

Study on Serum Calcium, Magnesium and Uric acid Levels in Preeclamptic and Healthy Pregnant Women - A Comparative Study

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ABSTRACT

Background & Objective: Pre-eclampsia is the most common medical complication of pregnancy associated with increased maternal and infant mortality and morbidity. Various dietary deficiencies or excesses have previously been linked to preeclampsia. Many studies have documented that the changes in the concentration of minerals like calcium, magnesium, and uric acid have a link to the etiopathogenesis of preeclampsia. The present study was undertaken to find the associations of serum calcium, magnesium, and uric acid with preeclampsia.

Methods: This cross-sectional comparative study was carried out in the Department of Physiology in collaboration with the Department of Biochemistry, Rajshahi Medical College, Rajshahi over a period of one year between July 2018 to June 2019. Pre-eclamptic and healthy pregnant women aged 18-35 years with single-tone pregnancies having a gestational age of 28-32 weeks were the study population. While preeclamptic pregnant women were included as cases, healthy pregnant women were included as controls. A total of 100 cases (pre-eclamptic women) and an equal number of controls (healthy pregnant women) were included. Serum calcium, magnesium, and uric acid levels of the subjects were compared between the case and the control groups to evaluate their association with preeclampsia.

Result: The findings of the study revealed that cases were older and heavier than the controls. However, both groups were alike in terms of gestational age. Both systolic and diastolic blood pressures were much higher in the case group than those in the control group. The serum calcium was significantly decreased in the case group than that in the control group ($p < 0.001$). The serum magnesium was also significantly dropped in the case group compared to the control group ($p < 0.001$). However, the serum uric acid was dramatically raised in the former group than that in the latter group ($p < 0.001$).

Conclusion: The study concluded that serum calcium and magnesium levels are significantly decreased and serum uric acid levels significantly increased in preeclamptic women.

Key words: Preeclampsia, calcium, magnesium, uric acid, association etc.

INTRODUCTION:

Pregnancy is essentially a period when a woman's body undergoes adaptive physiological changes to accommodate fetal growth.^{1,2} During pregnancy nutritional demand increases and many complex and interrelated biochemical, physiological, & anatomical alterations happen in the body.³ Biochemical parameters reflect these adaptive changes and are obviously distinct from those of the non-pregnant

state.⁴ The biochemical changes which occur in blood during normal pregnancy become exaggerated in complications of pregnancy like pre-eclampsia. Preeclampsia is one of the potential complications during this period, commonly associated with increased maternal and infant morbidity and mortality.^{4,5} It is a hypertensive disorder unique to pregnancy and is the second most common form of maternal morbidity. Its incidence in primigravidae is

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about 10% and in multigravidae about 5%.⁶ The prevalence of preeclampsia in developing countries ranges from 1.8-16.7%.⁷ WHO estimates the incidence of preeclampsia to be seven times higher in developing countries than that in developed countries.⁸ It is estimated that up to 30% of perinatal deaths are related to hypertensive disorders of pregnancy.

Preeclampsia is caused by multiple factors and the elimination of any one factor can reduce the mortality of mothers & infants. The pathophysiology of preeclampsia likely involves maternal-fetal physiological perturbations. Although the exact etiology is unknown,^{1,9} a number of dietary deficiencies or excesses have been linked as predisposing factors to preeclampsia. It has been observed that serum calcium level was significantly lower in preeclamptic women compared to normotensive pregnant women. Many studies have documented that the changes in the concentration of minerals like calcium, magnesium, and uric acid have a role in the etiopathogenesis of preeclampsia.^{3,10} As preeclampsia is more common in developing countries, it is assumed that nutritional deficiencies (diets that are low in minerals and vitamins) might have been implicated in its development.^{11,12}

