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RESEARCH ARTICLE

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SERUM HS-CRP AND URIC ACID AS INDICATOR OF SEVERITY IN PREECLAMPSIA

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ABSTRACT

The aim of the present study is to correlate hs-CRP and uric acid levels in preeclamptic women. This study was performed on three groups; mild preeclampsia (n=17), severe preeclampsia (n=13) and healthy pregnant women as controls (n=30). Hs-CRP and uric acid levels were measured in maternal serum by latex turbidimetric method and Uricase-PAP method respectively. In this study we found serum hs-CRP and Uric acid levels were higher in preeclamptic women (3.733±1.096, 8.007±1.077) as compared to normotensive pregnant women (1.216±0.552, 5.50±1.103). Similarly, serum hs-CRP and uric acid levels were significantly elevated in women with severe preeclampsia (4.769±0.807, 9.042±0.650) than mild preeclampsia cases. The positive and significant correlations were found in hs-CRP/Blood Pressure, Uric Acid /Blood Pressure and hs-CRP/Uric Acid. Our results shows that serum hs-CRP and Uric Acid levels have increased as disease progressed from mild to severe condition. Therefore, hs-CRP can be an additional marker to predict severity of disease.

KEYWORDS

Preeclampsia, hs-CRP, Uric acid, Inflammation

INTRODUCTION

Preeclampsia is one of the most common medical complications during pregnancy. It records one of the top five causes of maternal death in the world and it occurs in 4-5% of pregnant women[1]. The pathophysiology of preeclampsia remains uncertain despite many research efforts. Several etiologies have been implicated in the development of preeclampsia, those includes abnormal trophoblast invasion of uterine blood vessels, immunological intolerance between fetoplacental and maternal tissues, maladaptation to the cardiovascular changes or dietary deficiencies and genetic abnormalities[2]. Preeclampsia is characterized by the development of hypertension, proteinuria and edema at 20th weeks of gestation and in its most severe form is associated with thrombocytopenia, disseminated intravascular coagulation and hepatocellular damage[3].

Uric acid is the major end product of purine metabolism. In 1990 Fay described that increased breakdown of cells in the placenta may be the reason for over production of uric acid. An elevated level of uric acid reflects the degree of placental cell destruction as well as severity of disease[4]. Jeyabalan A et al reported that elevated levels of serum uric acid in preeclamptics as a result of reduced renal clearance[5]. Studies show that preeclampsia is a systemic inflammatory disease. Blann et al 1997 reported that inflammation plays a crucial role to induce endothelial cell dysfunction (ECD), accompanied by elevated levels of inflammatory markers such as Calpronectin, Plasminogen Activator Inhibitor-1 (PAI-1) and C-reactive Protein (CRP) etc[6]. The ECD and inflammatory processes has recently been implicated in the pathogenesis of preeclampsia. However, little is known about its correlation with the preeclampsia. CRP is a marker for acute inflammation, infection and tissue injury. Therefore, in the present study we have undertaken to determine the level of CRP by using highly sensitive method with a detection limit 0.05mg/L (hs-CRP), and its correlation with severity of disease.

The aim of present study is to correlate the hs-CRP and uric acid levels in preeclamptic women.

MATERIAL AND METHODS

For this study, 60 cases were included, of which 30 were preeclamptic patients and 30 were normal pregnant women as controls. These patients attended the Obstetrics and Gynecology department of the hospital. All patients were in the 19-30 years of age group and primigravidas. This study was approved by the institutional ethical committee.

This study was performed on three groups of women;

Group A: 17 women in the third trimester of pregnancy with mild preeclampsia at the time of admission.

Group B: 13 women in the third trimester of pregnancy with severe preeclampsia were included.

Group C: 30 healthy normotensive women in the third trimester of pregnancy were considered.

All controls were singleton, primigravidas monitored at the department of Obstetrics and Gynecology with gestational age of 28-40 weeks, having no chronic medical disorders and were not in labor. They were normotensive and had normal blood pressure throughout gestation.

