP which is 0.71567, ($p < 0.043$). The present study also show positive correlation between blood pressure and CRP which is 0.832, ($p < .001$) and this difference in p-value may be due to study design,study population, socio demographic status and genetic make up of participant.

TK Gosh 18 in 2011 studied in Bangladesh on 100 pregnant women. Of which 50 were hypertensive and 50 were control at same gestational age after 20 weeks. His data showed positive correlation of SBP, DBP, TLC (total leucocytic count), platelet count, urinary protein with CRP (42.02 mg/L±18 .01 mg/L), $P<0.001$ as compare to normal control (4.2 ±0.93 mg/L). This study proved that CRP and hypertension in pregnancy have positive correlation to find out the severity of the disease. The present data also showed positive correlation between SBP, DBP, CRP.

CONCLUSION

Based on all the available studies as well as the present study, it is concluded that CRP is elevated in hypertensive pregnant women, therefore it is a valuable and independent marker for early diagnosis of PE and eclampsia.

REFERENCES

1. Kashanian M, Aghbali F,Mehli N. Evaluation of diagnostic value of CRP for prediction of pre-eclampsia.J Obstet .Gynacology.Res.2013;39(12):1549-54.
2. Nawaz F, Sultan F, Sidique I ; Pregnancy outcome in Primigravida complicated with pregnancy induced hypertension ;J.Med Sciences:2014;22: 46-48.
3. Parmar U , Khubchandani A , Sharma P, Study of Changes in Levels of Serum Hs-Crp in Preeclampsia Patients, Int J Res Med 2017; 6(1) : 119-121.
4. Sultan N, Pregnancy in Pakistan. The Forgotten Millennium Development Goal.The Global Village 2013; 3:2.
5. Elizabeth K M, Association of serum C-Reactive protein concentrations with severity of preeclampsia and imminent eclampsia in pregnant women, J.Med Sciences 2013; 3-4.
6. Devi TS, A Penugonda, P Sujatha. Hs-c-reactive protein in Pre-eclampsia.Int.J Pharm BioSci. 2013;3: 27-32.
7. Nanda et al.CRP as a predictive factor of Pre-eclampsia.Int J Bio Med Res.2012;3:1307-10.
8. Markus G, Mohaupt. C - reactive protein and Its Role in Preeclampsia. Hypertension, 2015; 65: 285-86.
9. Ozler A,Turgut A et,al European. Serum levels of neopterin, tumor necrosis factor-alpha and Interleukin-6 in preeclampsia: relationship with disease severity Review for Medical and Pharmacological Sciences, 2012; 16: 1707-1712.
10. Ali Z, Zaki S, Tauseef A.C Reactive Protein levels are elevated in theThird Trimester in Preeclamptic pregnant Women. Int J Gynae Obst, 2013; 1:2.
11. Ali Z, B Feraz Ahmad, Z Saima,Correlation of CRP Levels in Third Trimester with Fetal Birth Weight in Preeclamptic and Normotensive Pregnant Women Journal of the College of Physicians and Surgeons Pakistan 2015, 25 .2: 111-14.
12. Amita A, Charlotte S, Gestational length assignment based on last menstrual period, first trimester crown-rump length, ovulation, and implantation timing Arch Gynecol Obstet. 2016; 294(4): 867–876.
13. Fisher T, C-reactive protein, inflammatory conditions, and cardiovascular disease risk, Am J Med 2007; 120(12): 1054-1062.
14. Ogedegbe G, Pickering T. Principles and techniques of blood pressure measurement, Cardiol Clin 2010; 28(4):571-86.
15. Abou Zahr C. Global burden of maternal death and disability. Br Med Bull 2003; 67:1–11.
16. Ferzana A, Minno R, et al, Comparison of C-Reactive Protein Concentrations of Patients with Preeclampsia and Normal Pregnancies , Life Science Journal 2013;10(11s).
17. Oancea Mihaela Daniela et al. Evaluation of Infl ammatory Markers in Pregnant Women at Risk, for the Prediction of Preeclampsia / Acta Medica Marisiensis, 2014; 60 (3):94-9.
18. TK Ghosh, S Ghosh, D Bhattacharjee. Bangladesh Journal of Medical Science : Vol 10, No 3 (2011).