Low serum calcium may cause high blood pressure by stimulating parathyroid hormone and renin release which, in turn, increases intracellular calcium in vascular smooth muscle, which causes vasoconstriction, increased vascular resistance, and rise of blood pressure in preeclamptic mothers.^{1,13,14} Calcium might have an indirect effect on smooth muscle function by increasing magnesium levels.¹⁵ Magnesium, by exerting its effect on tone, contractility, and reactivity of smooth muscles of blood vessels, causes peripheral vasodilatation. It thus plays a significant role in the physiological regulation of blood pressure.⁹ In addition, decreased magnesium increases the vasoconstrictor effect of angiotensin II and noradrenaline.¹⁶ Uric acid, a product of purine metabolism, is one of the most consistent and earlier detectable changes in preeclampsia. 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. Hyperuricemia induces endothelial dysfunction and may induce hypertension.¹⁶ Therefore, considering the physiological importance of calcium, magnesium, and uric acid levels, it appears that alteration in these micronutrients during pregnancy may be a risk or predisposing factor to preeclampsia. Despite numerous studies, the etiology of preeclampsia has not yet been fully elucidated.¹⁷ Thus, the present study was intended to investigate the associations of serum calcium, magnesium, and uric acid with preeclampsia.

METHODS:

This cross-sectional comparative study was conducted in the Department of Physiology in collaboration with the Department of Biochemistry, Rajshahi Medical College, Rajshahi over a period of one year between July 2018 to June 2019. Pre-eclamptic and healthy pregnant women aged 18-35 years with single-tone pregnancies having a gestational age of 28-32 weeks were the study population. While pre-eclamptic pregnant women served as the case group, healthy pregnant women served as the control group. Preeclampsia was defined as the new onset of hypertension to the extent of 140/90 mmHg and proteinuria or the new onset of hypertension plus significant end-organ dysfunction with or without proteinuria presenting after 20 weeks of gestation in a previously normotensive and non-proteinuric woman. Healthy pregnant women were termed as pregnant women with normal blood pressure without any systemic illness, gaining the right weight according to gestational period, and having no proteinuria. Pregnant women with a history of diabetes mellitus, renal disease, cardiovascular disease, known hypertension, severe anemia, twin pregnancy, diagnosed hydatidiform mole, hemophilia, and other preexisting medical conditions which may alter the study parameters were excluded from the study. A total of 100 cases and an equal number of controls were included.

Serum calcium, magnesium, and uric acid levels were measured by Semi Autoanalyzer Machine by

Enzymatic Colorimetric Method in the Department of Biochemistry, Rajshahi Medical College, Rajshahi. Data were processed and analyzed using SPSS (Statistics Package for Social Sciences) for Windows, version 23.0. The test statistics employed to analyze the data were descriptive statistics, Chi-square (χ^2), and Unpaired t-Test. While categorical data were compared between the study groups using Chi-square (χ^2) Test, the continuous data were analyzed using an Unpaired t-Test. The level of significance was set at 5% and a p-value < 0.05 was considered significant.

RESULTS:

The cases were significantly older and heavier than their control counterparts (p < 0.001 and p = 0.002 respectively). There was no difference between the groups in terms of gestational age with mean gestational age at entry being 30 weeks (p = 0.769). Both systolic and diastolic blood pressures were significantly higher in the former group than those in the latter group (p<0.001 and p<0.001 respectively) (Table I). The serum calcium was found to be significantly reduced in the case group compared to that in the control group (p<0.001). While the serum magnesium was observed to be drastically decreased, the serum uric acid was staggeringly high in the former group than that in the latter group (p < 0.001 and p < 0.001 respectively) (Table II).

Table I: Comparison of baseline characteristics between the study groups

Baseline characteristics	Group		p-value*
	Case (n=100)	Control (n=100)	
Age (years)	28.5 ± 4.0	26.6 ± 4.0	< 0.001
Gestational age (weeks)	30.4 ± 1.1	30.3 ± 1.2	0.769
BMI (kg/m ²)	23.0 ± 1.7	22.3 ± 1.2	0.002
Systolic BP (mmHg)	156.7 ± 8.3	111.2 ± 3.2	< 0.001
Diastolic BP (mmHg)	91.9 ± 4.3	74.6 ± 6.7	< 0.001

*Data were analyzed using an Unpaired t-Test and were presented as mean ± SD.

