Serum and Urinary Levels of Micronutrients in Preeclamptic and Healthy Pregnant Women: A Case-Control Study

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ABSTRACT
Introduction: Preeclampsia is the most common cause of prenatal and maternal mortality worldwide and the second most common cause of maternal death in Iran. Deficiency of some trace elements such as zinc, calcium and magnesium in pregnant women may play a role in preeclampsia. Therefore, the aim of this study was to measure serum and urinary levels of zinc, calcium and magnesium in preeclamptic and healthy pregnant women. Materials and Methods: This cross-sectional study was performed on 100 pregnant women (at second trimester of pregnancy) referred to the gynecology clinic of Sayyad Shirazi hospital in Gorgan, Iran, during 2014-15. The subjects were divided into a preeclampsia group (N=50) and an age-matched healthy control group (N=50). Serum and urinary levels of zinc, calcium and magnesium were measured by enzymatic method. Data were analyzed in SPSS (version 19) using t-test. P-values less than 0.05 were considered statistically significant. Results: Mean serum calcium level in the preeclampsia group (8.17± 0.64mg/dl) was significantly lower than that in the control group (8.70±0.40mg/dl) (P<0.001). Moreover, mean urinary calcium level in the preeclampsia group (222.33± 19.35mg/dl) was significantly higher than that in the control group (158.61± 40.16 mg/dl) (P<0.001). Conclusions: Women with preeclampsia have significantly lower serum calcium level compared to healthy pregnant women, but the level is still within the normal range. Moreover, preeclampsia has no significant effect on the serum zinc and magnesium concentrations. Women with preeclampsia have significantly higher urinary calcium and significantly lower urinary magnesium levels compared to healthy pregnant women.

KEYWORDS: Preeclampsia, serum and urine, zinc, magnesium, calcium

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INTRODUCTION
Preeclampsia is a disorder characterized by hypertension, edema and proteinuria, affecting about 2 to 8% of pregnant women worldwide [1-7]. Deficiencies of trace elements such as calcium, magnesium, zinc and copper are thought to be associated with risk of preeclampsia [8-13]. These micronutrients are all essential for the antioxidant defense system [10]. Disruption in the balance between oxidant-generating system and antioxidant defense system results in oxidative stress. Oxidative stress-induced endothelial dysfunction is one of the main events proposed in the pathogenesis of preeclampsia [10]. Despite numerous studies, there is not sufficient evidence about the exact role of trace elements [14]. Calcium has a major role in development of clinical hypertension. A balance between calcium and magnesium (vasodilation and vasoconstriction) level is required for the normal regulation of blood pressure. Therefore, magnesium may be considered as a calcium channel blocker that increases intracellular calcium concentrations, resulting in vasodilatation [1]. The aim of this study was to evaluate serum and urinary level of zinc, calcium and magnesium in preeclamptic and healthy women in Gorgan, Northeast of Iran.

MATERIALS AND METHODS
This cross-sectional study was performed on 100 pregnant women (at second trimester of pregnancy) referred to the gynecology clinic of Sayyad Shirazi hospital in Gorgan, Iran, during 2014-15. The subjects were divided into a preeclampsia group (N=50) and an age-matched healthy control group (N=50).
Informed consent was taken from all participants and a questionnaire was completed to collect data on age and gravidity. The subjects were free to withdraw from the study at any time. Inclusion criteria were blood pressure of >140/90 mmHg and proteinuria after 20 weeks of gestation. Exclusion criteria were presence of eclampsia and other epileptic disease, pregnancy-induced hypertension and other hypertensive disorders, and cardiovascular disease requiring medication. A questionnaire was completed to collect data on age and gravidity. Calcium, magnesium and zinc levels were measured by enzymatic method using Pars Azmun kits (Iran) for calcium and magnesium, and Dialab kits (Austria) for zinc. Urinary level of the trace elements was assessed by 24-hour urine collection. Data were analyzed in SPSS (version 19) using t-test. P-value of less than 0.05 was considered statistically significant.

**RESULTS**
The mean age (±standard deviation) of subjects was 28.42 (±6.03) years. Table 1 represents the serum level of calcium, zinc and magnesium in both study groups. Serum calcium level was significantly lower in the preeclampsia group compared to the control group (P<0.001), but no calcium deficiency was found. There was no significant difference in the serum zinc and magnesium levels between the two study groups.

