Research Article

Estimation of C - Reactive Protein, Magnesium and Uric Acid Levels in Pre-Eclampsia Patients in Comparison with Normal Pregnant Women

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Abstract: Efforts to diagnose Preeclampsia have been hampered by inability to predict which women are likely to be affected. Because there is no standard diagnostic test yet available for preeclampsia, the present work used biomarkers to evaluate this condition. The aim of this study was to determine the level of C-reactive protein (CRP) in PE mothers along with normal pregnant mothers. Another objective of this study is to find out the major markers to diagnose PE mothers among biochemical and hematological parameter. A case control study was conducted at Dept. of Obstetrics and Gynecology of our Hospital. 25 cases of PE mothers and age and gestational matched 25 cases of normal control pregnant mothers were included in this present study. CRP was estimated by NycoCard CRP reader. Serum Uric acid, SGPT, magnesium, calcium and Creatinine were estimated by fully automated analyzer. Neutrophils count, Total leucocyte count and Platelet counts were done in cell counter with peripheral direct smear and manual count correlation. Urine protein was detected by dipstick method. Results show a significantly increased mean C-reactive protein in PE mothers (12.5 ± 3.8 mg/l) in comparison to normal control mother (1.2 ± 0.93 mg/L) with p value 0.03. Mean Serum magnesium observed lower in PE women (1.1± 0.4 mg/dl) than normal pregnant women (2.4± 0.2 mg/dl) with p value 0.02. We also found significance difference in SGPT, uric acid levels, whole blood count and neutrophil count between two groups. Among the all screened biochemical & hematological markers, Serum C-reactive protein, magnesium and uric acid levels along with blood cell count cumulatively can be measured and may be used as markers for early diagnosis of PE and can be reduced maternal as well as fetal morbidity and mortality.

Keywords: C-reactive protein, Preeclampsia, Magnesium, Pregnancy.

INTRODUCTION

Preeclampsia (PE), a complication of late pregnancy, is characterized by hypertension, proteinuria and varying degrees of ischemic end-organ damage [1]. It is one of the leading causes of maternal and fetal morbidity and mortality and currently there is no cure other than termination of the pregnancy. World wide about 50,000 mothers die due to pregnancy induced hypertension per year. It is responsible 25% of all fetal growth retardation and 15% preterm birth in developed countries [2]. Though PE varies from region to region and from different hospitals the incidence of it in India is 8-10% and maternal mortality is reported 8% amongst all maternal mortality [3]. The incidences is gradually increasing over last few decades [4]. It is common below 25 years of age [5]. The causes of preeclampsia are complex and are not fully understood but the condition may be associated with poor placentation [6]. Various studies demonstrated the relationship between hypertensive complication and changes in concentration of various biochemical parameters such as serum uric acid, calcium and magnesium in preeclamptic women [7-10]. Physiologically, calcium plays role in muscle contraction and regulation of water balance in the cells. The low serum calcium and the increase in intracellular calcium lead to elevation of blood pressure in preeclampsia. Magnesium plays an important role in neurochemical transmission and peripheral vasodilatation. Besides serum calcium and serum magnesium, the hyperuricemia is believed to result from the decreased renal excretion that occurs as a consequence of the preeclampsia and also increased production secondary to tissue ischemia and oxidative stress. Therefore, modification of calcium, magnesium and uric acid metabolism during pregnancy could be one of the potential causes of preeclampsia [7, 11-15]. C-reactive protein (CRP) is an acute phase protein which is synthesized in hepatocytes and present in trace amount in normal healthy person and rise significantly following injury and inflammation [15]. Endothelial cell dysfunction and inflammation are considered to have a crucial role in the pathophysiology of PE [13] It has been shown that serum levels of C-
reactive protein (CRP) and inflammatory cytokines are elevated in women with PE. CRP in the third trimester is elevated in women with preeclampsia compared to those with normal pregnancies, and levels have been shown to correlate with disease severity [16]. The objective of the present study was to determine various biochemical and hematological parameters in women with PE and compare the values with that of normal pregnant women.

**MATERIALS AND METHODS**

A cross sectional case control study was conducted at Dept. of obstetrics and gynecology of our Hospital. Study was carried out between June 2012 to July 2013. The study population consisted of 50 pregnant women, 25 preeclampsia and 25 normal pregnant women as control.

**Preeclampsia group**

Mothers were diagnosed as PE when the systolic blood pressure were persistently ≥ 140 mm of Hg and diastolic blood pressure ≥ 90mmof Hg, on two occasion each 6 hours apart , accompanied by proteinuria at least 1+ on dip stick testing at third trimester of gestation.

