Comparison of Serum Uric Acid, Iron and Total Iron Binding Capacity (TIBC) Levels in Pre–eclamptic and Normal Pregnant Women

Bita Eslami, M.P.H.; Ashraf Moeini, M.D.; Relhaneh Hosseini, M.D.; Mojtaba Sedaghat, M.D.

1 Department of Gynecology and Obstetrics, Arash Women’s Hospital, Tehran University of Medical Sciences, Tehran, Iran
2 Department of Endocrinology and Female Infertility, Royan Institute, ACECR, Tehran, Iran
3 Department of community medicine, Tehran University of Medical Sciences, Tehran, Iran

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Abstract
Objective: The objective of our study was to compare uric acid, iron and TIBC levels in normal and preeclamptic pregnant women and determine their relations with maternal and fetal complications.

Materials and methods: A case control study was conducted in 200 normal and preeclamptic pregnant women. At 32–40 weeks of pregnancy (third trimester) a blood test was taken in order to measure the uric acid, iron and TIBC and their relation with maternal and fetal complications.

Results: Uric acid level showed significant difference (4.58 ± 0.73, 4.87 ± 0.58, \( p = 0.002 \)) between two groups of pre–eclamptic and normal women. The iron and TIBC level had no significant difference in either group. The uric acid level and iron had significant differences between two groups with and without maternal complication, respectively (4.69 ± 0.66, 5.05 ± 0.59, \( p < 0.05 \)) (387.42 ± 82, 405.24 ± 57, \( p < 0.05 \)). There was not any difference in three parameters between groups with and without fetal complication. The BMI was significantly higher in preeclamptic group and has positive relation with uric acid level. If we consider 29 as BMI cut–off point; it will be associated with 73% sensitivity and 67% specificity in preeclampsia determination. Using 4.55 as uric acid cut–off point, the sensitivity is 76% and specificity is 49%.

Conclusion: Although the higher level of uric acid, higher BMI scale and positive roll–over test are associated with preeclampsia, but they are not very strong predictors as single test.

Keywords: Serum uric acid, Iron, TIBC, Roll–over test, Preeclampsia

Introduction
Preeclampsia is a multisystemic obstetric disorder with unknown etiology (1) and it affects 5 to 10 percent of all pregnancies (2). It’s the most significant cause of maternal and fetal morbidity and is responsible for approximately 15% of maternal mortality (3).

Early detection of preeclampsia has been investigated by several biological and biochemical tests. Although none of them have not enough accuracy in order to detect preeclampsia as early as possible.

Some studies evaluated serum uric acid levels and correlation between serum uric acid with maternal and fetal morbidity (4–6).

In normal pregnancy, serum uric acid concentra-
tion decreased (7) and concentrations usually are in the 3–4 mg/dl range (180–240 µmol/l) (7, 8) and then slowly increase reaching 4–5 mg/dl (240–300 µmol/l) by term (9).

In preeclamptic women, serum uric acid concentration is increased in compare with normal pregnancy due to reduction in renal excretion of urate, which is probably mediated by the systemic vasoconstriction, reduction in renal blood flow and decrease in glomerular filtration rate that accompany this disease (10).

There are several other potential origins for uric acid in preeclampsia; increased tissue breakdown, acidosis and increased activity of the enzyme xanthine oxidase /dehydrogenase (11).

The causes of preeclampsia are complex and not fully understood, but the condition may be associated with poor placentation (12). The effect of poor placentation is to leave the spiral arteries smaller than normal for the second half of pregnancy (12). Iron may arise in the ischemic placenta by destruction of red blood cells from thrombotic, necrotic, and hemorrhagic areas (13), which, if uncontrolled, may result in endothelial cell damage, as hypothesized by Hubel et al. (14).

Disturbances in iron hemostasis have already been observed in preeclampsia (15, 16).

Meanwhile, the roll–over test has also been found useful in identifying patients at risk (4).

Therefore in this study serum uric acid, serum iron and TIBC and roll–over test are examined as screening tests in order to compare in preeclamptic cases against normal pregnant women.

**Materials and Methods**

A total of two hundreds obstetric patients at Arash hospital were enrolled in an ongoing investigation. The study was approved by the ethics institutional review board of Arash Hospital and informed consent was obtained from all participants. Women were excluded from the study if they had multiple fetuses, chronic hypertension, renal disease, any form of anemia, diabetes, and other preexisting medical condition or history of drug use. Neither of mothers had received iron supplements until 20 weeks of pregnancy and then all women received 30 mg elemental iron daily.

One hundred women with normal pregnancy and 100 patients with preeclampsia were recruited in this study.

In the roll–over test, between 32–40 weeks of pregnancy, diastolic BP was recorded while the patient was at rest and after she turned over on her back. An increase of more than 20 mm Hg in diastolic BP was considered a positive test result (4).

Five millimeters of venous blood was taken from these women in 32–40 weeks of pregnancy (third trimester) in order to measure the iron and uric acid (photometric) and TIBC (immunoturbidimetric) by Pars Azmoon kit (Iran). Serum was prepared from venous blood collected and stored at −40°C until assayed. The patients were followed until 48 hours after delivery and maternal and neonatal outcomes were reported.

The maternal complications included HELLP syndrome, eclampsia and maternal death. Fetal complications were IUGR, preterm labour, low Apgar score and IUFD.

Statistical analysis was performed with SPSS software (Version 16). The appropriate statistical test including Chi–Square and Student’s t–test were used to compare the results. A two–tailed p–value of less than 0.05 was considered significant.

**Results**

General characteristics (age, BMI, parity) of patients and infants are shown in Table 1.

