Original Research Article

Assessment of Serum Magnesium and Uric Acid Levels in Women with Normal Pregnancy and Pre-Eclampsia in Rohilkhand Region in Uttar Pradesh, India

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ABSTRACT

The present study have been undertaken to evaluate and compare the maternal serum concentrations of magnesium and uric acid among non-pregnant healthy women, women with uncomplicated pregnancy and pregnant women with pre-eclampsia and also to find if there is any importance of serum magnesium and uric acid levels in management of pre-eclampsia.

The present study included 120 women divided into three groups (group-A, group-B and group-C). Estimation of maternal serum magnesium and uric acid were analyzed by using Calmagite method and Modified Trinder Peroxidase method.

The mean ± SD systolic, diastolic and mean arterial blood pressure (MAP) of group-B women were significantly higher than group-A women (128.0 ± 6.8 vs 119.0 ± 10.3 mm of Hg, 75.1 ± 7.5 vs. 70.3 ± 8.7 mm of Hg and 92.7 ± 5.48 vs. 86.5 ± 6.68 mm of Hg) and group-C women were significantly higher than group- B women ( 172.2 ± 13.1 vs. 128.0 ± 6.8 mm of Hg, 107.4 ± 7.3 vs. 75.1 ± 7.5 mm of Hg and 129.03 ± 6.5 vs. 92.7 ± 5.48 mm of Hg ). The mean serum magnesium levels were significantly decreased in women with uncomplicated pregnancy when compared with non-pregnant healthy women, p< 0.05. The mean serum concentrations of uric acid in normotensive pregnant was significantly higher when compared to healthy non-pregnant women, p< 0.05. There was highly significant decrease in the mean value of serum magnesium in pre-eclamptic pregnant women when compared to normotensive pregnant women. The mean value of serum uric acid in pre-eclamptic pregnant women was significantly elevated when compared to normotensive pregnant women, p< 0.05.

We conclude that magnesium and uric acid homeostases are altered during pregnancy and these alterations appear to be more pronounced in women with pre-eclampsia.

Key words: Gestational age, calmagite method, non-pregnant, normotensive, hypomagnesemia

INTRODUCTION

Pregnancy is a normal physiological state which shows many changes in metabolic and biochemical processes in the maternal environment.1,2 Around the world, an estimated 529,000 women die during...
pregnancy or childbirth. Pre-eclampsia is a non-convulsive form of hypertensive disorder of pregnancy. Its general prevalence is between 2-8% of pregnancies. It is a multisystem endothelial disease that leads to glomeruloendotheliosis, and in severe cases it may lead to renal impairment and failure. In many studies authors showed a relationship between the aggravation of the hypertensive complication and the change in levels of various parameters like magnesium, calcium, uric acid etc in pre-eclamptic mother’s serum.

Magnesium is an important element for health and disease. It is currently a subject of major interest in biology and medicine. Magnesium, the second most abundant intracellular cation after potassium, has been identified as a cofactor in over 300 enzymatic reactions involving energy metabolism, protein and nucleic acid synthesis. Various studies have suggested the significant influence of magnesium on fetal and maternal morbidity both prepartum and postpartum. Magnesium has a significant effect on tone, contractility, and reactivity of blood vessels and, thus, has a significant role in physiological regulation of blood pressure. In addition, decrease magnesium concentration increases the vasoconstrictor effect of angiotensin II and nor-adrenaline. Magnesium also plays a substantial beneficial effect in preeclampsia for the prevention and treatment of convulsions. Therapeutic magnesium sulphate which is used in PIH inhibits phosphatidyl inositol-4, 5-bisphosphate specific phospholipase C activity and subsequent calcium release in the cells, thus leading to decreased intracellular calcium levels and a decrease in blood pressure.

Uric acid (2, 6, 8-trihydroxypurine) is the end product of purine metabolism and its elevated level induces endothelial dysfunction and may induce hypertension and vascular disease. An association between elevated serum uric acid levels and preeclampsia was first reported by Slemons and Bogert in 1917. In women who go on to develop preeclampsia, uric acid concentration is elevated as early as 10 weeks of gestation, at a time much earlier than clinical presentation of the disorder. There are several proposed mechanisms for elevation of uric acid in the pre-eclampsia, such as abnormal renal clearance, increased tissue breakdown, acidosis and a rise in the activity of the xanthine oxidase / dehydrogenase enzyme. On the basis of some studies claim that elevated concentrations of circulating uric acid are not uniformly seen in every woman with pre-eclampsia, they do appear to identify a subset of pre-eclamptic that are at a greater risk for maternal and fetal morbidities. Also it is one of the most consistent and earliest detectable changes in pre-eclampsia and has been cited as a better predictor of fetal risk than blood pressure.

