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Putative Role of Serum Uric Acid and hsCRP in Preeclampsia

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Abstract | **Original Research Article**

Preeclampsia is one among the leading cause for maternal and fetal morbidity and mortaility. Its pathophysiology is poorly understood in spite of intensive research. This case-control study was aimed to determine the level of inflammatory biomarker hsCRP and uric acid and the association of these biomarkers and preeclampsia. Serum uric acid and hsCRP were measured in 30 women in the third trimester of pregnancy with mild preeclampsia, 20 women in the third trimester of pregnancy with severe preeclampsia and compared statistically with 50 healthy age matched normotensive women in the third trimester of pregnancy. The statistical analysis was done by Student t-test and Anova in SPSS version 17.0. Both serum hsCRP and uric acid were found to have significant positive correlation with the severity of preeclampsia. From this study it may be concluded that hsCRP and uric acid levels were increased and contribute to the pathogenesis of preeclampsia. They may be used as additional biomarkers to predict the severity of preeclampsia.

Keywords: Preeclampsia, biomarkers, hsCRP, uric acid.

INTRODUCTION

Preeclampsia is a pregnancy-specific disorder with adverse maternal and fetal outcomes with global incidence of 5% to 7% of all pregnancies [1]. Blood pressure ≥ 140/90 mmHg and proteinuria occurring after 20 weeks gestation in women who were not previously known to be hypertensive are the cardinal clinical features of preeclampsia [2]. Preeclampsia is a multisystem disorder of pregnancy. According to WHO Estimates the incidence of Preeclampsia is seven times higher in developing countries (2.8% of live births) than in developed countries (0.4%) [8]. The incidence of preeclampsia, in India is reported to be 5-15% of the pregnancies [3]. The incidence in primigravidae is about 10% and in multigravidae about 5% [3].

Numerous maternal, fetal and paternal factors have been implicated in the pathophysiology of preeclampsia [4]. The most important and accepted factors include (i) abnormal placental implantation [5-7], (ii) maternal immunologic intolerance, (iii) genetic [8] nutritional and environmental factors[7] and (iv) cardiovascular and inflammatory changes. Of all these factors, endothelial dysfunction and inflammation tends to play a crucial role in the pathophysiology of preeclampsia which leading to alteration in vascular reactivity, loss of vascular integrity ultimately leading to activation of coagulation cascade [9].

Previous studies have documented that the levels of serum uric acid, the end product of purine metabolism was elevated in preeclampsia which may be due to either increased production or decreased excretion of uric acid. Hyperuricemia due to increased production was attributed to increased breakdown of cells in the placenta, and due to reduced renal clearance was also reported in various studies [10-12].

Various clinical and biochemical evidence suggests that disturbance of normal endothelial cell function may be a primary cause in the pathogenesis of preeclampsia [9]. This endothelial dysfunction leads to elevation of inflammatory markers. One among them is CRP which is a sensitive marker of systemic inflammation. CRP is synthesized in response to infection and tissue injury by the hepatocytes. Estimation of hsCRP has been suggested to be more sensitive than conventional CRP measurement and provides better sensitivity in confirmation of inflammation. Serum hsCRP positively correlated with severity of pre-eclampsia [13].

Therefore this study was designed to determine the levels of serum uric acid and hsCRP in the pathogenesis and severity of preeclampsia.

Aim

This study was aimed to determine the level of inflammatory biomarker hsCRP and uric acid and the association of these biomarkers and preeclampsia.

MATERIALS AND METHODS

100 cases were included in this study, of which controls were 50 normal pregnant women and 50 were pre-eclamptic patients. Informed consent was obtained from the controls and patients.

Pre-eclampsia patients

The pre-eclamptic patients were subdivided into 2 subgroups depending upon the severity of preeclampsia.

Group 1: 30 women in the third trimester of pregnancy with mild preeclampsia

Group 2: 20 women in the third trimester of pregnancy with severe preeclampsia

Control subjects

Controls comprised of 50 healthy normotensive women in the third trimester of pregnancy (Group 3).

Exclusion criteria

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

Sample collection and processing

Under aseptic precautions, about 5ml of venous blood sample was collected after 12 hours of fasting. The blood was allowed to clot and the serum was separated by centrifugation. The samples were analysed for Serum Uric acid by an enzymatic method based on Uricase PAP and serum hsCRP by high sensitivity CRP kits using a latex turbidimetric method with a detection limit of 0.05 mg/L.

Statistical analysis

The statistical analysis was done in SPSS version 17.0. The results were expressed as mean ± SD and analyzed by Student t-test and Anova. p value < 0.05 was considered significant.