Table 2 shows the comparison of uric acid, iron and TIBC level in each group. As it was shown the iron and TIBC level had no significant difference in either group. Only uric acid level was significantly increased in preeclamptic women (4.58 ± 0.73, 4.87 ± 0.58, p= 0.002).

According to the data of table 3 seventeen patients were known as sever preeclampsia with BP >160/110 and there is no significant difference in uric acid, iron and TIBC levels between two groups of mild and severe preeclampsia.

As it was evident, maternal complication was manifested in 14 patients of preeclamptic group and 2 persons of normal group. Twenty persons in preeclamptic group and 5 persons in normal group had fetal complications.

The uric acid level (4.69 ± 0.66, 5.05 ± 0.59, p<0.05) and iron (387.42 ± 82, 405.24 ± 57, p<0.05) had significant differences between two groups with and without maternal complication. There was no significant difference in three parameters between groups, with and without fetal complication.

There was significant relationship between positive roll–over test and preeclampsia. One person in normal group and 14 persons in preeclamptic group had positive roll–over test (p<0.001).

**Discussion**

The results of our study manifested the theoretical sig-
significant differences of uric acid level between normal and preeclamptic women. Although preeclampsia is theoretically associated with iron disturbance metabolism, there is no significant difference in iron and TIBC levels. It may be due to low power of study or perhaps some more items (such as ferritin or transferrin) must be introduced. On the other hand, the disturbance of iron metabolism is in placental level and may has no systemic effects. However, Rayman et al have reported significantly higher serum iron (68%) and lower TIBC (12%) in preeclamptic subjects (16). It should be mentioned their study sample size was 40 and the mean gestational age was 33 weeks. However in our study the sample size is higher and the mean gestational age was 38 weeks which may explain the results’ differences.

Although Williams and Galerneau and also Thangaratinam et al have reported that uric acid level is a poor predictor of maternal and fetal complications, but our study revealed a correlation between uric acid levels and maternal complications which supports Koopmans et al study’s results (4–6).

The iron level shows correlation with maternal complications too. It may be due to a rise in heme catabolism after increased destruction of maternal red blood cells (17).

According to our results there was no relation between uric acid, iron and TIBC and fetal complication as reported in Williams and Galerneau and also Thangaratinam et al studies (4, 5). Considering the uric acid level which is related with maternal complication as we reported above it seems to be paradox with previous studies.

BMI also is higher in preeclamptic group and also has significant relationship with uric acid level. Raja- singam et al believe that plasma uric acid level is related to body mass index as a biomarker of oxidative stress (18).

Delić and Stefanović also reported correctly classified 79.6% patients using uric acid and urea (19). Kaypour and coworkers revealed 54.76% sensitivity and 96% specificity for uric acid 40.47% and 90.90% for BMI (20).

It seems that no single test can predict preeclampsia.

Table 1: Characteristics of patients and infants

<table>
<thead>
<tr>
<th></th>
<th>Preeclampsia (n = 100)</th>
<th>Normal (n =100)</th>
<th>P–Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28.2 ± 5.6</td>
<td>25.8 ± 4.7</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI** (kg/m²)</td>
<td>31.6 ± 6.1</td>
<td>27.8 ± 3.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Parity</td>
<td>2.2 ± 0.4</td>
<td>2.3 ± 0.4</td>
<td>0.35</td>
</tr>
<tr>
<td>GA*** (weeks)</td>
<td>37.13 ± 2.8</td>
<td>39.66 ± 1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Infant’s birth weight (gr)</td>
<td>2980 ± 605</td>
<td>3231 ± 336</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* P–value refers to t-test. ** BMI: Body Mass Index  *** GA: Gestational Age

Table 2: Comparison of biochemical parameters between two groups

<table>
<thead>
<tr>
<th></th>
<th>Preeclampsia</th>
<th>Normal</th>
<th>P–Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uric acid (mg/dl)</td>
<td>4.87 ± 0.58</td>
<td>4.58 ± 0.73</td>
<td>0.002</td>
</tr>
<tr>
<td>Serum iron (mg/dl)</td>
<td>107.74 ± 23</td>
<td>107.34 ± 32</td>
<td>0.92</td>
</tr>
<tr>
<td>TIBC** (mg/dl)</td>
<td>384.70 ± 77</td>
<td>393.17 ± 84</td>
<td>0.46</td>
</tr>
</tbody>
</table>

* P–value refers to t-test. ** TIBC: Total Iron Binding Capacity

Table 3: Comparison of data between mild and severe preeclampsia

<table>
<thead>
<tr>
<th></th>
<th>Mild preeclampsia (n =83)</th>
<th>Severe preeclampsia (n = 17 )</th>
<th>P–Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uric acid (mg/dl)</td>
<td>4.71 ± 0.63</td>
<td>4.89 ± 0.64</td>
<td>0.29</td>
</tr>
<tr>
<td>Serum iron (mg/dl)</td>
<td>107.27 ± 28</td>
<td>110.41 ± 30</td>
<td>0.37</td>
</tr>
<tr>
<td>TIBC** (mg/dl)</td>
<td>387.36 ± 79</td>
<td>405.88 ± 100</td>
<td>0.67</td>
</tr>
</tbody>
</table>

* P–value refers to t-test. ** TIBC: Total Iron Binding Capacity
sia correctly. The combination of uric acid level, roll–over test and BMI may improve the predictive value.

The primary outcome of our study was comparison of uric acid level between two groups of pre eclamptic and normal pregnant women (4.58 ± 0.73, 4.87 ± 0.58 respectively). Based on our result the power of our study will be 87.5% by using the Epi Info Web site (www.cdc.gov/epiinfo). However by considering the other outcomes the power will be low.

So, further studies at the first or second trimesters with larger sample size are suggested to find a specific marker in preeclampsia and focus on it to reduce maternal and fetal complications.

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Nothing

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References