

Status of Serum Calcium and Magnesium Level among Preeclamptic Patients

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Abstract

Background: Preeclampsia is a disorder of widespread vascular endothelial dysfunction. Like other developing countries, in Bangladesh it is one of the major complications during pregnancy. Preeclampsia is caused by multiple factors and elimination of any one factor can reduce the mortality of mothers and infants. **Objective:** The purpose of the present study was to assess the status of serum calcium and magnesium level among preeclamptic patients. **Methodology:** This was a cross-sectional comparative study which was carried out in the Department of Biochemistry of Mymensingh Medical College, Mymensingh, Bangladesh in co-operation with the Department of Obstetrics and Gynaecology of Mymensingh Medical College from July 2018 to June 2019. All patients of preeclampsia who were admitted to the Department of Obstetrics and Gynaecology at Mymensingh Medical College Hospital, Mymensingh, Bangladesh were investigated for serum calcium and magnesium levels on admission. Patients with other serious co-morbid diseases and chronic diuretic therapy were excluded. An automated biochemical analyser (Sysmex XS 1000i) will be used in this study for whole blood analysis in our laboratory. **Results:** The analysis revealed a highly significant decrease in serum calcium and magnesium levels in preeclamptic patients compared to controls. **Conclusion:** In conclusion, serum calcium and magnesium levels are significantly reduced in preeclamptic women, suggesting their potential role in the pathophysiology and management of preeclampsia.

Keywords: Preeclampsia; calcium; magnesium; pregnancy.

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Introduction

Pregnancy is a biological stress associated with many complex and interrelated biochemical, physiological, and anatomical alterations happening in the body¹. Biochemical changes seen in the blood during normal pregnancy are exaggerated in various complications of pregnancy like preeclampsia². Preeclampsia is an abnormality in pregnancy characterized by an increase in blood pressure levels and changes in blood trace element levels. Preeclampsia is commonly defined by a systolic blood pressure ≥ 140 mmHg or diastolic pressure ≥ 90 mmHg. Additionally, proteinuria may serve as a marker for preeclampsia when protein

level in a sample of urine exceeds 30 mg/dL. Preeclampsia can lead to organ disorders such as brain, liver and kidney injury. Although the mechanism of preeclampsia remains unknown, some evidence suggests a relationship with placentation and endothelial disorders³. Despite active research for many years, the etiology of this disorder remains unknown. It is the major cause of maternal and perinatal morbidity and mortality in developing countries. Approximately 10.0% to 15.0% of maternal mortality in developing countries are associated with preeclampsia. In Bangladesh, the incidence of preeclampsia is alarmingly high, about 16% of maternal deaths are associated with it.

Calcium is an important element in our body and plays an important role in muscle contraction and regulation of water balance in cells. Modification of plasma concentration leads to the alteration of blood pressure. The lowering of serum calcium and increase of cellular calcium can cause an elevation of blood pressure in preeclamptic women. The increase of cellular serum concentration when serum calcium went lower led to constriction of smooth muscle of blood vessels and increased vascular resistance. Serum calcium concentration measurement is a relatively easy, minimally invasive test and not very costly⁴.

On the other hand, Magnesium acts as a cofactor of many enzymes and also plays an important role in neurochemical transmission and peripheral vasodilation. Magnesium has a relaxant effect on blood vessels of pregnant women, and changes in the concentration of this element can lead to alteration of blood pressure, causing preeclampsia⁵. Serum magnesium level may decrease due to poor dietary intake, hemodilution or expansion of extracellular space. Reduction in the level of extracellular magnesium causes partial membrane depolarization and decreased repolarization along with opening of membrane calcium channels, leading to a shift of calcium intracellularly. This phenomenon produces vasoconstriction and raise blood pressure⁶. Further, it has been said that low serum magnesium increases endothelin-1-mediated smooth muscle contraction and hampers the release of prostacyclin from the endothelial cells of umbilical arteries, again manifesting as an increase in blood pressure.

Therefore, considering the above-mentioned facts, the present study was designed for evaluation of serum calcium and magnesium levels in pregnant women with preeclampsia and comparing them with those of the control group to verify the possible association between serum calcium, magnesium and preeclampsia.