Table II: Comparison of Biochemical parameters between the study groups

Biochemical parameters	Group		p-value
	Case (n=100)	Control (n=100)	
Serum calcium (mg/dl)	6.2 ± 0.7	9.9 ± 0.4	< 0.001
Serum magnesium (mg/dl)	0.8 ± 0.1	2.0 ± 0.2	< 0.001
Serum uric acid (mg/dl)	8.1 ± 0.6	3.8 ± 0.6	< 0.001

*Data were analyzed using an Unpaired t-Test and were presented as mean ± SD.

DISCUSSION:

The present study was designed to compare the status of serum calcium, magnesium, and uric acid between preeclamptic and healthy pregnant women and thereby evaluate the role of these three micronutrients in the pathogenesis of preeclampsia. The study demonstrated that serum calcium and magnesium were decreased and serum uric acid was significantly increased in preeclamptic pregnant women. The data supported the hypothesis that a decrease in serum calcium might be a predisposing factor in the development of preeclampsia. Similar findings were reported by many investigators.^{2, 3,13,18-24} However, several investigators ruled out the association of serum calcium with preeclampsia.^{5,25-27} They refuted the involvement of low calcium in the pathogenesis of preeclampsia.

This difference in the findings may explain that preeclamptic pregnant women also might have relatively reduced^{1,25} dihydroxycholecalciferol levels compared to healthy pregnant women with a consequent increase in parathyroid hormone levels causing reabsorption of calcium from the distal renal tubules and the intestine causing no significant changes in the serum calcium level in preeclamptic pregnant women. The differences in the findings may also be attributed to the method of assay of serum calcium, differences in dietary habits, genetic pools as well as the socioeconomic status of the study populations. The dietary history of the participants in this study was, however, not elucidated. Additionally, differences in the sample size may also account for the observed differences in findings.

The serum magnesium in pre-eclamptic women was also significantly lower in comparison to healthy pregnant women, which is consistent with the findings of a number of recent studies.^{2,3,10,13,14,16-20,24,28} An increase in renal clearance during pregnancy, poor dietary intake, consumption of minerals by growing fetal skeletal systems, and haemodilution, all contribute to hypomagnesemia. However, several studies reported no association of magnesium with preeclampsia.^{9,11,26,29,30} The difference in the findings reported by different investigators could be

explained by the variation in the study population and dietary intake. The level of serum magnesium might be affected by dietary habits, physiological or pathological state, and the method of estimation used.

In the present study, serum uric acid level was raised in pre-eclamptic women when compared with healthy pregnant women. This finding is compatible with the previous studies.^{3,24,31,32,33} Two studies^{34,35} however did not find any significant association between serum uric acid and preeclampsia. In their study, all subjects were primigravida with singleton pregnancy and were recruited before their 20th week of gestation. It was possible that the effects of preeclampsia on the renal system early in pregnancy might be minimal to produce any detectable change in the serum uric acid level. However, the present study had several limitations, which must be taken into account before drawing a conclusion. The study was done on a smaller sample size using a cross-sectional design. The effect of supplementation of calcium and magnesium in preeclamptic pregnant women can be seen as a part of testing the hypothesis further. Moreover, many other clinical parameters such as urinary uric acid, and serum albumin had not been done, which could have been correlated with preeclampsia. One of the strengths of our study was that we included preeclamptic pregnant women who were diagnosed by a qualified obstetrician. We also included healthy pregnant women who were under antenatal care.

The overall findings of our study suggest that serum calcium and magnesium levels significantly decreased and serum uric acid levels significantly increased in preeclamptic women. Thus, assessment of these parameters during pregnancy could be useful in the early diagnosis of pregnant women at risk of preeclampsia, for early detection and supplementation of these micronutrients may reduce the incidence of preeclampsia. A regular periodic screening program with follow-up of the pregnant women is, therefore, recommended to properly define the value of estimation of these micronutrients during pregnancy to establish its link in the pathogenesis of preeclampsia.

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