Preeclamptic women of third trimester were included. Patients were selected after diagnosis of preeclampsia by hospital

Gynecologists. Preeclampsia was diagnosed according to American college of Obstetrics and Gynecology (ACOG) criteria; a blood pressure higher than 140/90 mm of Hg, edema and Proteinuria > 300 mg/24 hours or ≥ 1+ dipstick method after 20th week of gestation. The patients with blood pressure >140/90 mmHg but <160/110 mmHg without proteinuria were included in mild cases. And patients with blood pressure ≥ 160/110 mmHg, proteinuria and presence of headache, visual disturbances, upper abdominal pain, Oligouria and thrombocytopenia were included in severe cases.

Patients with history of hyperuricemia, diabetes, renal diseases, hypertension, cardiovascular illness, and symptomatic infectious diseases were excluded from both the study groups.

Venous blood sample was collected in a plain bulb with aseptic conditions. After allowing for clotting, the sample was centrifuged at 3000 rpm for 5 minutes. Serum was separated and collected in polythene tubes with cork. The sera with no sign of hemolysis were used for the analysis of parameters.

In both the groups, Uric Acid and hs-CRP levels were determined. Serum hs-CRP levels were measured by high sensitivity CRP kits using a latex turbidimetric method with a detection limit of 0.05 mg/L[7]. Serum Uric acid was measured by an enzymatic method based on Uricase-PAP method[8].

The results were expressed as mean ± SD and analyzed by student t-test.

RESULTS

Table no. 1 shows the gestational age and blood pressure of control and preeclampsia patients. The clinical parameters are summarized in table no - 2. In our study, hs-CRP level was significantly ($p<0.001$) higher in preeclamptic women (3.733 ± 1.096 mg/L) when compared with normal pregnant women (1.216 ± 0.552 mg/L). We observed, gradual increase in hs-CRP level as disease progresses from mild (2.941 ± 0.390) to severe preeclampsia (4.769 ± 0.807).

When serum uric acid level was taken into account, we found significant ($p<0.001$) elevation in the uric acid level in preeclamptic women (8.007 ± 1.077) as compared to normotensive pregnant women (5.50 ± 1.103). However, within the preeclampsia group uric acid level was found to be significantly ($p<0.001$) elevated in severe cases compared to mild preeclampsia cases.

Blood pressure is an indicator for the severity of the preeclampsia. In the present study along with blood pressure, hs-CRP and uric acid levels increased with the severity. Therefore, we correlated these two parameters with blood pressure within preeclampsia group. We found, hs-CRP and uric acid levels are significantly ($p<0.001$) correlated with blood pressure [hs-CRP/SBP $r=0.7232$, hs-CRP/DBP $r=0.7465$ and uric acid/SBP $r=0.6407$, uric acid/DBP $r=0.7325$] respectively. In addition, we found significant ($p<0.001$) correlation between hs-CRP and uric acid concentrations in pregnancies complicated with preeclampsia ($r = 0.6628$).

Table No – 1
Demographic and clinical parameters of Control and preeclamptic groups

Demographic Criteria	Control Group	Preeclampsia Group	Preeclampsia Patients	
	Normal pregnant women (n=30)	PE (n=30)	Mild PE (n=17)	Severe PE (n=13)
Gestational Age in Weeks	30.99 ± 6.72	32.92 ± 3.58	32.89 ± 2.72	32.96 ± 4.58
Systolic Blood Pressure (mmHg)	116.26 ± 4.35	149.6 ± 10.12	142.70 ± 3.46	162.23 ± 8.73
Diastolic Blood Pressure (mmHg)	75.33 ± 4.37	97.33 ± 7.52	91.76 ± 2.44	104.61 ± 5.25

Values are given as mean ± SD, PE- Preeclampsia

Table No – 2
Biochemical parameters of Control and preeclamptic groups

Demographic Criteria	Control Group Normal pregnant women (n=30)	Patients		
		PE (n=30)	Mild PE (n=17)	Severe PE (n=13)
Uric Acid (mg/dL)	5.50 ± 1.103	8.007 ± 1.077*	7.211 ± 0.491	9.042 ± 0.650**
Hs-CRP (mg/L)	1.216 ± 0.552	3.733 ± 1.096*	2.941 ± 0.390	4.769 ± 0.807**

Values are given in mean ± SD, PE- Preeclampsia, * p<0.001 – compared with normal pregnant women, ** p<0.001- compared with mild Preeclampsia

DISCUSSION

From the beginning of scientific research the etiology of preeclampsia has been the subject of more investigations and speculations. Although, one should note that a unifying etiology of preeclampsia has not been identified, investigations performed during the last two decades have substantially advanced. Improvement in health and increase in the rate of survival of mother and fetus is essential for global health equity.

