Serum Calcium, Magnesium and Uric Acid in Preeclampsia and Normal Pregnancy

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Objective: To compare serum calcium, magnesium and uric acid in mild, severe preeclamptic women and normal pregnant women.

Study design: Cross-sectional study.

Setting: Section of Obstetrics and Gynecology, Taksin Hospital.

Material and Method: The data was collected from 36 normal pregnant women, 35 mild preeclamptic women and 33 severe preeclamptic women who were admitted in the Section of Obstetrics and Gynecology at Taksin Hospital between April 2006 and June 2007. The blood samples were collected and analyzed for calcium, magnesium and uric acid. The data was analyzed using Analysis of Variances (ANOVA).

Results: The serum calcium in severe preeclamptic women was significantly lower $(8.7 \pm 0.59 \text{ mg/dl} \text{ vs. } 8.99 \pm 0.31 \text{ mg/dl}, p = 0.045; and 9.05 \pm 0.52 \text{ mg/dl}, p = 0.014)$ and serum uric acid was significantly higher (7.01 $\pm 1.93 \text{ mg/dl} \text{ vs. } 5.33 \pm 1.23 \text{ mg/dl}, p < 0.001 \text{ and } 5.95 \pm 1.9 \text{ mg/dl}, p = 0.044$) than in normal pregnant women and mild preeclamptic women respectively, but there was no difference between normal and mild preeclamptic women. There was no difference in serum magnesium among normal pregnancy and both groups of preeclampsia. **Conclusion:** Hypocalcemia and hyperuricemia correlated to severe preeclampsia.

Keywords: Serum calcium, Serum magnesium, Serum uric acid, Preeclampsia, Normal pregnancy

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Preeclampsia is one of the most common causes of maternal and fetal morbidities and mortalities⁽¹⁾. Its incidence is 4-8% of pregnancies^(2,4). The pathophysiological mechanism is characterized by a failure of the trophoblastic invasion of the spiral arteries, leading to maladaptation of maternal spiral arterioles, which may be associated with an increased vascular resistance of the uterine artery and a decreased perfusion of the placenta^(4,5). However, the exact etiology of preeclampsia is still unknown. The results from many clinical studies show the relationship between the aggravation of the hypertensive complication and the change in concentration of various chemistries in mother's serum⁽⁴⁻¹⁰⁾. Interestingly, variable serum calcium, magnesium and uric acid are found in preeclamptic mothers^(5,6,11-13).

On the physiological basis, calcium plays an important role in muscle contraction and regulation of water balance in cells. Modification of plasma calcium concentration leads to the alteration of blood pressure. The lowering of serum calcium and the increase of intracellular calcium can cause an elevation of blood pressure in preeclamptic mothers. The serum magnesium also decreases in women with preeclampsia^(6,12). Generally, magnesium has been known as an essential cofactor for many enzyme systems. It also plays an important role in neurochemical transmission and peripheral vasodilatation. Magnesium sulfate appears to be safe and effective for the prevention of seizures and has been used as the drug of choice in severe

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preeclampsia and eclampsia treatment^(5,14). Besides the serum calcium and magnesium, the hyperuricemia is believed to result from the decreased renal excretion that occurs as a consequence of the preeclampsia but this result is probably also increased production secondary to tissue ischemia and oxidative stress. Soluble uric acid impairs nitric oxide generation in endothelial cells. Hyperuricemia induces endothelial dysfunction and may induce hypertension and vascular disease. Therefore, the modification of calcium, magnesium and uric acid metabolism during pregnancy could be one of the potential causes of preeclampsia^(4,5,15-21). However, the role and status of serum calcium, serum magnesium and serum uric acid in pregnant women are still being discussed. The aims of the present study were to measure serum levels of calcium, magnesium and uric acid in mild and severe preeclamptic pregnancy and compared with normal pregnancy.

