Hyperuricemia as a Predictor of Poor Fetal Outcome in Pre-Eclamptic Women

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Abstract

Background: To evaluate the relation between raised serum uric acid level and fetal outcome.

Methods: This Cohort study was conducted at Department of Obstetrics and Gynaecology, Services Hospital, Lahore, to compare the risk of poor fetal outcome in hyperuricemic and normouricemic pre-eclamptic patients. A total of 300 patients with the diagnosis of pre-eclampsia were included in the study and serum uric acid levels were obtained in all the patients. They were divided into two groups: Group A: Pre-eclamptic Normouricemic; Group B: Pre-eclamptic Hyperuricemic. All patients were followed after delivery for fetal outcome and results were compared in both groups.

Results: The mean maternal age was 28.60 ± 3.308 years. The mean gestational age was 36.85 ± 0.59 weeks. The mean uric acid level of the patients at presentation was 5.067 ± 1.74 mg/dl. The mean uric acid level in group A was 3.64 ± 0.73 mg/dl and in group B was 7.98 ± 0.85 mg/dl. In group A, 9.3% newborns were found small-for-gestational-age (SGA), whereas in Group B, 23.3% newborns were found having SGA. The relative risk was calculated for development of SGA in hyperuricemia and was found significant (RR=2.5; 95% CI: 1.40-4.45).

Conclusion: Serum uric acid level measurement is a useful and inexpensive marker for predicting pre-eclampsia and fetal growth retardation in women presenting with gestational hypertension.

Key Words: Hyperuricemia, Pre-eclampsia, Fetal outcome

Introduction

Gestational hypertension is a medical disorder worldwide that complicates approximately 12-22% of the pregnancies.1 Pre-eclampsia is one of the subtypes of gestational hypertension, which is defined as the development of hypertension, proteinuria, or both after 20 weeks in a woman with previously normal blood pressure. Elevated uric acid is a component of pre-eclampsia syndrome that was recognized many years ago. Not only the hypertensive disorders in pregnancy are linked with elevated serum uric acid, but also the essential hypertension is also associated with the abnormalities in the levels of serum uric acid and lipid profile.2 The association of pre-eclampsia with gestational diabetes has also been well established in many trials.3 Interpretation of uric acid level requires the exact knowledge of the duration of gestation, as its levels in normal pregnancy increases with the increasing gestation, i.e. 2-4.2 mg/dl, 2.4-4.9 mg/dl and 3.1-6.3 mg/dl in 1st, 2nd and 3rd trimester of pregnancy respectively.4 Women with gestational hypertension and hyperuricemia have evidence of endothelial dysfunction and deliver growth-retarded babies.5 In women with gestational hypertension, hyperuricemia (>5.5 mg/dl) was associated with smaller birth weight centiles and increased risk of small-for-gestational-age (SGA) 6. According to a study, the prevalence of SGA in hyperuricemic pre-eclamptic women was 23.9% as compared to 12.3% for normouricemic pre-eclamptics, with RR[95% CI]: 2.0 (0.8-4.8).6

Patients and Methods

It was a cohort study conducted at Department of Gynaecology and Obstetrics Unit-III, Services Hospital, Lahore over a period of one year from January 2014 to December, 2014. In this study, Pre-eclampsia was defined as the development of hypertension (diastolic blood pressure > 90mm of Hg or systolic blood pressure > 140mm of Hg), proteinuria (presence of 300mg/dl or more protein in 24 hour urine specimen which correlates with a finding of +1 of greater), or both, after 20 weeks of gestation in women with previously normal blood pressure. Hyperuricemia was defined as serum uric acid level more than 5.5mg/dl. The cut-off value of 5.5 mg/dl was decided by the authors because in most of the previous studies normal range for pregnant females is considered as >5.2-5.5 mg/dl. Poor fetal outcome was measured in terms of fetus with SGA. Pre-eclamptic patients with all the gravida, between 25-35 years of age were included in the study. Patients with multiple gestations were excluded from the study as the incidence of SGA is reportedly high in multiple
pregnancies. Also patients with other co-existing medical disorders like maternal diabetes, renal, respiratory and hepatic dysfunction and placental abruption were excluded. A sample size of total 300 patients with 150 being in each group was calculated, with 10% margin of error, 80% power of study, taking expected %age of SGA i.e. 23.9% in hyperuricemia and 12.3% in normouricemia. The pre-eclamptic patients were divided into normouricemic (Group-A) and hyperuricemic (Group-B) groups after getting serum uric acid levels. A detailed history was taken and gestational age was calculated from the last menstrual period and dating scan. Fetal monitoring was done by maintaining SGA chart and ultrasonography. Patients were kept in follow up and baby was delivered according to gynaecological merits. Fetal weight was recorded at birth. Serum uric acid levels were done spectrophotometrically. Summaries were presented qualitatively in frequencies and percentages in both hyperuricemic and normouricemic groups. Quantitative summaries of age, gestational age, and baby weight were presented in terms of mean and standard deviation. Relative risk (RR) was calculated to see any association between hyperuricemic and small-for-gestational-age. RR>2 was considered as significant.