In spite of numerous studies; the etiology of pre-eclampsia has not yet been fully elucidated. According to many authors in recent studies observes that the changes in levels of serum magnesium and uric acid appear to be of immense value in understanding the pathogenesis of pre-eclampsia. In this context, the present study has been undertaken to evaluate and compare the changes in serum level of magnesium and uric acid in healthy non-pregnant women, normal pregnant women and pregnant women complicated with pre-eclampsia and also to find if there is any relationship between serum magnesium and uric acid levels in this study group of Rohilkhand region of Uttar Pradesh.

MATERIALS AND METHODS

Case control study was conducted at the Department of Biochemistry, Rohilkhand Medical College and Hospital.
(RMCH), Bareilly, Uttar Pradesh. The duration of study was 12 months, from September 2012 to August 2013. Total 120 women were recruited for the study. They were divided in the following three groups, each group consisting of 40 subjects. **Group A:** Comprised healthy non-pregnant women with age’s ranges from 22-35 years taken as controls, **group B:** comprised of normotensive pregnant women with age’s ranges from 22-34 years, receiving antepartum care at the out patients department and **group C:** consisted of pre-eclamptic women with age’s ranges from 23-37 years who were admitted to the Department of Obstetrics and Gynecology, RMCH, Bareilly. All cases were selected by taking a detailed medical history, physical examination and other relative investigations. While selecting the subjects, care was taken that none of them was suffering from diabetes mellitus, cardio-vascular diseases, renal diseases, chronic hypertension, and co-agulation disorders. Before performing the various tests subjects consent had been taken. All the procedures reported here in the study have followed the guidelines approved by the locally appointed ethical committee.

Pre-eclampsia was defined as development of blood pressure > 140/90 mmHg after 20 weeks of gestation and proteinuria of ≥ 300 mg as confirmed by 24h urine collection in women with no known history of hypertension, renal disease, endocrine abnormalities and had single pregnancy and had no family history of lipid or carbohydrate disorders (Lampinen et al 2008). Pre-eclampsia was defined as development of blood pressure > 140/90 mmHg after 20 weeks of gestation and proteinuria of ≥ 300 mg as confirmed by 24h urine collection in women with no known history of hypertension, renal disease, endocrine abnormalities and had single pregnancy and had no family history of lipid or carbohydrate disorders (Lampinen et al 2008). Pre-eclampsia was defined as development of blood pressure > 140/90 mmHg after 20 weeks of gestation and proteinuria of ≥ 300 mg as confirmed by 24h urine collection in women with no known history of hypertension, renal disease, endocrine abnormalities and had single pregnancy and had no family history of lipid or carbohydrate disorders (Lampinen et al 2008).

Blood pressures of our selected subjects were measured by standard mercury sphygmomanometer and blood samples were collected from antecubital vein with all aseptic precautions in glass tubes free from electrolytes. Blood samples were allowed to clot at room temperature and the serum was separated by centrifugation. The samples were analysed for serum magnesium by calmagite method and for serum uric acid by Modified Trinder Peroxidase method.

**Statistical analysis:** The values of studied parameters are presented as the mean ± SD. A student’s unpaired t-test was used for cross sectional comparisons of continuous variables between the 2 groups. The results were considered statistically significant when the probability of the null hypothesis was less than at least 5% (p < 0.05). The main statistical comparisons were performed between healthy non-pregnant and healthy pregnant women, between healthy pregnant women and pre-eclamptic women.

**RESULTS**

Table 1.1 and 1.2, Fig. 1.1, 1.2 and 1.3 shows the maternal characteristics of the study groups. The mean maternal age of group-A, group-B and group-C women were 24.5 ± 3.2, 25.9 ± 3.4 and 26.5 ± 2.8 years. A majority of the women were in the age group of 25 to 30 years. The results showed that the mean maternal age for normotensive pregnant women (group-B) was statistically significant in comparison to healthy non-pregnant women (group-A) [25.9 ± 3.4 year vs 24.5 ± 3.2 year]; p = 0.04. There was no statistical difference (p > 0.05) in maternal age between pre-eclamptic pregnant women (group-C) in comparison to normotensive pregnant women (group-B) [26.5 ± 2.8 year vs. 25.9 ± 3.4 year]. Of the 40 pre-eclamptic patients 28 were primigravida (70%) and 12 were multigravida (30%). The mean gestational age of pre-eclamptic women in group-C was statistically significant in comparison to normotensive pregnant women in group-B (31.17 ± 4.08 week vs. 33.00 ± 4.37 week) [Table 1.1].
Table-1.1 Maternal characteristics of the study groups.