Material and Method

The cross-sectional study was conducted in the Section of Obstetrics and Gynecology at Taksin Hospital between April 2006 and June 2007. The present study was approved by the Ethics Committee for Researches Involving Human Subjects, the Bangkok Metropolitan Administration. The studied population consisted of 36 normal pregnant women, 35 pregnant women with diagnosis of mild preeclampsia and 33 pregnant women with diagnosis of severe preeclampsia. All participants were \geq 28 weeks of pregnancy. Mild preeclampsia is defined as a blood pressure of at least 140/90 mmHg measured on two occasions each 6 hours apart, accompanied by proteinuria of at least 300 mg per 24 hours, or at least 1+ on dipstick testing⁽¹⁾. Severe preeclampsia is defined as having one or more of the following criteria: blood pressure of at least 160/110 mmHg measured on two occasions each 6 hours apart, proteinuria of at least 5 g per 24 hours, or at least 3+ on dipstick testing, oliguria of lesser than 500 ml per 24 hours, cerebral or visual disturbances, pulmonary edema or cyanosis, epigastric or right upper quadrant pain, impaired liver function, thrombocytopenia, fetal growth restriction⁽¹⁾. Fetal growth restriction is defined as the condition in which the newborn has a birth weight lesser than 10% for gestational age⁽²²⁾. Patients with a history of chronic or transient hypertension, history of renal disease or cardiovascular disease, thyrotoxicosis, hemophilia, diabetes mellitus class > C were all excluded.

On admission, venous serum samples were collected when the patients were in the supine position,

prior to their commencement to intravenous therapy. The venous blood was aspirated from the participant's antecubital vein, placed in a plain vacuum tube. At the time of blood collection, urine protein, edema and deep tendon reflexes were assessed. Urine protein was measured by dipstick and was graded on a scale of 0 to 4+ (0, none; 1+, 30 mg/dl; 2, 100 mg/dl; 3+, 300-1,999 mg/dl; 4+, at least 2,000 mg/dl). Deep tendon reflexes were assessed by striking the patellar tendon and grading the response on a scale of 1+ to 4+(1+, slight)movement of the foot; 2+, mild leg withdrawal; 3+, marked leg and foot movement; 4+, abrupt leg jerk and extension). The blood sample obtained on admission was also sent for complete blood count, serum calcium, magnesium, uric acid, prothrombin time and partial thromboplastin time.

Blood samples were allowed to clot at room temperature and then centrifuged at 2,000 rpm for 7 minutes. Serum aliquots were stored at 2-8 degree Celcius until analysis. Serum calcium was measured by photometric color test with Olympus calcium Arsenazo III OSR60117. The coefficient of variance within run and between run of serum calcium were 0.65% and 0.96% respectively. Serum magnesium was measured by colorimetric method by Roche Cobas Integra 800. The coefficient of variance within run and between run of serum calcium were 2.8% and 2.9% respectively. Serum uric acid was measured by enzymatic color test with Olympus OSR6098. The coefficient of variance within run and between run of serum uric acid were 1.55% and 2.44% respectively.

The data was analyzed with the SPSS software package version 15.0 and expressed in terms of mean, standard deviation (SD). Continuous variables of serum calcium, magnesium and uric acid concentrations of the three groups were compared by F-test from Analysis of Variances (ANOVA). Then Scheffe was used for post hoc comparisons if F-test had statistical significance. A p-value < 0.05 was considered to be statistically significant.

The sample size was calculated by using serum calcium and magnesium from the study of Sukonpan K et al⁽¹⁵⁾ and serum uric acid from the study of Pasaoglu H et al⁽²³⁾. The formula, used for calculating the sample size, was for a study using the student's t-test and considering alpha = 0.05 and beta = $0.1^{(24)}$. The calculated sample size was 30 cases/group.

