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Original Research Article

Correlation of Serum hs-CRP with Biochemical and Clinical Parameters in Preeclamptic Pregnant Females: A Case-Control Study

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Abstract

Background: Preeclampsia is a serious complication & presents as an important cause of fetomaternal morbidity and mortality. Assessment of the circulatory inflammatory markers in the second half of pregnancy can help in the detection of females at high risk.

Aims & Objectives: The present case-control study is designed to assess the levels of hs-CRP & correlate it with biochemical & clinical parameters in preeclamptic pregnant females.

Materials & Methods: This case-control study recruited 20 preeclamptic and 20 healthy pregnant females who came to the Department of Obstetrics & Gynaecology of our tertiary care hospital. Pregnant females with pre-gestational hypertension, diabetes mellitus and other chronic disorders were excluded. According to the guidelines of the American College of Obstetric and Gynecology, patients were classified as preeclamptic and severe preeclamptic. Group A consisted of a preeclamptic pregnant female (n=20) and Group B consisted of a healthy pregnant female (n=20). The parameters noted were demographic, body mass index, and total protein excretion in 24 h. Venous blood samples were collected, at least 6 hours before delivery. Biochemical tests were conducted to assess the hs-CRP, Blood Urea Nitrogen (BUN), Creatinine, Aspartate transaminase, Alanine transaminase, and Lactate dehydrogenase levels.

Results: Demographic parameters and BMI were comparable in both groups ($p > 0.05$). Mean SBP&DBP was statistically significantly higher in Group A as compared to Group B ($p < 0.05$). In group A, 9% of cases were mild, 62% were severe, 11% had eclampsia and 18% had HELLP syndrome. Hemoglobin levels, serum hs-CRP, BUN, creatinine, AST, ALT, LDH and urinary protein excretion were statistically significantly higher in Group A as compared to Group B ($p < 0.05$). A strong positive correlation was noted between serum hs-CRP levels and diastolic blood pressure and urinary protein excretion. Serum calcium levels and weight and length of the newborns were statistically significantly lower in Group A ($p< 0.05$). A negative correlation was noted between serum hs-CRP and the weight & length of the newborns in both groups.

Conclusion: There was significant increase in serum hs-CRP level in preeclamptic pregnant females as compare to healthy pregnant females. Therefore serum hs-CRP estimation may

serve as a useful, inexpensive & potential tool to assess the preeclamptic status and maternal and neonatal outcomes.

Keywords: C-Reactive Protein, Preeclampsia, Pregnancy, Inflammatory Markers.

Introduction

The most common complications in pregnancy are preeclampsia that occurs in around 5-14% of pregnancies. Increased severity of preeclampsia is a frequent cause of maternal & fetal morbidity and mortality around the globe [1]. The disease is characterized by hypertension, dyslipidemia, and increased systemic inflammatory response with urinary loss of proteins, edema, and activation of hemostatic mechanisms [2]. There is a rise in blood pressure ≥ 140/90 mmHg with proteinuria which develops after 20 weeks of pregnancy. Preeclampsia subsequently converts to eclampsia with the development of convulsions, hemolysis, raised liver enzymes, and low platelet count (HELLP) syndrome. Other associated complications are cerebral hemorrhage, lung edema, renal failure and liver hemorrhage.[3]

In the first trimester of pregnancy, placental dysfunction may occur which may lead to endothelial cell damage. This may subsequently give rise to increased levels of various inflammatory markers. These inflammatory markers may be a potential diagnostic tool for the early identification and triage of such patients. Early detection might minimise systemic complications and maternal death due to inflammatory response. [4] C-reactive protein, an acute-phase reactant is one such marker, which is a highly sensitive, low-grade inflammatory marker. It has a substantial role in the phagocytic clearance of pathogens and dead cells. The high sensitivity CRP (hs-CRP) (range 0 to 3 mg/L) is equivalent to routine CRP (range 0 to 200) in structure and function, but it has a lower detection limit in assays. It gives an accurate estimation of the underlying inflammation and tissue damage.[5] It is also a potential tool for the differentiation of acute inflammation and severity of inflammation.[6]

Previous evidences support the fact that high CRP levels are observed in healthy pregnant females but to a lesser extent than in preeclamptic females. Behboudi- Gandevani et al 2012 demonstrated that raised levels of hs-CRP can be utilized to predict preeclampsia development in the first half of pregnancy.[7] Sayyed AA et al 2020 reported that raised hs-CRP levels during the first trimester of pregnancy could be an early indicator of intrauterine growth restriction and pre-eclampsia.[4] With this background, the present case-control study was designed to assess the levels of hs-CRP and correlate it with biochemical and clinical parameters in preeclamptic pregnant females.