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Group-A (40)</th>
<th>Group-B (40)</th>
<th>Group-C (40)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>Mean ± SD</td>
<td>24.5 ± 3.2</td>
<td>26.5 ± 2.8</td>
<td>25.9 ± 3.4</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>23-37</td>
<td>23-37</td>
<td>22-34</td>
</tr>
<tr>
<td>Estimated</td>
<td>24-28</td>
<td>29-33</td>
<td>34-38</td>
<td></td>
</tr>
<tr>
<td>Gestational</td>
<td>09(22.5%)</td>
<td>14(35%)</td>
<td>17(42.5%)</td>
<td></td>
</tr>
<tr>
<td>weeks</td>
<td>10 (25%)</td>
<td>12 (30%)</td>
<td>18(45%)</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>33.00 ± 4.37</td>
<td>31.17 ± 4.08</td>
<td>129.03 ± 6.5</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>Gr. A vs Gr.B p &lt; 0.05, Gr.B vs Gr.C p &gt; 0.05</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td>Primi</td>
<td>28 (70%)</td>
<td>24 (60%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Multi</td>
<td>12 (30%)</td>
<td>16 (40%)</td>
<td></td>
</tr>
</tbody>
</table>

Table-1.2 Mean systolic, diastolic and mean arterial pressure (MAP) for the three groups of participants.

<table>
<thead>
<tr>
<th>Blood Pressure (mm of Hg)</th>
<th>Group-A</th>
<th>Group-B</th>
<th>Group-C</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic (mean ± SD)</td>
<td>119.0 ± 10.3</td>
<td>128.0 ± 6.8</td>
<td>172.2 ± 13.1</td>
<td>Gr. A vs Gr.B p &lt; 0.05, Gr.B vs Gr.C p &lt; 0.05</td>
</tr>
<tr>
<td>Diastolic (mean ± SD)</td>
<td>70.3 ± 8.7</td>
<td>75.1 ± 7.5</td>
<td>107.4 ± 7.3</td>
<td>Gr. A vs Gr.B p &lt; 0.05, Gr.B vs Gr.C p &lt; 0.05</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>86.5 ± 6.68</td>
<td>92.7 ± 5.48</td>
<td>129.03 ± 6.5</td>
<td>Gr. A vs Gr.B p &lt; 0.05, Gr.B vs Gr.C p &lt; 0.05</td>
</tr>
</tbody>
</table>

Fig. 1.1 showing the maternal age of study groups

Fig. 1.2: No. of participants in gestational weeks of gr B & gr C Cases

Fig. 1.3. Mean gestational age of group-B and group-C cases

Fig. 1.4 Mean systolic, diastolic and MAP of group-A, B and C cases

Fig. 2.1 Mean serum magnesium level (meq/L) in group A, B and C cases

Fig. 2.2 Serum uric acid levels in study groups

Fig. 2.3 Serum uric acid levels in study groups
In this study we compared the results of mean systolic, diastolic and mean arterial blood pressure (MAP) of group-B women with group-A women and group-C women with group-B women (Table-1.2, Fig. 1.4). The mean ± SD systolic, diastolic and mean arterial blood pressure (MAP) of group-B women were significantly higher than group-A women (128.0 ± 6.8 vs. 119.0 ± 10.3 mm of Hg, 75.1 ± 7.5 vs. 70.3 ± 8.7 mm of Hg and 92.7 ± 5.48 vs. 86.5 ± 6.68 mm of Hg) and group-C women were significantly higher than group-B women (172.2 ± 13.1 vs. 128.0 ± 6.8 mm of Hg, 107.4 ± 7.3 vs. 75.1 ± 7.5 mm of Hg and 129.03 ± 6.5 vs. 92.7 ± 5.48 mm of Hg).

Table-2.1 shows the comparison between mean serum concentrations for magnesium and uric acid in normotensive pregnant women (group-B) and healthy non-pregnant women (group-A).

The mean serum magnesium concentration was significantly decreased in group-B women than group-A women (1.53 ± 0.16 meq/L vs. 1.62 ± 0.18 meq/L, p <0.05). But the mean serum concentration of uric acid in normotensive pregnant women (group-B) cases was significantly higher in comparison to healthy non-pregnant women (group-A) [5.17 ± 0.94 mg/dl vs. 3.82 ± 0.64 mg/dl, p <0.05].