Results

The present study enrolled 104 pregnant women. The clinical characteristics of the participants

are shown in Table 1. Age, hematocrit, platelet count and APGAR scores among normal pregnant women, mild and severe preeclamptic women were not significantly different. Normal pregnant women had mean gestational age more than both mild and severe preeclamptic women significantly $(38.3 \pm 1.97 \text{ weeks vs.})$ 36.31 ± 3.2 weeks, p = 0.035; and 36.24 ± 3.58 weeks, p = 0.03 respectively), but there was no significant difference between mild and severe preeclamptic women. There was no significant difference in BMI between normal pregnant women and severe preeclamptic women but the BMI of mild preeclamptic women was more than normal pregnant women and severe preeclamptic women significantly $(34.45 \pm 6.24 \text{ kg/m}^2 \text{ vs. } 27.99 \text{ kg/m}^2 \text{ vs. } 27.99$ $+5.49 \text{ kg/m}^2$, p = 0.002; and 27.26 + 8.95 kg/m², p < 0.001 respectively). The fetal birth weight of severe preeclamptic women was less than normal pregnant women significantly $(2593.28 \pm 749.74 \text{ g vs.} 3000 \pm 499.1 \text{ g, p} =$ 0.039) but there was no significant difference between mild preeclamptic women when compared to normal pregnant women and severe preeclamptic women.

In Table 2, the serum calcium in severe preeclamptic pregnant women was significantly less than normal pregnant women and mild preeclamptic women $(8.7 \pm 0.59 \text{ mg/dl vs}. 8.99 \pm 0.31 \text{ mg/dl}, p = 0.045; \text{ and}$ 9.05 ± 0.52 mg/dl, p = 0.014 respectively), but there was no significant difference in serum calcium between normal pregnant women and mild preeclamptic women. The serum uric acid in severe preeclamptic women was significantly more than normal pregnant women and mild preeclamptic women $(7.01 \pm 1.93 \text{ mg/dl vs.} 5.33 \pm$ 1.23 mg/dl, p < 0.001; and 5.95 ± 1.9 mg/dl, p = 0.044respectively). There was no significant difference in serum uric acid between normal pregnant women and mild preeclamptic women. Unlike serum calcium and uric acid, the serum magnesium in normal pregnant women was not significantly different when compared to mild and severe preeclamptic women.

Table 1. Comparisons of the clinical characteristics for the three groups of particip	pants
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	Normal pregnancy	Mild preeclampsia	Severe preeclampsia
	(n = 36)	(n = 35)	(n = 33)
Age (years) Gestational age (weeks) BMI (kg/m ²) Hematocrit (%) Platelet count (thsd/cumm) Birth weight (g) APGAR scores	$\begin{array}{c} 25.60 \pm 6.97 \\ 38.30 \pm 1.97 \\ 27.99 \pm 5.49 \\ 37.39 \pm 3.06 \\ 250.47 \pm 57.2 \\ 3000.00 \pm 499.1 \end{array}$	$\begin{array}{c} 29.09 \pm 8.01 \\ 36.31 \pm 3.20 * \\ 34.45 \pm 6.24 * * \\ 36.65 \pm 4.19 \\ 245.37 \pm 75.4 \\ 2938.50 \pm 450.8 \end{array}$	$\begin{array}{c} 25.60 \pm 7.04 \\ 36.24 \pm 3.58 * \\ 27.26 \pm 8.95 ^{*++} \\ 36.43 \pm 5.05 \\ 222.91 \pm 71.35 \\ 2593.28 \pm 749.74 * \end{array}$
1 minute	$\begin{array}{c} 8.89 \pm 0.31 \\ 9.57 \pm 1.89 \end{array}$	8.80 ± 0.41	8.16 ± 1.87
5 minutes		9.80 ± 0.41	9.22 ± 1.88

Values are given as mean \pm SD; n: number

Significance different by Scheffe:

* p < 0.05, ** p < 0.01, *** p < 0.001 compared with normal pregnancy

 $^{\scriptscriptstyle +}$ p < 0.05, $^{\scriptscriptstyle ++}$ p < 0.01, $^{\scriptscriptstyle +++}$ p < 0.001 compared between mild and severe preeclampsia