Results

A total of 300 patients were included in the study. The two groups were comparable in terms of demographic details. The uric acid level in group A ranged from 2.7 to 5.3 mg/dl and mean value was found to be 3.64 ± 0.73 mg/dl while in group B it ranged from 5.9 to 9.9 mg/dl and mean value was found to be 7.98 ± 0.85 mg/dl (Table 1).

Table 1: Demographics of patients in both groups

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (years)</td>
<td>28.05±2.960</td>
<td>28.71±2.834</td>
</tr>
<tr>
<td>Gestational Age (weeks)</td>
<td>36.96±0.53</td>
<td>36.74±0.62</td>
</tr>
<tr>
<td>Hb (mg/dl)</td>
<td>3.64±0.73</td>
<td>7.98 ±0.85</td>
</tr>
<tr>
<td>Uric Acid (mg/dl)</td>
<td>3.64±0.73</td>
<td>7.98 ±0.85</td>
</tr>
</tbody>
</table>

Discussion

Pre-eclampsia is a type of hypertension which is unique and confined to pregnancy. It is a common problem and occurs among 3-10% of nulliparous women during pregnancy. It is globally prevalent and contributes as a major cause to morbidity and mortality during pregnancy. It is a multi-system disorder and mainly involves kidneys. Due to endothelial damage in the kidneys, it causes proteinuria, hypertension and derangement of renal function. Studies reveal equal prevalence of preeclampsia among nulliparous and multiparous women. Whenever defining pre-eclampsia, hyperuricemia is not a commonly used criteria, but many studies have suggested that hyperuricemia during pregnancy suggests gestational hypertension and can lead to an untoward outcome.

Pre-eclampsia is a known cause of low birth weight and premature birth. The hyperuricemic group was found with a mean birth weight of 2.91 ± 0.51 Kg, lower than Group A in which mean birth weight was 3.18 ± 0.44. Our results are comparable with such a study carried out in Dhaka, which showed a mean birth weight of 2.31 ± 0.71 Kg in pre-eclamptic women with hyperuricemia. A rising serum uric acid is now recognized as an early feature of pre-eclampsia and its measurement greatly increases the diagnostic accuracy of pre-eclampsia. The level of uric acid above 4.5 mg/dl is indicative of pre-eclamptic process and in such cases, the patients deserve careful and close clinical follow up. Increasing higher concentration of uric acid i.e. 5.7 mg/dl, 6.3
mg/dl, and 6.7 mg/dl was observed in pregnancy with chronic hypertension and pre-eclampsia. Serum uric acid could be used as a sensitive indicator of severity of pre-eclampsia. Lim KH found that the concentration of serum uric acid also correlated well with severity of the glomerular lesion. D'Anna R and colleagues concluded that the level of serum uric acid appears to be a sensitive index of the severity of pre-eclampsia.

The frequency of SGA in our study was seen in 47 newborns. Among all these 23.33% were from the hyperuricemic pre-eclamptic group. In a similar study there were 28% newborns found SGA in pre-eclamptic women with a mean serum uric acid level more than 6.4 mg/dl. In that study, no newborn was found SGA in pre-eclamptic women who were with a mean serum uric acid levels of 5.6 ± 0.3 mg/dl at delivery. However, in our study SGA was noted in 9 newborns in pre-eclamptic normouricemic group. High uric acid levels with pre-eclampsia during pregnancy leads to a spectrum of maternal and fetal outcomes. According to Parrish M and colleagues, adverse maternal outcomes occurred in 15.3% of 258 patients in their cohort trial. The positive likelihood ratio (LR) for adverse maternal outcome was found 5.3 with Urac acid levels ≥ 76.3 μmol/l. Also adverse perinatal outcomes occurred in 45.2% of births. In another study, it was found that hyperuricemic pre-eclamptic mothers were associated with higher probability of delivery by caesarean section (33% versus 12%; p = 0.007). In a study conducted on Japanese normotensive pregnant women, Akahori et al. documented that hyperuricemia in the third trimester of pregnancy is an independent risk factor for SGA delivery. In our study the relative risk for the development of SGA with hyperuricemia was calculated and found 2.2. It means that the pre-eclamptic hyperuricemic patients are 2.2 times as likely as normouricemic pre-eclamptic to develop SGA. It was more than 2 and statistically significant making present study reliable in commenting about the association between hyperuricemia and SGA.

**Conclusion**

Serum uric acid level measurements are a useful and inexpensive marker for predicting pre-eclampsia and fetal growth retardation in women presenting with gestational hypertension.

**References**