Materials and Methods

This case-control study recruited 20 preeclamptic and 20 healthy pregnant females who came to the Department of obstetrics & gynecology of our tertiary care hospital. Pregnant females with pre-gestational hypertension, diabetes mellitus and other chronic disorders were excluded from the study. A complete obstetric examination was conducted and pregnancy was confirmed by ultrasonography. According to the guidelines of the American College of Obstetrics and Gynecology, patients were classified as preeclamptic and severe preeclamptic.[8]

Group A - preeclamptic pregnant female (n=20)

Group B - healthy pregnant female (n=20)

Demographic parameters, body mass index (BMI), and total protein excretion in 24 hours were assessed. Proteinuria was grouped as no (0), mild (1 and 2), and severe (3 and more) positive proteinuria. Venous blood samples were collected, at least 6 h before delivery and before magnesium sulphate application. Biochemical tests were conducted to assess the hs-CRP, Blood Urea Nitrogen (BUN), Creatinine, Aspartate Transaminase (AST), Alanine Transaminase (ALT), and Lactate Dehydrogenase (LDH) levels. No antihypertensive or any other medication was prescribed and patients were not undergoing labour at the time of sample collection. The blood samples were centrifuged and analyzed using an autoanalyser. The lowest limit of detection was 0.175 mg/l.

Statistical analysis:

The collected data were tabulated and put into statistical analysis using SPSS (Indian version). The data were presented as frequency and percentage. The data were expressed as mean and standard deviation. Independent paired t-test was done for analysis. P-value <0.05 was considered statistically significant. The Chi-square test was applied for finding a correlation among various parameters.

Results

Demographic parameters and BMI were comparable in both groups ($p > 0.05$). Mean systolic blood pressure and diastolic blood pressure was statistically significantly higher in Group A as compared to Group B ($p < 0.05$). (Table 1)

In group A (Preeclamptic group), out of 20, mild Preeclampsia in 9%, severe Preeclampsia in 62% and eclampsia in 11%, and 18% of patients were in the HELLP syndrome category were observed. No statistically significant difference was observed in hematocrit values, leukocyte, and platelet count. Hemoglobin levels, serum hs-CRP, BUN, creatinine, AST, ALT, LDH and urinary protein excretion were statistically significantly higher in Group A as compared to Group B ($p < 0.05$). A strong positive correlation was noted between serum hs-CRP levels and diastolic blood pressure and urinary protein excretion. (Table 2)

Serum calcium levels were statistically significantly lower in Group A as compared to Group B ($p < 0.05$). The weight and length of the newborns were statistically significantly lower in Group A as compared to Group B ($p < 0.05$). A negative correlation was noted between serum hs-CRP and the weight and length of the newborns in both groups. (Table 2).

Table 1: Showing Demographic parameters in Group A and Group B

	Group A	Group B	p-Value
Maternal Age(yrs)	34.7±9.2	28.5±5	P >0.05
BMI (kg/m2)	28.8± 3.6	27.6±4.3	P >0.05
SBP(mm Hg)	174±14	112±10.3	P <0.05
DBP (mm Hg)	106 ±12	68.4±8.7	p <0.05

Table 2: Showing Hematocrit Values, Biochemical parameters, Newborn characteristics

Various parameters	Group A (Preeclamptic group)	Group B (Healthy controls)	P value
Hemoglobin (gm/dl)	12.6±2.7	11.6±0.8	P <0.05
Hematocrit (v/v, %)	38.2±6	33.7±2.4	p <0.05
Leukocytes (x 10^9 /L)	11764 ± 3856	8.65 ± 2.73	p>0.05
Platelets (x 10^3/L)	223 ± 43	276± 86	p>0.05
BUN (mg/dl)	25.8± 17.9	17±5.5	p>0.05
Creatinine (mg/dl)	0.8±0.3	0.7±0.6	p<0.05
hs-CRP	9.7±1.1	3.6±2.8	p<0.001
AST (U/L)	90.1±110.5	32±12	p<0.05
ALT (U/L)	84.7±130.7	15.7±4.1	p<0.05
Lactate dehydrogenase (U/L)	1332.2±642.4	621.2±217.1	p<0.05
Calcium (mg/dl)	7.5±0.2	8.8±0.3	p<0.05
Proteinuria (score)	3.1±0.3	-	p<0.001
Gestational age (weeks)	37.8±2.4	36.2±3.1	p>0.05
Birthweight (g)	2463±338	3226±651	p<0.001
Birth length (cm)	46.8±2.4	48.2±4.2	p<0.05