Methodology

Study Settings and Population: This cross-sectional study was carried out at the Department of Biochemistry, Mymensingh Medical College and the subjects were collected from the Department of Obstetrics & Gynecology, Mymensingh Medical College Hospital, Mymensingh, Bangladesh. This study was carried out from July 2018 to June 2019. A total of 120 subjects were included in this studied. Out of them 60 were case (Group-II) and 60 were in control (Group-I). Group-I (control) consisted of 60 apparently normal healthy pregnant women aged between 20 to 40 years and gestational age more than 20 weeks, selected as controls in this study. Group-II (case) consisted of 60 diagnosed preeclamptic patients aged between 20-40 years and gestational age more than 20 weeks, selected as

cases in this study. Exclusion Criteria for both case and control were pre-existing hypertension before pregnancy from history, renal disease from history and other clinical findings, subjects taking any drugs containing calcium and magnesium for the last 5 months from history, drug that causes hyperuricemia and nephrotoxicity for the last 5 months from history.

Data Collection tools: A survey questionnaire was designed. Data were collected through a preformed data collection sheet (questionnaire). Measurements of height, weight were done with light clothes and without shoes. Blood pressure was taken after 10 minutes rest with standard cuffs for adults fitted with a mercury sphygmomanometer.

Data collection procedure: Data were collected after direct interview from patients or attendants. Informed consent were obtained from all participants. Blood was collected and analyzed for investigation. Structured case record forms were included.

Study procedure: For the purpose of the study, subjects both normal pregnant and preeclamptic patients were collected from the antenatal obstetric ward of Mymensingh Medical College Hospital, Mymensingh. The study subjects were selected on the basis of inclusion and exclusion criteria. Their informed written consent were taken. Age, gestational age, occupation, socio-economic status, residential address, family history of diabetes, hypertension, drug history, height, weight and other relevant data were collected and recorded in a preformed data collection sheet. For laboratory investigations, required amount of blood was collected, processed and preserved for estimation of different biochemical parameters. Data were then processed and analyzed to draw a conclusion.

Anthropometric measurements: Anthropometric measurements including height in meter (m), body weight in kilogram (kg) were measured using standardized techniques. Body mass indexes (BMI) of the subjects were calculated using standard formula, $BMI = \text{Weight (kg)} / [\text{Height (m)}]^2$.

Laboratory investigations: Serum calcium was determined by colorimetric method using the test kit. Serum magnesium was determined by colorimetric method using the test kit

Standardization of analytical technique: Analyses of different concentration of standard solution of serum calcium, magnesium, uric acid and creatinine were performed to obtain a calibration chart.

Quality control: Control sera (both normal and abnormal), duplicate standard and duplicate test serum were run in every batch of the test procedure.

Statistical Analysis: All biochemical values were expressed as mean $\pm$ SD (Standard deviation). Statistical significance of difference between two groups were evaluated by using Student's unpaired 't' test. All statistical analysis were done by using SPSS (Statistical Package for Social Science) version 21 windows package.

Ethical issues: Ethical implications were followed as per guidelines of BMRC. The study protocol was approved by the institutional review committee. Due permission will be taken from proper authority. All concerned were informed about the study. Informed written consent was taken from each participant. Data was collected from approved data collection form.

Results

In the present study, a total number of 120 subjects were participated. Out of them 60 normal healthy pregnant women were as control group (Group-I) and another 60 preeclamptic patients were selected as case group (Group-II). Different variables of the subjects were being analyzed and compared between Group-I and Group-II. Serum calcium, magnesium, levels were estimated from blood samples collected from 120 subjects. Some physical aspects such as maternal age, gestational age, BMI, systolic blood pressure (SBP) and diastolic blood pressure (DBP) of the subjects were also analyzed.

Serum calcium, magnesium, were expressed in mg/dl. Maternal age expressed in years, gestational age in weeks, BMI in Kg/m², systolic blood pressure (SBP) and diastolic blood pressure (DBP) in mm of Hg. All the values were expressed as mean $\pm$ SD and statistical significance of difference between two groups were evaluated by Student's unpaired 't' test. $P < 0.001$ considered as highly significant result. $P < 0.05$ considered as significant result. $P \geq 0.05$ considered as not significant (NS) result.

