

# The Role of Serum Uric Acid in Preeclampsia

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## Abstract

**Objective:** The goal of this study was to assess the utility of serum uric acid in preeclampsia diagnosis and its correlation with some maternal and fetal outcomes.

**Materials and methods:** A case-control study was performed on 26 term pregnant women with preeclampsia and 52 normal pregnant women. Serum uric acid, platelet count, hematocrit, gestational age, and birth weight of all patients were measured. Data distribution was assessed with the one sample Kolmogorov-Smirnov test. Mann-Whitney U test was used to assess differences between groups. Correlations between plasma uric acid and other parameters were evaluated with the Spearman's Rho or Pearson correlation test, where appropriated. Receiver-operating characteristics (ROC) curves were used to assess the ability of plasma uric acid to distinguish the preeclampsia from normal subjects. Significance was set at  $P < 0.05$ .

**Results:** The mean level of plasma uric acid was  $5.8 (\pm 2)$  mg/dl in cases and 4.9 mg/dl in controls ( $P=0.04$ ). ROC curve analysis demonstrates the absence of obvious cut off point for plasma uric acid to distinguish preeclampsia. Sensitivity and specificity for uric acid level of 5.5 mg/dl were 61.5% and 78.8%, respectively. There was no significant linear correlation between the plasma uric acid level and other measured parameters in each group.

**Conclusion:** On the basis of our data, the clinical utility of measuring serum uric acid levels in diagnosing preeclampsia is limited.

**Key words:** Uric acid, Preeclampsia, Pregnancy Diagnostic test

## Introduction

Preeclampsia is an obstetric disease that involves different systems and organs and is of unknown certain etiology (1). Preeclampsia affects almost 2-8% of all pregnancies and several complications have been reported with this disease (2). Preeclampsia is known to have a preclinical phase before signs and symptoms become overt in the second half of pregnancy (3). Unavailability of a precise test for identifi-

cation of pregnant women at risk of developing preeclampsia is a major reason for the high morbidity of this disease (4).

In 1917 the association between elevated serum uric acid and preeclampsia was reported for the first time (5). From that time on, uric acid measurement was considered a component in the work up of pregnant women with preeclampsia to monitor the severity of the disease and helped to manage it. There are several proposed mechanisms for elevation of uric acid in preeclampsia such as abnormal renal clearance, increased tissue breakdown, acidosis and a rise in the activity of the xanthine oxidase/dehydrogenase enzyme (6). Reduction in the clearance of uric acid due to the reduction in the glomerular filtration rate, increased

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**Table 1:** Comparison of measured parameters in preeclampsia and control groups

|                                 | Preeclampsia group<br>(n=26)<br>Mean ± SD | Control group<br>(n=52)<br>Mean ± SD | P-Values |
|---------------------------------|---|--------------------------------------|----------|
| Systolic blood pressure (mmHg)  | 162.1 ± 26.2                              | 110.5 ± 9.8                          | < 0.001  |
| Diastolic blood pressure (mmHg) | 100 ± 15.5                                | 70.7 ± 9.5                           | < 0.001  |
| Hematocrit (%)                  | 38.2 ± 4.9                                | 38.4 ± 3.5                           | 0.870    |
| Platelet count                  | 195923.1 ± 66357.2                        | 192153.9 ± 46235.7                   | 0.771    |
| Birth weight (gr)               | 2653.9 ± 337.9                            | 3145.6 ± 402.8                       | < 0.001  |

absorption and a decrease in the secretion may be the cause for the rise in the level of serum uric acid in preeclamptic women (2).

Different sensitivity and specificity of the serum uric acid values have been posed in diagnosing and predicting preeclampsia and its complications, ranging from being the most sensitive indicator of preeclampsia available (7) and having equal importance to proteinuria in identifying fetal risk in women with preeclampsia (8), to being of little or poor value in diagnosing and predicting preeclampsia (4, 9). This study aimed to compare the values of serum uric acid in preeclamptic and normal pregnant women and its correlation with some important maternal and fetal outcomes.

## Materials and methods

A case-control study was performed on 26 pregnant women with preeclampsia as cases and 52 normal pregnant women as controls, all at term (37 to 40 gestational weeks). The study was approved by hospital's ethics committee. All women were recruited from Shariati Hospital prenatal care clinic between 2006- and 2008. All women were delivered at the same hospital. Informed consent was obtained from patients before blood sampling. The defined sample size will be sufficient to detect a difference of 2 mg/dl in serum uric acid level, assuming a standard deviation of 3 mg/dl, a power of 80%, and a significance level of 5%.

The criteria for diagnosing preeclampsia was due to National Working Group (10) on Hypertension in Pregnancy classification which was hypertension (either 149/90 mmHg or relative increase in systolic pressure of 30 mm Hg or increase in diastolic pressure 15 mm Hg compared with blood pressure values obtained before 20 weeks gestation) accompanied by proteinuria (either > 0.3 gm/24 hr or 30 mg/dl [1+ dipstick]), edema, or both occurring after 20 weeks of gestation.

Only women with singleton term pregnancy and without past history of any chronic disease such as

renal diseases, diabetes, and pregestational hypertension were included.

Serum uric acids of the patients were measured at the laboratory of Shariati Hospital with Uricase/Peroxidase method with Bio System kits (Spain). In addition to comparing the uric acid levels in women with and without preeclampsia, we investigated the correlation of uric acid levels with some fetal and maternal outcomes, platelet count, hematocrit, gestational age, and birth weight.