Table 2.	Comparisons	of serum	calcium,	magnesium	and	uric aci	id for	the three	groups of	partic	ripants
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	Normal pregnancy	Mild preeclampsia	Severe preeclampsia
	(n = 36)	(n = 35)	(n = 33)
Serum calcium (mg/dl) Serum magnesium (mg/dl) Serum uric acid (mg/dl)	$\begin{array}{c} 8.99 \pm 0.31 \\ 2.04 \pm 0.19 \\ 5.33 \pm 1.23 \end{array}$	$\begin{array}{c} 9.05 \pm 0.52 \\ 2.04 \pm 0.21 \\ 5.95 \pm 1.90 \end{array}$	$\begin{array}{c} 8.70 \pm 0.59^{*, \text{\tiny +}} \\ 2.24 \pm 0.62 \\ 7.01 \pm 1.93^{***, \text{\tiny +}} \end{array}$

Values are given as mean \pm SD; n: number

Significance different by Scheffe:

* p < 0.05, ** p < 0.01, *** p < 0.001 compared with normal pregnancy

 $^+$ p < 0.05, $^{++}$ p < 0.01, $^{+++}$ p < 0.001 compared between mild and severe preeclampsia

Discussion

In the present study, the mean serum calcium levels of normal pregnant women $(8.99 \pm 0.31 \text{ mg/dl})$ were less than the range (9.34-9.66 mg/dl) given by the previous report⁽²⁵⁾. The serum calcium level did not change throughout pregnancy in previous studies^(16,26), but the mean serum calcium level in severe preeclamptic women was less than normal pregnant women and mild preeclamptic women from the present study. The data supported the hypothesis that calcium might be a cause in the development of preeclampsia. The effect of serum calcium on changes in blood pressure could be explained by the level of intracellular concentration of calcium. The increase of intracellular calcium concentration when serum calcium went lower led to constriction of smooth muscles in blood vessels and increase of vascular resistance^(27,28). The present finding is similar to the previous studies^(18,25). However, the present finding was contradictory to some studies that the mean serum calcium levels in preeclampsia were not different from normal pregnancy^(16,26,29,30).

The mean serum magnesium level of normal pregnant women in the present study $(2.04 \pm 0.19 \text{ mg/dl})$ was within the range (1.35-2.23 mg/dl) given by previous report⁽³¹⁾. In the present study, the mean serum magnesium levels in both groups of preeclampsia were not significantly different from normal pregnancy. The present finding was similar to the findings of previous studies⁽³¹⁻³³⁾. This result is contradictory to some studies which reported that the mean serum magnesium level in preeclampsia was lower than normal pregnancy^(13,15,16). Generally, the hypomagnesemia in most pregnant women is associated with hemodilution, renal clearance during pregnancy and consumption of minerals by the growing fetus^(6,34). Previous studies reported a relationship between hypomagnesemia and pregnancy induced hypertension. Magnesium levels may have significant effects on cardiac excitability and on vascular tone, contractility and reactivity. They proposed that magnesium promoted vascular muscle relaxation^(16,17,35). Some studies showed that serum magnesium was even higher in the preeclamptic group than in normal pregnancy^(16,36). The difference may be explained by the variations of the studied population and the dietary intake.

The mean serum uric acid level of normal pregnant women in the present study $(5.33 \pm 1.23 \text{ mg/dl})$ was more than the range (3.5-5.1 mg/dl) given by a previous report⁽³⁷⁾. The mean serum uric acid in severe preeclamptic women was more than normal pregnant women and mild preeclamptic women. But there was no significant difference between normal pregnant women and mild preeclamptic women. The present finding is similar to the findings of previous studies^(30,34,38). Elevated serum uric acid levels due to decreased renal urate excretion are frequently found in women with preeclampsia^(4,19). Soluble uric acid impairs nitric oxide generation in endothelial cells. Thus, hyperuricemia can induce endothelial dysfunction⁽²⁰⁾. However, the present result is contradictory to some studies that the mean serum uric acid level in preeclampsia was not different from normal pregnancy^(39,40).

