Maternal Serum Uric Acid Level during Pregnancy: A Biomarker for Preeclampsia

*RUKHSHAN KHURSHID, *ADINA SHAMSI, **IRUM FAYYAZ, *MUDDASIR ZIA

ABSTRACT

Background: Pre-eclampsia is a frequent obstetrical problem responsible for adverse effects on pregnancy outcome.

Aim: To find role of serum uric as an early predictor of preeclampsia.

Methods: A case control study was conducted on 30 pre-eclamptic women and 20 age matched women with normal pregnancy. Patients were taken from Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital Lahore, from January 2015 to December 2016. Pre-eclampsia was diagnosed by pregnancy with gestational age ≥20 weeks, with blood pressure ≥140/ ≥90 mm Hg and 24-hour urinary protein ≥300 mg. Blood samples were collected for estimation of serum uric acid. Serum uric acid was measured by Autoanalyzer using standard kit of Merck.

Results: Mean age of normal pregnancy group was 28.43±4.11 with mean gestational age was 30.90±3.9 weeks. Mean age of pre-eclampsia group was 29.07±5.54 with mean gestational age was 28.70±4.0 weeks. Level of serum uric acid was increased in pre-eclampsia group as compared to level of serum uric acid of group of normal pregnant women and it showed a highly significant difference (P<0.001). Serum uric acid as a biomarker showed 65% sensitivity and 95% specificity with 95% positive predictive value.

Conclusion: It is concluded that age may be an independent risk factor for developing preeclampsia. Serum uric acid level may be a biomarker of preeclampsia and also may help to monitor the disease.

Keywords: Preeclampsia, serum uric acid, biomarker.

INTRODUCTION

Pre-eclampsia is the third frequent cause of maternal death and it complicates ~ 5-7% of pregnancy. Its prevalence rate in Pakistan is 19%. It is also associated with fetal morbidity and mortality. Pre-eclampsia is considered as “a disease of hypotension” and its exact reason is weakly understood. However it is proposed that endothelial dysfunction is mainly associated with pathophysiology of preeclampsia lead to increased risk of morbidity and mortality in mother and child. The link between endothelial dysfunction and inflammation, oxidative stress and the hypercoagulable state is complex in the disease of preeclampsia as these condition may augment the effect of each other, resulting an increased vascular damage.

Pre-eclampsia is multisystem disorder in pregnant women and distinguished by the development of proteinuria and hypertension, impaired liver function and raised serum uric acid after 20 weeks of gestation. It is proposed that increased serum uric acid is related with hypertension, renal disease and adverse cardiovascular events in the non-pregnant women and endothelial dysfunction, inflammation and unfavorable fetal outcomes in pregnant women. Endothelial dysfunction may lead to breakdown of trophoblast, cytokine release and ischemia, results a raised level of uric acid.

In early pregnancy, serum uric acid fall to <3mg/dl due to the uricosonic effects of estrogen and increase in renal blood flow. Lately it increases during the third trimester, reaching levels of 4 to 5 mg/dl by term. The damaging effects of uric acid are to decreased nitric oxide bioavailability and enhanced superoxide generation.

An increased level of uric acid in preeclamptic women is not only a indicator of disease severity but it also have a direct role with the pathogenesis of the disease as uric acid unfavorably effect both placenta and maternal vasculature. Increased level of serum uric acid may lead hypertension by an increase in salt sensitivity and proliferation of vascular smooth muscle and proteinuria.

Hypertension was reported to account complications for 15% of pregnant women. Complications of preeclampsia include an increased risk of acute renal failure, abruptio placentae, cardiovascular problems and maternal mortality.

In Pakistan the rate of eclampsia is high. Early detection, proper monitoring and treatment of preeclampsia is necessary in preventing maternal mortality. Our study aimed to confirm that maternal...
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serum uric acid level during pregnancy can be used as a biomarker for Preeclampsia and increased level of serum uric acid levels can be associated with the severity of Preeclampsia. A biomarker which is cheap and may be used to save the valuable lives of fetus and mother.

Present study was designed to find out role of serum uric as an early predictor of preeclampsia.

MATERIALS AND METHODS

A case control study was conducted on 30 pre-eclamptic women and 20 age matched women with normal pregnancy. Patients were taken from Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital Lahore, from January 2015 to December 2016. Letter of consent was taken from each subject. Study was approved by Ethical Committee of Sir Ganga Ram Hospital Lahore.

Pre-eclampsia was diagnosed by pregnancy with gestational age >20 weeks, with blood pressure ≥140/≥90 mm Hg noted on two 6 hours apart and 24-hour urinary protein ≥300mg. Pregnant women with pre-existing hypertension, renal disease, cardiovascular disease, diabetes mellitus or any endocrinopathies were excluded from the study.

Blood samples were collected for estimation of serum uric acid. Serum uric acid was measured by Autoanalyzer using standard kit of Merck.

Statistical analysis was performed using SPSS. 18. Variables were expressed as mean±SD. Comparison of parameters were carried out by student ‘t’ test. P<0.05 was considered statistically significant. Sensitivity and Specificity, positive and negative predictive value of serum uric acid as a biomarker of disease was calculated.