**Normal pregnant group**

Normal pregnancy was diagnosed on the basis of biochemical, clinical and ultrasound findings. All women had gestational ages of 23-37 weeks preferably primigravida, single ton fetus included.

None of the patients either PE or normal pregnant women was treated with any antihypertensive or medication known to interfere with inflammation. Due to not possible to get the total protein excretion in 24 hr from all patients, proteinuria was measured in spot urine and presented as no (0) and mild (1+ and 2+) positive proteinuria. Patients with systolic blood pressure was 160 mm Hg or higher or diastolic blood pressure was 110 mmHg or higher; and proteinuria greater than 1000 mg/24 h were excluded before grouping. Mother with history of diabetes, renal disease, any cardiovascular disease, chronic hypertension, symptomatic infectious disease, obesity, periodontitis, premature membrane rupture, clinical chorioamnionitis, mothers taking corticosteroid <7days, patient in labour are not included in this study. Blood samples were collected from all of the patients for serum uric acid, calcium, magnesium, etc. The serum uric acid, SGPT, serum magnesium, serum calcium were measured by fully automated analyzer (HUMASTAR600, USA). The Platelet counts and Total leucocytes count in hematological cell counter were correlation from peripheral direct smear and manual was measured by Dip Stick. C- reactive protein estimated by NycoCard CRP reader (Axis-Shield, Scotland).

Statistical analysis

Data were analyzed by Student's t test using SPSS software, version 20.00. p value <0.05 was considered to be statistically significant.

**RESULTS**

The demographic and clinical characteristics of the groups are summarized in Table 1. There is no statistically significant difference was observed in mean age, gestational age and BMI between the two groups (p values 0.36, 0.59 and 0.69 respectively, Table 1). Mean systolic blood pressure was significantly higher in women with preeclampsia than in normal pregnant women (p value 0.01). Mean diastolic blood pressure was also showed significantly higher in women with preeclampsia than in normal pregnant women (p value 0.03). Biochemical analysis showed that serum uric acid higher in preeclampsia women (7.6± 0.5) than normal pregnant women (3.70 ± 0.00) (p value 0.03). There is no significance observed in serum creatinine (p value 0.12) and SGPT (p value 0.06) values in both groups. Whereas, mean of Serum CRP showed significantly high and directly related with PE mothers (12.5 ± 3.8 mg/L) than normal pregnant mother (1.2 ± 0.93 mg/L) with p value 0.003 (Figure 1). Positive proteinuria was found in women with PE mothers (1+, 2+), whereas not observed in normal pregnant mothers. The mean serum magnesium in preeclamptic women (1.1± 0.4) was less than normal pregnant women (2.4±0.2) with p value 0.02 (Figure 2). The mean serum calcium was also observed less in preeclamptic women (7.6± 0.5) than normal pregnant women (8.9± 0.4), but does not showed difference (p value 0.21). The platelet counts were reduced in PE womens than normal pregnant mothers, but does not showed difference (p value 0.12). Whereas TLC and neutrophil count was also observed higher in preeclamptic women than normal pregnant women with p value 0.04 & p value 0.04. SGPT also shown significantly higher in preeclampsia compared to control group values (p value0.05) (Table 1).
Table 1: Demographic and Clinical Characteristics of Study Groups