The present study showed that serum calcium in severe preeclamptic women was lower and serum uric acid was higher than normal pregnant women and mild preeclamptic women respectively but there was no difference between normal pregnant women and mild preeclamptic women. There was no difference in serum magnesium among normal pregnancy and both groups of preeclampsia. These findings support that hypocalcemia and hyperuricemia correlate to severe preeclampsia.

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ระดับแคลเซียม แมกนีเซียม และกรดยูริกในซีรัมของผู้ป่วยโรคพิษแห่งครรภ์กับสตรีตั้งครรภ์ปกติ

ชาญวิทย์ พันธุมะผล, บุญศรี กิตติโชติพาณิชย์

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบระดับแคลเซียม แมกนีเซียม และกรดยูริกในซีรัมของผู้ป่วยโรคพิษแห่งครรภ์ ชนิดไม่รุนแรงและชนิดรุนแรงกับสตรีตั้งครรภ์ปกติ

ประเภทงานวิจัย: Cross-sectional study

สถานที่ทำการวิจัย: กลุ่มงานสูติ-นรีเวชกรรม โรงพยาบาลตากสิน

วัสดุและวิธีการ: โดยการเก็บข้อมูลจากสตรีตั้งครรภ์ปกติ 36 ราย ผู้ป่วยโรคพิษแห่งครรภ์ชนิดไม่รุนแรง 35 ราย และ ผู้ป่วยโรคพิษแห่งครรภ์ชนิดรุนแรง 33 รายซึ่งรับเป็นผู้ป่วยในกลุ่มงานสูติ-นรีเวชกรรม โรงพยาบาลตากสิน ระหว่าง เดือนเมษายน พ.ศ. 2549 ถึงเดือน มิถุนายน พ.ศ. 2550 เก็บตัวอย่างเลือดจากหลอดเลือดดำ และนำไปวิเคราะห์ หาระดับแคลเซียม แมกนีเซียมและกรดยูริกในซีรัม นำข้อมูลมาวิเคราะห์ความแปรปรวน (ANOVA)

ผลการศึกษา: ในผู้ป่วยโรคพิษแห่งครรภ์ชนิดรุนแรงพบว่ามีค่าระดับแคลเซียมในซีรัมค่าต่ำกว่า (8.7 ± 0.59 มก./ดล. เปรียบเทียบกับ 8.99 ± 0.31 มก./ดล., ค่าพี = 0.045; และ 9.05 ± 0.52 มก./ ดล., ค่าพี = 0.014) และมีค่าระดับ กรดยูริกในซีรัมสูงกว่า (7.01 ± 1.93 มก./ดล. เปรียบเทียบกับ 5.33 ± 1.23 มก./ ดล., ค่าพี < 0.001 และ 5.95 ± 1.9 มก./ดล., ค่าพี = 0.044) เมื่อเปรียบเทียบกับสตรีตั้งครรภ์ปกติและผู้ป่วยโรคพิษแห่งครรภ์ชนิดไม่รุนแรง แต่ไม่มี ความแตกต่างของค่าเหล่านี้ระหว่างสตรีตั้งครรภ์ปกติและผู้ป่วยโรคพิษแห่งครรภ์ชนิดไม่รุนแรง การศึกษานี้ไม่พบ ความแตกต่างในระดับแมกนีเซียมในซีรัมระหว่างสตรีตั้งครรภ์ปกติและผู้ป่วยโรคพิษแห่งครรภ์ชนิดไม่รุนแรง สรุป: ภาวะแคลเซียมในซีรัมต่ำและกรดยูริกในซีรัมสูงมีความสัมพันธ์กับภาวะโรคพิษแห่งครรภ์ชนิดรุนแรง