The study showed that serum calcium, magnesium, levels were lower in case (Group-II) when compared with control (Group-I) group. It was observed that mean serum calcium, magnesium, levels were 6.07 ± 0.80 mg/dl, 1.24 ± 0.28 mg/dl, in Group-II (case) and 9.23 ± 0.40 mg/dl, 2.17 ± 0.11 mg/dl, in Group-I (control) respectively. Statistical analysis of these parameter showed that the difference of mean values between case and control were and highly significant ($P < 0.001$).

In this study mean maternal age of the Group-II (case) and Group-I (control) were 29.70 ± 4.02 and 27.23 ± 4.40 years and mean gestational age of the Group-II (case) and Group-I (control) were 31.52 ± 2.76 and 31.70 ± 2.66 weeks respectively. The difference of mean values were not significant ($P > 0.05$). Mean BMI, SBP and DBP of the subjects were higher in case than control. Mean BMI, SBP

and DBP were 28.41 ± 1.25 kg/m², 148.50 ± 6.44 mm of Hg and 95.97 ± 4.80 mm of Hg in Group-II (case) and 26.27 ± 1.11 kg/m², 112.3 ± 6.93 mm of Hg and 72.73 ± 5.32 mm of Hg in Group-I (control) respectively. The difference of mean values were highly significant ($p < 0.001$) when case and control were compared.

Gestational age: Gestational age more than 20 weeks was selected both case and control group. It was observed that mean gestational age in Group-II (case) and Group-I (control) were 31.52 ± 2.76 and 31.70 ± 2.66 weeks respectively and the level of significance was 0.712 ($P > 0.05$). Thus the difference in mean gestational age was not significant between preeclamptic patients (case) and normal healthy pregnant women.

BMI: In this study, it was observed that mean BMI of the Group-II (case) and Group-I (control) were 28.41 ± 1.25 and 26.27 ± 1.11 Kg/m² respectively. A highly significant ($P < 0.001$) increase in BMI was observed in preeclamptic patients (case) compared to that of the healthy pregnant women.

Blood pressure: The study was revealed that the systolic blood pressure were higher in preeclamptic (case) group than in normal healthy pregnant control group. The mean systolic blood pressure of the Group-II and Group-I were 148.50 ± 6.44 and 112.30 ± 6.93 mm of Hg respectively. A highly significant ($P < 0.001$) increase in systolic blood pressure was observed in preeclamptic patients (case) compared to that of the healthy pregnant women. It was observed that the diastolic blood pressure were higher in preeclamptic (case) group than in normal healthy pregnant control group. The mean diastolic blood pressure of the Group-II and Group-I were 95.97 ± 4.80 and 72.73 ± 5.32 mm of Hg respectively. A highly significant ($P < 0.001$) increase in diastolic blood pressure was observed in preeclamptic patients (case) compared to that of the healthy pregnant women.

The values of all the clinical and biochemical parameters of the study subjects (case and control) were presented in Table- 1

Calcium Estimation: In this study, it was observed that mean serum calcium levels were 6.05 ± 0.82 and 9.20 ± 0.38 mg/dl in Group-II (case) and Group-I (control), respectively. A significant ($P < 0.05$) decrease in serum calcium levels were observed in preeclamptic patients (case) when compared to that of the normal healthy pregnant women. Analysis of mean serum calcium levels of study population were presented in Figure I.

Magnesium Estimation: In this study, it was observed that the mean values of serum magnesium levels were 1.24 ± 0.28 and 2.17 ± 0.11 mg/dl in Group-II (case) and Group-I (control) respectively. A highly significant ($P < 0.001$)

Table 1: Clinical Parameters of the Study Population (Mean $\pm$ SD)

Variables	Group-I (Control)	Group-II (Case)	P value
Maternal age(years)	27.23 $\pm$ 4.40	29.70 $\pm$ 4.02	0.002 ^{NS}
Gestational age (weeks)	31.70 $\pm$ 2.66	31.52 $\pm$ 2.76	0.712 ^{NS}
BMI (Kg/m ²)	26.27 $\pm$ 1.11	28.41 $\pm$ 1.25	P<0.001**
Systolic Blood Pressure (mm of Hg)	112.3 $\pm$ 6.93	148.50 $\pm$ 6.44	P<0.001**

P less than 0.05 taken as the level of significance; P<0.001 considered as highly significant result; P<0.05 considered as significant result; P $\geq$ 0.05 considered as not significant (NS) result; SD= Standard deviation.

decrease in serum magnesium levels was observed in preeclamptic patients (case) when compared to that of the normal healthy pregnant women. Analysis of mean serum magnesium levels of the study population was presented in Figure II.