Table-2.1, Fig. 2.1 also shows the comparison of mean serum concentrations for magnesium and uric acid between pre-eclamptic pregnant women (group-C) and normotensive pregnant women (group-B). There was highly significant decrease in the mean value of serum magnesium in pre-eclamptic pregnant women (group-C) in comparison to normotensive pregnant women (group-B) [1.34 ± 0.09 meq/L vs 1.53 ± 0.16 meq/L, p <0.05]. But the mean value of serum uric acid in pre-eclamptic pregnant women (group-C) was significantly elevated than normotensive pregnant women (group-B) [6.9 ± 0.54 mg/dl vs 5.17 ± 0.94 mg/dl, p < 0.05].

**DISCUSSION**

In this study we investigated clinical characteristics and serum magnesium and uric acid levels in non-pregnant healthy women (group-A), normotensive pregnant women (group-B) and pre-eclamptic women (group-C). Mean maternal age of normotensive pregnant women (group-B) were statistically significant than non-pregnant healthy women (group-A), (p < 0.05). There was no statistical differences in the mean maternal age between pre-eclamptic women and normotensive pregnant women (p > 0.05). The mean gestational age was highly significant in pre-eclamptic women (group-C) in comparison to normotensive pregnant women (group-B) (p < 0.05). The mean systolic, diastolic and mean arterial blood pressure (MAP) in pre-eclamptic women (group-C) was significantly higher than normotensive pregnant women (group-B) and non-pregnant healthy women (group-A), (Table 1.1, 1.2, Fig. 1.1, 1.2, 1.3 & 1.4).

From table-2.1, and Fig. 2.1, 2.2; we observed that the mean serum magnesium levels were significantly decreased in normotensive pregnant women (group-B) in comparison to non-pregnant healthy women (group-A), p < 0.05. Further, a highly significant decrease was observed in pre-eclamptic women (group-C) as compared to...
normotensive pregnant women (group-B).
The present finding was similar to the findings of previous studies. (22-24) Kesteloot et al, reported that in normal pregnancy hemodilution effect of estrogen and increased demand of minerals by the growing fetus decreases the serum magnesium level and in pre-eclampsia, urinary excretion of magnesium also increases, so the level decreases further. (25) But our results are contrary to some authors, who did not find any significant difference in the concentrations of serum magnesium levels between cases (group-B and group-C) and controls (group-A). (26-28) The difference may be explained by the variations of the studied population and the dietary intake. (29) Hypomagnesemia causes hemodynamic abnormalities such as abnormal vascular tone, thickening of arterial wall and endothelial dysfunction. (26) Magnesium acts peripherally to produce peripheral vasodilatation and a fall in blood pressure. In addition, Magnesium is known to increase the prostacycline release from the endothelial cells of the blood vessels, which acts as a potent vasodilator. Magnesium depletion increases the vasoconstrictor effect of angiotensin II and nor-adrenaline. (24) Therapeutic magnesium sulphate is used for the prevention and treatment of pre-eclampsia.
The mean serum uric acid levels in the present study significantly lower in group-A (non-pregnant healthy women) than group-B (normotensive pregnant women), p < 0.05. Our results agree with previous findings of some authors. (30,31) A decreased glomerular filtration rate may contribute to an increased uric acid, but this likely occurs later in pregnancy closer to the time of pre-eclampsia diagnosis. (31) In the present study, we also found significantly elevated mean serum uric acid level in pre-eclamptic women (group-C) compared to normotensive pregnant women (group-B). Similar results were observed by other authors. (29, 32-44) Hyperuricemia is believed to be resulted from decreased renal excretion as a consequence of pre-eclampsia, also results from increased production secondary to tissue ischemia and oxidative stress. (25) Soluble uric acid impairs nitric oxide generation in endothelial cells. Thus hyperuricemia induces endothelial dysfunction and may induce hypertension and vascular disease. (35) But in some authors namely Salako BL et al., Weerasekera DS et al. (36, 37) did not find any significant difference in mean serum uric acid levels between pre-eclamptic women (group-C) and normotensive pregnant women (group-B).

CONCLUSION
Based on the results of the present study and data available from literature, it is clear that alteration in magnesium and uric acid metabolism during pregnancy could be one of the potential causes of pre-eclampsia. Our findings are comparable with previous studies. It is emphasized from this study that a regular evaluation of serum magnesium and uric acid after 20 weeks of gestation may be an effective screening method for impending pre-eclampsia and may identify population at greater risk to be included in primary prevention programmes.

REFERENCES

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