RESULTS

Age distribution is study subjects is tabulated as table 1. It was observed that mean age of normal pregnancy group was 28.43±4.11 with mean gestational age was 30.90±3.9 weeks. Mean age of pre-eclampsia group was 29.07±5.54 with mean gestational age was 28.70±4.0 weeks.

Comparison of level of serum uric acid in study groups is tabulated as table 2. Mean level of serum uric acid was increased in pre-eclampsia group as compared to level of serum uric acid of group of normal pregnant women and it showed a highly significant difference (P<0.001).

Serum uric acid as a biomarker based on sensitivity, specificity, positive predictive value and negative predictive value was calculated (Table 3). It was observed that sensitivity was 65%, specificity was 95%, positive predictive value was 94% and negative predictive value of uric acid was 60%.

<table>
<thead>
<tr>
<th>No of cases in parenthesis</th>
<th>Values are expressed as mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
<td>Normal pregnancy group (20)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>28.43±4.11</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>30.90±3.9</td>
</tr>
</tbody>
</table>

Table 2: Comparison of level of serum uric acid in study groups

<table>
<thead>
<tr>
<th></th>
<th>Mean level of Uric acid(mg/dl)</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal pregnancy group</td>
<td>4.39</td>
<td>0.72</td>
</tr>
<tr>
<td>Pre-eclampsia group</td>
<td>7.29</td>
<td>1.24</td>
</tr>
</tbody>
</table>

P value <0.001

Table 3: Serum uric acid as a Biomarker

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<table>
<thead>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>65%</td>
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<tr>
<td>Specificity</td>
<td>95%</td>
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<tr>
<td>Positive predictive value</td>
<td>94%</td>
</tr>
<tr>
<td>Negative predictive value</td>
<td>60%</td>
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DISCUSSION

Pre-eclampsia is a pregnancy precise, multisystem syndrome differentiated by decreased organ perfusion resulting to vasospasm and coagulation cascade activation. This syndrome has been related to multiple factors. However, exact cause of preeclampsia is not known13,14.

Mean age of pre-eclampsia group was 29.07±5.54 with mean gestational age was 28.70±4.0 weeks. There is mild difference between the mean age and gestational weeks of normal pregnant women and of pre-eclamptic group. A study found that pre-eclampsia is reported in both younger and the middle aged women15. A study also stated that rate of pre-eclampsia was decreased in women with age <30 years and it increased in women with age 30-34 years16. In addition some studies found that maternal age found to be an independent risk factor for early development of preeclampsia and impaired growth of fetus17,18.

Our study is in accord with a study who found that preeclampsia develops before 33 weeks of gestation increased the risk of adverse maternal and perinatal outcome19. It is stated that early-onset of pre-eclampsia, with <34 gestational weeks, may be associated with placental pathology. However, gestational age ≥34 weeks may present late onset preeclampsia which may be triggered by intrinsic pathology involving overcrowding of microvillus. It is suggested that oxidative stress proteins change the maternal response via regulating many growth factors and preventing early onset of preeclampsia20.

Mean level of serum uric acid was increased in pre-eclampsia group as compared to level of serum uric acid of group of normal pregnant women and it showed a highly significant difference (P<0.001).

It is reported that in normal pregnant women the level of serum uric acid is 25-35% decreased of than the level of uric acid of non-pregnant women. However the level of uric acid increased and come to normal level. It is proposed that there is raised glomerular filtration in pregnant women and reduced reabsorption of uric acid from proximal tubules of kidney during pregnancy.

In women with pre-eclampsia there is impaired trophoblastic invasion in the placenta and ischemic metabolite formation. These ischemic metabolite are responsible for peripheral vasoconstriction in glomeruli and glomerular endotheliosis results in decreased GFR and increased uric acid net reabsorption from proximal convoluted tubule leading to increased level of serum uric acid.

A study found that raised uric acid reabsorption, increased sympathetic activity, repressed the activity of angiotensin system and decreased the level of estrogen. Some studied suggested that in pre-eclampsia increased level of serum lactate may reduced the secretion of uric acid through renal tubules. Though some studies show that uric acid may itself have a pathogenic role in pre-eclampsia resulting in a vicious cycle of disease. However, the role of serum uric acid as a marker of preeclampsia is not confirmed.

Serum uric acid as a biomarker based on sensitivity, specificity, positive predictive value and negative predictive value showed it has high positive predictive value and high specificity.

Uric acid level >6 mg/dl in the third trimester showed that the chance of developing Preeclampsia is 94%. According to a study in preeclampsia high levels of uric acid, may be resulting from the body's effort to manage oxidative stress.

**Limitation:** Levels of serum uric acid in women with first and second trimester of pregnancy were not estimated. It is therefore not clear that the level of serum uric acid was raised in acute phase of disease or it may slowly rise from the initial stage of pregnancy.

**CONCLUSION**

It is concluded that age may be an independent risk factor for developing preeclampsia. Serum uric acid level may be a biomarker of preeclampsia and also may help to monitor the disease.

**REFERENCES**