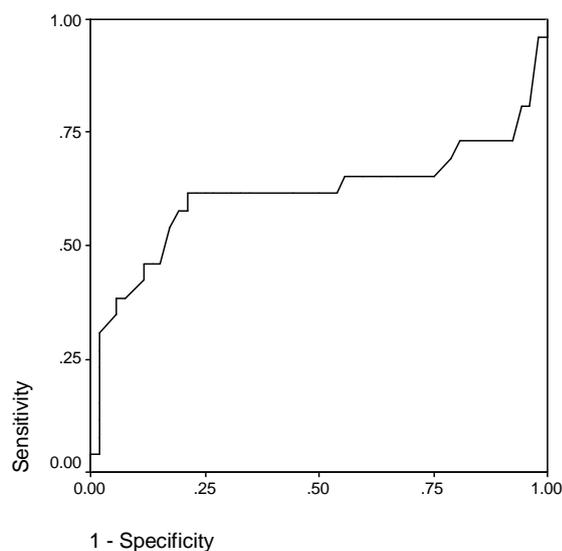
Data was presented as mean ± standard deviation (SD) and its distribution was assessed with the one sample Kolmogorov-Smirnov test. Systolic and diastolic blood pressure and Gestational age were nonparametric variables, and Mann-Whitney U test was used to assess differences between groups. The other variables displayed a normal distribution, and compared with independent t-test. Correlations between plasma uric acid levels and other measured parameters were evaluated with the Spearman's rho or Pearson correlation, where appropriated. Receiver-operating characteristics (ROC) curves were used to assess the ability of plasma uric acid to distinguish the preeclampsia of normal subjects. Significance was set at  $P < 0.05$ .

## Results

Twenty six women in preeclampsia group, with the median (range) gestational age of 37 (37–40) weeks were compared with 52 women without preeclampsia as the control group with the median (range) gestational age of 39 (37–40) weeks. Other subjects' characteristics are summarized in table one. The preeclamptic group had a significantly lower mean of birth weight compared to control group ( $P = 0.04$ ) (Table 1).

The mean ±SD of plasma uric acid (UA) was 5.8 ±2 mg/dl (range 2.5 to 10.1) in preeclampsia group; and 4.9 ±1.1 mg/dl (range 2.7 to 8.9) in control group ( $P = 0.04$ ).

Figure 1 shows the results of the ROC curve ana-



**Figure 1:** Receiver-operator characteristic curve for various plasma uric acid levels in distinguishing preeclampsia of normal subjects.

lysis which demonstrates the absence of obvious cut off point for plasma UA level to distinguish preeclampsia from normal subjects. The area under the receiver-operating characteristic (ROC) curve was 0.61 and was not statistically significant ( $P = 0.101$ ). Sensitivity and specificity for plasma UA levels of 5.5 mg/dl were 61.5% and 78.8%, respectively.

There were no significant linear correlations between the plasma uric acid level and other measured parameters in each group (Table 2).

### Discussion

Several tests have been proposed as an indicator

**Table 2:** Correlation of plasma uric acid levels with measured parameters in preeclampsia and control groups

| Measured parameter              | Preeclampsia group (n=26)<br>R (P-Values) | Control group (n=52)<br>R (P-Values) |
|---------------------------------|---|--------------------------------------|
| Systolic blood pressure (mmHg)  | 0.23 (0.263)                              | 0.22 (0.121)                         |
| Diastolic blood pressure (mmHg) | 0.29 (0.148)                              | 0.18 (0.208)                         |
| Gestational age (weeks)         | - 0.2 (0.936)                             | 0.01 (0.982)                         |
| Hematocrit (%)                  | 0.11 (0.585)                              | -0.01 (0.981)                        |
| Platelet count                  | - 0.29 (0.158)                            | 0.08 (0.587)                         |
| Birth weight (gr)               | - 0.16 (0.424)                            | 0.06 (0.685)                         |

of the development of preeclampsia, and one of these tests that has been investigated many times and caused a lot of controversy is serum uric acid. Although the data in this study suggest a statistically significant difference between the mean serum uric acid values of the case and control groups (0.9 mg/dl difference,  $p = 0.04$ ), the clinical importance of it is questionable. We were unable to identify an obvious cut off point on the receiver operator curve (ROC) for uric acid level that was sufficiently sensitive and specific to distinguish preeclampsia. The best sensitivity (61.5%) and specificity (78.8%) was related to cut off of 5.5 mg/dL. These figures are close to the values of some other studies, and the findings are consistent with those studies that did not find a clinical utility for serum uric acid in prediction of preeclampsia (7, 4, 3) and in contrary to some other studies (8). This might be because most of the studies that have reported a strong correlation between elevated serum uric acid and the severity of preeclampsia, have examined pregnant women with the most severe form of the disease (11). Thus, in the relatively less prevalent women with severe preeclampsia, levels of serum uric acid might correlate with certain measures of outcome; however, in milder form of the disease, which is more prevalent, the correlation of serum uric acid levels and outcomes is weak, such as in the study by Paternoster et al. concluding that the rate of protein excretion, the oldest laboratory test used for diagnosis, appeared to be more useful in the prediction of preeclampsia than serum uric acid (12).

No significant correlation was found between uric acid measures and platelet count, and hematocrit as two markers of severity of the disease. No significant correlation was found with birth weight either. On the basis of our data, the utility of serum uric acid level in preeclampsia is limited. As a diagnostic test uricemia is a late sign and moderately sensitive but not specific enough when used to diagnose preeclampsia. Further studies including all types of hypertensive disorders of pregnancy are needed to achieve more data about the role of serum uric acid in determining preeclampsia.

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