Discussion

In the present study, demographic parameters and BMI were comparable in both groups with no statistical difference (p>0.05). Mean diastolic pressure and mean systolic blood pressure was statistically significantly higher in Group A as compared to Group B (p < 0.05). (Table 1)

In the present study, in the Preeclamptic group, mild preeclampsia was observed in 9%, severe preeclampsia in 62%, eclampsia in 11% and HELLP syndrome in 18% of patients were observed. This is in accordance with the studies conducted by Kumru et al 2006, wherein out of 20 patients in the preeclamptic group 2(10%) were with mild preeclampsia, 12 (60%) severe preeclampsia, 2 (10%) eclampsia and 4 (20%) HELLP syndrome.[9]

In the present study, no statistically significant difference was observed in hematocrit values, leukocyte, and platelet count (p>0.05). Hemoglobin levels, BUN, creatinine, AST, ALT, LDH and urinary protein excretion were statistically significantly higher in Group A as compared to Group B (p < 0.05). Serum calcium levels were statistically significantly lower in Group A as compared to Group B (p < 0.05). (Table 2)

In the present study, serum hs-CRP was statistically significantly higher in Group A as compared to Group B (p < 0.05). Similar findings were noted by Kumru et al 2006. [9] Watts et al 1991 explained that raised hs-CRP is due to decreased plasma volume in such patients. A substantial increase in serum hs-CRP could also be attributed to proteinuria and high blood pressure.[10] Oshi K et al 2022 also stated that CRP levels increased in pregnant females than in healthy controls.[11] In contrast, Savvidou et al 2002 were not able to appreciate any correlation between preeclampsia & CRP concentration in the late second trimester of pregnancy.[12]

In the present study, a positive correlation was observed between hsCRP and DBP and proteinuria in Group A (preeclampsia group). Similar findings were noted by Kumru et al. [9] The severity of preeclampsia can be estimated by proteinuria and blood pressure. Saito M et al 2003 found a positive correlation between hs-CRP levels with blood pressure. Also, a significant correlation between hs-CRP and albumin excretion in urine was observed in type 2 diabetes mellitus cases. [13] Erren et al stated that the degree of endothelial damage correlated with inflammation severity.

Endothelial damage occurs due to oxidation–reduction imbalance and results in the development of preeclampsia.[14]

In the present study, serum calcium levels were statistically significantly lower in Group A as compared to Group B ($p < 0.05$). Similarly, results were noted by Gargari BP et al [15] and Kumru et al [9] who observed changes in serum calcium levels to be related to the pathogenesis of preeclampsia.

Literature supporting decreased calcium levels in preeclampsia is minimal. But still, studies hypothesized an increased urinary calcium excretion or a reduced parathyroid hormone secretion. Tolvanen et al 1998 reported the use of calcium supplementation can improve vascular tone by increasing smooth muscle sensitivity to nitric oxide and decreasing the production of vasoconstrictor prostanoids in the prevention of preeclampsia.[16]

In the present study, the weight and length of the newborns were statistically significantly lower in Group A as compared to Group B ($p < 0.05$). A negative correlation was noted between serum hs-CRP and the weight & length of the newborns observed in both groups. (Table 2) In Similar findings noted by Kumru et al preeclampsia can lead to intrauterine growth restriction (IUGR) and low birth weight newborns due to diminished trophoblastic cell invasion. [9] High apoptotic rate noted in placentas of preeclamptic females which may stimulate the release of CRP. CRP also acts as a scavenger for chromatin released from apoptotic cells. [17]

Conclusion

Hs-CRP levels have been shown to rise in preeclamptic pregnant females. The hs-CRP levels have been observed to correlate with biochemical parameters like liver enzymes (aspartate aminotransferase and alanine aminotransferase, lactate dehydrogenase) with associated proteinuria and low calcium levels. The study concludes that hs-CRP can be used as a potential inflammatory marker to predict the severity of preeclampsia and decreased weight & length in newborns.

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