<table>
<thead>
<tr>
<th>Demographic/clinical parameters</th>
<th>Preeclampsia (n=25)</th>
<th>Normal Pregnant (n=25)</th>
<th>Reference value</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (years)</td>
<td>27.5 ± 3.4</td>
<td>26.8 ± 2.7</td>
<td>--</td>
<td>0.36, NS</td>
</tr>
<tr>
<td>Gestational age (week)</td>
<td>33.7 ± 3.9</td>
<td>34.5 ± 4.2</td>
<td>--</td>
<td>0.59, NS</td>
</tr>
<tr>
<td>Body mass index (kg/m²+)</td>
<td>24.3 ± 1.8</td>
<td>23.5 ± 1.7</td>
<td>20-25</td>
<td>0.69, NS</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>146 ± 4.2</td>
<td>115.6 ± 6.3</td>
<td>120</td>
<td>0.01*</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>92.5 ± 3.7</td>
<td>78.2 ± 1.9</td>
<td>80</td>
<td>0.03*</td>
</tr>
<tr>
<td>Serum uric acid (mg/dl)</td>
<td>6.5 ± 1.2</td>
<td>3.70 ± 0.7</td>
<td>4-6</td>
<td>0.03*</td>
</tr>
<tr>
<td>Serum calcium (mg/dl)</td>
<td>7.6 ± 0.5</td>
<td>8.9± 0.4</td>
<td>9-11</td>
<td>0.21,NS</td>
</tr>
<tr>
<td>Serum magnesium (mg/dl)</td>
<td>1.1± 0.4</td>
<td>2.4± 0.2</td>
<td>1.8-3.0</td>
<td>0.02*</td>
</tr>
<tr>
<td>SGPT (IU/L)</td>
<td>67.5 ± 12.6</td>
<td>38.9 ± 5.8</td>
<td>5-40</td>
<td>0.05*</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>1.8± 0.25</td>
<td>1.1± 0.21</td>
<td>0.5-1.5</td>
<td>0.12, NS</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>1.2 ± 0.93</td>
<td>12.5 ± 3.8</td>
<td>0.06-3.0</td>
<td>0.003*</td>
</tr>
<tr>
<td>WBC (/ml)</td>
<td>17.2 ± 2.7 x 10³</td>
<td>8.5 ± 2.1 x 10³</td>
<td>4 x10⁷-11x10⁷</td>
<td>0.04*</td>
</tr>
<tr>
<td>Absolute Neutrophil count (/ml)</td>
<td>9.2 ± 1.4 x 10³</td>
<td>5.9 ± 0.8 x 10³</td>
<td>1.5 x 10⁷-7.8x10⁷</td>
<td>0.04*</td>
</tr>
<tr>
<td>Platelet count (/ml)</td>
<td>1.9 ± 0.52 x 10³</td>
<td>2.6±0.41 x10³</td>
<td>1.5 x 10⁷-4x10⁵</td>
<td>0.12, NS</td>
</tr>
<tr>
<td>Proteinuria (dipstick)</td>
<td>1+, 2+</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Data expressed as Mean ± SD; NS: Non-significant, *p < 0.05 is considered to be statistically significant

DISCUSSION

Elevated serum uric acid levels was observed in women with preeclampsia which also correlate with the previous studies [15, 17]. This may be due to due to decrease renal uric acid excretion. Soluble uric acid impairs nitric oxide generation in endothelial cell, leads to hyperuricemia which can induce endothelial dysfunction [18, 19]. Commonly, uric acid is a marker of oxidative stress, tissue injury and renal dysfunction and several studies have reported a positive correlation between elevated maternal serum uric acid levels and adverse pregnancy outcomes [20]. Serum magnesium and calcium are intracellular ions important for cellular metabolism like muscle contractibility, secretion and neuronal activity as well as cellular death [21]. In our study, reduced magnesium levels observed in preeclampsia patient, which also correlate with the previous studies [22-25]. In the most of the pregnant women, the hypomagnesaemia is associated with hemodilution and renal clearance during pregnancy and consumption of minerals by growing foetus. Magnesium levels may have significant effects on cardiac excitability and on vascular tone, contractility and reactivity [14, 26]. The consequences of low magnesium leads to a reduction in the cerebral blood flow, cerebral vasospasm and neuronal burst increases. Macdonald et al. [25] shown that magnesium has a vasoprotective effect. These findings supports that hypomagnesaemia and hyperuricemia correlate to preeclampsia. There is increasing evidence that preeclampsia is a systemic inflammatory disease [27]. CRP, a sensitive marker of tissue damage and
inflammation, has been proposed to play a role in eliciting the inflammatory response characteristics of preeclampsia [27]. The potential role of CRP measurement in the early prediction of preeclampsia has been less well defined. For example, Garcia et al. [28] reported elevated levels at 22 weeks gestation in women who subsequently developed pre-eclampsia, while Teran et al. [29] reported no difference when levels were checked at 16 gestational weeks. In this study, we have shown that serum CRP levels are higher in PE women when compared to normal pregnant women. In this study elevated liver enzyme SGOT and renal functional tests indicates the severity of preeclampsia, so also the CRP increases. Elevated CRP levels in PE demonstrated in the present study in the absence of oral/infectious diseases conceivably reflect the presence of an underlying systemic inflammatory process. Total leukocyte count and Absolute Neutrophil Count, were also increased in women with PE. This study assumes that serum CRP shows positive finding in PE and also proves that inflammation also plays an important role in the pathogenesis of PE.

CONCLUSION
Among the all screened parameters, Serum uric acid, Serum magnesium, C-reactive protein, WBC and Absolute Neutrophil count showed significance difference between the two groups. Among these, Serum C-reactive protein, magnesium and uric acid levels showed a very higher significance rate. In conclusion, serum C-reactive protein, magnesium and uric acid levels along with blood cell count cumulatively can be measured and may be used as markers for early diagnosis of PE and can be reduced maternal as well as fetal morbidity and mortality.

REFERENCES