Preeclampsia is a complex condition, which cannot be attributed by any single cause. The primary cause to develop a disease may be due to insufficient invasion by trophoblast cells in uterine wall in early pregnancy. There is no unifying scientific evidence to explain the pathophysiology of disease. But, a possible hypothesis for its pathogenesis is reduced placental perfusion as a result of shallow invasion this leads to increased lipid peroxidation and the release of oxygen radicals without counter regulation by antioxidants. In addition to this activation of neutrophils and macrophages, this promotes cytokine production and further leads to maternal endothelial dysfunction[9].

Preeclampsia is a disease of pregnancy associated with endothelial cell damage. There is an increasing evidences that preeclampsia is a systemic inflammatory disease. Activation of haemostatic system and endothelial activation are the key components of systemic inflammatory response. The hs-CRP is a sensitive marker of tissue damage and inflammation. Its production is stimulated by inflammatory cytokines, Interleukin-6 and α-Tumor Necrosis Factor[10]. The hs-CRP plays important role in eliciting the inflammatory processes[11]. It acts as a scavenger and responsible for clearance of membranes and nuclear antigens[12]. Hs-CRP is useful in differentiating acute inflammation as well as assessment of severity of inflammation.

In our study, we found significantly increased level of Serum hs-CRP in preeclampsia patients as compared to normal pregnant women. This finding correlates with the previous reports of Ustun et al 2005 and Kumru et al 2006. Teran et al 2001 and Belo et al et al 2003 reported higher CRP levels in patients with preeclampsia[13,14]. We found positive significant correlation between hs-CRP levels and blood pressure which shows the elevation of hs-CRP level is proportional to severity of preeclampsia. Present results support the hypothesis that systemic inflammation is involved in the pathogenesis of preeclampsia and serum hs-CRP level may be a marker to predict severity of disease.

The present study shows that uric acid level is significantly higher in preeclampsia patients than in the normal pregnant women. Similarly from mild to severe preeclampsia, the serum uric acid level increased significantly in severe cases than mild preeclampsia cases. Redman et al 1976, Boneu et al 1980, Acien et al 1990, and Yoshimura et al 1990 reported the association of increased uric acid level and preeclampsia[15,16,17,18]. Kee-Hak Lim et al 1998 also found an increase in serum uric acid level as severity of disease progresses[19].

Uric acid is marker of oxidative stress, tissue injury and renal dysfunction. Abnormal trophoblast invasion is reported in preeclampsia, because of which placenta receives less blood supply from uteroplacental artery. Subsequently placenta becomes hypoxic. This hypoxia causes placental tissue breakdown and provides additional source of purines. Placenta and damaged placental tissues are the rich sources of purines for generation of uric acid by xanthine oxidase[20].

We found a positive significant correlation between uric acid and blood pressure. In preeclampsia, the epithelial lining of glomerulus may be damaged due to high blood pressure and formation of blood clot[21]. This may lead to decrease in the renal tubular excretion. The decreased tubular excretion or placental tissue breakdown may be responsible for increase in uric acid level in patients with preeclampsia. In this study, serum hs-CRP and uric acid levels were concomitantly increased from mild to severe disease condition. We also found positive and significant correlation between hs-CRP and uric acid levels. Thus, our findings suggest a strong association between hs-CRP, uric acid levels and blood pressure. Elevated hs-CRP and uric acid reflects ECD and involvement of inflammation in preeclampsia.

We therefore conclude that hs-CRP and uric acid levels may be helpful to predict severity of disease. Further study will be required to assess prognostic value of hs-CRP in first trimester of pregnancy to identify the future risk for developing preeclampsia. Early detection might reduce systemic complications and maternal deaths due to preeclampsia.

REFERENCES

1. Selahattin Kumru, Ahmet Godekmerdan, Selim Kutlu, Zeynep Ozcan, Correlation of maternal serum high-sensitive C-reactive protein levels with biochemical and clinical parameters in preeclampsia, Eur J Obstet Gynecol Reprod Biol, 124: 164-167, (2006).