RESULTS

Blood pressure of control and pre-eclamptic patients is shown in table 1. Serum uric acid and hsCRP levels are summarized in Table No. 2.

Tabl-1: Blood pressure levels in various study groups

Criteria	Group 1 Mild PE (n=30)	Group 2 Severe PE (n=20)	Group 3 Control (n=50)
Systolic BP (mm of Hg)	144 ± 4	165 ± 9	112 ± 4
Diastolic BP (mm of Hg)	92 ± 3	106 ± 5	74 ± 5

Values are expressed as mean ± SD, PE –preeclampsia.

The average blood pressure of women with mild preeclamptic was 144 ± 4/ 92 ± 3 mm Hg and severe preeclampsia was 165 ± 9 / 106 ± 5 at the time of admission. The normotensive pregnant women were age matched and had an average blood pressure of 112 ± 4 / 74 ± 5 mm Hg.

Table-2: Serum hscrp and uric acid in various study groups

Criteria	Group 1 Mild pe (n=30)	Group 2 Severe pe (n=20)	Group 1 & 2 Pe (n=50)	Group 3 Control (n=50)
Uric acid (mg/dl)	6.73 ± 1.53	8.98 ± 0.70	7.65 ± 1.54	5.28 ± 0.91
HSCRP (mg/l)	2.74 ± 0.96	5.37 ± 1.43	3.68 ± 1.71	1.12 ± 0.55

Values are expressed as mean ± SD, PE – preeclampsia.

As shown in Table No.2, Serum Uric acid was found to be significantly elevated (P<0.001) in PE women (7.65±1.54mg/dL) as compared to normotensive women (5.28±0.91 mg/dL) and was found to be significantly elevated in severe PE (8.98±0.70 mg/dL) than mild PE (6.73±1.53 mg/dL) women (p value <0.01).

Serum hsCRP was also significantly (P <0.001) higher in preeclamptic pregnant women (3.68±1.71 mg/L) when compared to normal pregnant women (1.12±0.55mg/L). hsCRP also correlates well with severity of the disease with gradual increase in hsCRP level as disease progresses from mild (2.74±0.96) to severe (5.37±1.43) preeclampsia.

DISCUSSION

Pre-eclampsia stands out among the hypertensive disorders of pregnancy for its impact on both maternal and fetal health. It is one of the leading causes of maternal and perinatal mortality and morbidity worldwide. Several etiologies have been implicated in the development of pre-eclampsia. Endothelial cell dysfunction and inflammation are considered to have a crucial role in the pathophysiology of pre-eclampsia [14].

One among the hypothesis postulated for the development of pre-eclampsia is systemic inflammation. Several studies have demonstrated the role of inflammatory markers in pre-eclampsia. CRP is responsible for clearance of membrane and nuclear antigens and acts like a scavenger. The production of hs-CRP which is a sensitive marker of tissue damage and inflammation is stimulated by inflammatory cytokines, Interleukin-6 and Tumor Necrosis Factor- [15]. hs-CRP is useful in differentiating acute inflammation as well as assessment of severity of inflammation [16]. Qui C et al in their study have shown that elevated CRP levels in the first trimester of pregnancy to be an independent predictor of pre-eclampsia [17]. In our study there is a significant positive correlation between hs-CRP levels and blood pressure and the increase in hs-CRP level is proportional to severity of preeclampsia. This result is in supportive of the hypothesis that systemic inflammation plays a major role in the etiopathogenesis of pre-eclampsia.

In the present study there is a significant positive correlation between serum uric acid and severity of preeclampsia. Uric acid is a marker of oxidative stress, tissue injury and renal dysfunction. Abnormal trophoblast invasion which is considered the primary cause of pre-eclampsia, may be due to insufficient invasion by trophoblastic cells in uterine wall in early pregnancy. This leads to reduced uteroplacental blood flow and causes placental hypoxia. This hypoxia causes placental tissue break down. So the sources of purines for generation of uric acid in pre-eclampsia are placenta and

damaged placental tissues [18]. The other reason for hyperuricemia is attributed to the renal changes that occur in preeclampsia. There is a decrease in both the glomerular filtration rate and renal blood flow in preeclampsia. Fractional urate clearances decrease, often before overt disease, with hyperuricemia being an important feature of preeclampsia [16].

Conclusion

Serum uric acid and hsCRP levels are increased in pre-eclampsia and their levels correlate well with the severity of pre-eclampsia and they can be used as biomarkers for assessing the severity of pre-eclampsia.

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