**Table 1. Mean (±standard deviation) serum levels of micronutrient in the preeclampsia and control group**

<table>
<thead>
<tr>
<th>Micronutrients</th>
<th>Women with preeclampsia</th>
<th>Healthy pregnant women</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mg/dl)</td>
<td>8.17 (±0.64)</td>
<td>8.70 (±0.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Zinc (mg/dl)</td>
<td>70.50 (±19.94)</td>
<td>75.89 (±18.96)</td>
<td>0.17</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>1.82 (±0.53)</td>
<td>1.83 (±0.18)</td>
<td>0.895</td>
</tr>
</tbody>
</table>

Mean urinary level of calcium was significantly higher in the preeclampsia group, but mean urinary level of zinc was significantly lower in the preeclampsia group. There was no significant difference in the urinary level of magnesium between the patients and controls (Table 2).

**Table 2. Mean (±standard deviation) urinary level of micronutrients in the preeclampsia and control group**

<table>
<thead>
<tr>
<th>Micronutrients</th>
<th>Cases with preeclampsia</th>
<th>Healthy control group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (mg/dl)</td>
<td>222.33 (±19.35)</td>
<td>158.61 (±40.16)</td>
<td>0.012</td>
</tr>
<tr>
<td>Zinc (mg/dl)</td>
<td>647.11 (±58.33)</td>
<td>950.99 (±80.13)</td>
<td>0.003</td>
</tr>
<tr>
<td>Magnesium (mg/dl)</td>
<td>187.11 (±36.60)</td>
<td>148.75 (±23.79)</td>
<td>0.682</td>
</tr>
</tbody>
</table>

**DISCUSSION**
The present study was designed to evaluate the alterations in the serum levels of calcium, zinc and magnesium in women with preeclampsia. Our findings showed that preeclamptic women had significantly lower serum calcium levels compared to healthy pregnant women. This is in line with results of some previous studies [4, 6, 9, 10, 15]. Increased intracellular calcium in smooth muscle cells has been reported during pregnancy, which could be due to elevated secretion of parathyroid hormone and renin in response to hypocalemia. This rise in calcium leads to vasoconstriction and increased vascular resistance, which results in the subsequent development of high blood pressure in pregnancy [4].
In this study, serum zinc level was lower in preeclamptic women compared to healthy controls. However, this difference was not statistically significant. In addition, the urinary level of zinc was significantly lower in women with preeclampsia. Similar to our study, most previous studies reported decreased serum zinc levels in patients with preeclampsia [4, 9]. Low serum concentration of zinc leads to oxidative stress and reduces the activity of the antioxidant enzyme-superoxide dismutase, which itself may increase blood pressure [4]. Due to the increased transfer of zinc from mother to the growing fetus, decreased serum zinc level and increased urinary zinc excretion are observed in preeclamptic women [4]. On the other hand, elevated lipid peroxidation in preeclampsia lowers concentrations of transporter protein and estrogen, resulting in a decrease in serum zinc level [4].

Unlike previous reports, we found no significant difference in the serum and urinary magnesium levels between the two groups [4,9,10]. It has been reported that preeclamptic women have lower serum magnesium, calcium and zinc levels. Concentrations of magnesium significantly affects the tone and contractility of vascular smooth muscles [4].

Pregnancy-induced hypertension could be due to increased vascular resistance, and low serum concentrations of calcium and magnesium may play a role in constriction of vascular smooth muscles. Moreover, decreased magnesium concentrations may have a vasodilatory effect that results in increased blood pressure [4].

CONCLUSION
Women with preeclampsia have significantly lower serum calcium level compared to healthy pregnant women, but the level is still within the normal range. Moreover, preeclampsia has no significant effect on the serum zinc and magnesium concentrations. Women with preeclampsia have significantly higher urinary calcium and significantly lower urinary magnesium levels compared to healthy pregnant women. Since this was a cross-sectional study, conducting longitudinal and cohort studies would further clarify the possible association of micronutrient deficiency and preeclampsia.

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CONFLICT OF INTEREST
There is no conflict of interest to declare.

REFERENCES