2. Sibai, Baha M, Diagnosis and management of Gestational Hypertension and Preeclampsia, Obstetrics and Gynecology, 102 (1): 181-192, (2003).
3. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in pregnancy, Am J Obstet Gynecol, 183(1): S_1-S_{22}, (2000).
4. Fay R A, Uric acid in pregnancy and preeclampsia: an alternative hypothesis, Aust N Z I Obstet Gynecol, 30(2):141-142, (1990).
5. Jeyabalan A, Conrad K P. Renal function during normal pregnancy and preeclampsia, Front Biosci, 1(12): 2425-2437, (2007).
6. Blann A D, Lip G Y, Relation between endothelial cell activation and infection, inflammation and infarction, Lancet, 350: 293-294, (1997).
7. Chenilot O et al, Clin Chem Lab Med, 38: 1003-1011,(2000).
8. Henry, Common C, Winkelman J W (eds). Clinical Chemistry: Principles and techniques. Harper and Row, Hagerstown MD, (1974).
9. Christopher W G Redman, Gavin P Sacks, Ian L Sargent, Preeclampsia: An excessive maternal inflammatory response to pregnancy, Am J Obstet Gynecol, 180: 499-506 (1999).
10. Braekke K, Holthe MR, Harsem NK, Fagerhol MK, Staff AC, Calprotectin, a marker of inflammation, is elevated in the maternal but not in the fetal circulation in preeclampsia, Am J Obstet Gynecol, 193 (1): 227-233, (2005).
11. Yusuf Ustun, Yapral Engin-Ustun, Mansur Kamaci, Association of fibrinogen and C-reactive preotein with severity of preeclampsia, Eur J Obstet Gynecol Reprod Biol, 121: 154-158, (2005).
12. Du Clos TW, The interaction of C-reactive preotein and serum amyloid P component with nuclear antigens, Mol Biol Rep, 23 (3-4): 253-260, (1996).
13. Teran E, Escudero C, Moya W, Flores M, Vallance P, Lopez-Jaramillo P, Eleveted C-reactive preotein and pro-inflammatory cytokines in Andean women with preeclampsia, Int J Obstet Gynecol, 75 (3): 243-249, (2001).
14. Luis Belo, Alice Santos-Silva, Murlel Caslake, Josephine Cooney, Luis Pereira-lelte, Alexandre, Quintanilha and Irene Rebelo, Neutrophil Activation and C-reactive protein concentration in preeclampsia, 22 (2): 129-141, (2003).
15. Redman C W, Beilin L J, Bonnar J, Wilkinson R H, Plasma-Urate measurements in predicting fetal death in hypertensive pregnancy, Lancet, 1 (7974):1370-1373, (1976).
16. Boneu B, Fourine A, Sie P, Grandjean H, Bierme R, Pontonnier G, Platelet production time, uricemia and some hemostasis tests in preeclampsia, Eur J Obstet Gynecol Reprod Biol, 11 (2): 85-94, (1980).
17. Acien P, Lloret G, Lioret M, Perinatal morbidity and mortality in Pregnancy hypertensive disorders: prognostic value of the clinical and laboratory findings, Int J obstet gynecol , 32 (3): 229-235, (1990).
18. Yoshimura A, Ideura T, Iwasaki S, Koshikawa S, Significance of uric acid clearance in preeclampsia, Am J Obstet Gynecol, 162 (6): 1639-40, (1990).
19. Kee-Hak Lim, Steven A Friedman, Jeffrey L, E Cker, The clinical utility of serum uric acid measurements in hypertensive diseases of pregnancy, Am J Obstet Gynecol, 178 (5): 1067-1071, (1998).
20. Saugstad O D, Hypoxanthine a measurement of hypoxia, Pediatr Res, 9: 158-161, (1975).
21. Powers Robert W, Bodnar Lisa M, Ness Roberta B, Cooper Katheryn M, Gallaher Marcia J, Frank Michael P, Daftary Ashi R, Roberts James M, Uric acid concentration in early pregnancy among preeclamptic women with gestational hyperuricemia at delivery, Am J Obstet Gynecol, 194 (1): 160-166, (2006).