Figure I: Comparison of Mean Serum Calcium Levels in the Study Population

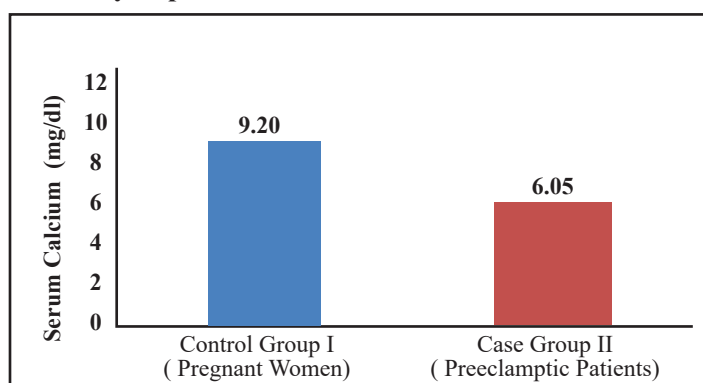
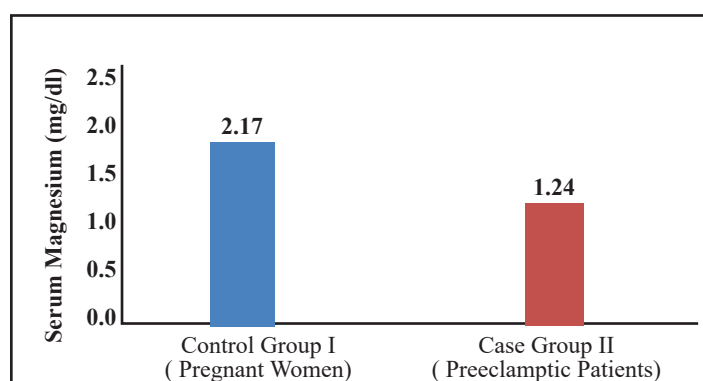


Figure II: Comparison of mean serum magnesium levels in the study population



Discussion

In the present study, mean $\pm$ SD of serum calcium was found 9.20 $\pm$ 0.38 mg/dl and 6.05 $\pm$ 0.82 mg/dl in Group-I (control) and Group-II (case), respectively. There was a highly significant (P<0.001) decrease in serum calcium in preeclamptic patients when compared to that of the control group. This finding was well correlated with other studies. A valid study suggested that there is an association between calcium consumption and preeclampsia. Changes in blood pressure during preeclampsia are attributable to changes in

serum calcium levels, which could be best explained by the level of intracellular calcium. The increase in intracellular calcium or decrease in serum calcium level leads to constriction of smooth muscle in blood vessels and subsequent increase in vascular resistance.

Ionized calcium is also crucial for synthesis of nitric oxide and prostacyclin and hence deficiency also aggravates oxidative stress. It has been found that the lowering of serum calcium and increase in concentration of cellular calcium may lead to elevation of blood pressure in a preeclamptic pregnant female. Another study showed that abnormalities in calcium homeostasis may contribute to the increased vascular sensitivity as documented in preeclampsia. According to a study, in preeclampsia, there is cellular injury and cellular death may occur which results in an influx of calcium ions into cells, leading to increased intracellular calcium ions and loss of calcium homeostasis. Another study showed that low serum calcium may cause high blood pressure by stimulating PTH and renin release and also by vasoconstriction by increasing its level in vascular smooth muscle. Another study suggested that low calcium in the serum also elicits calcitriol response, which stimulates calcium influx into vascular endothelial cells, thus increasing blood pressure⁷⁻¹².

However, controversial studies found no significant differences in the serum levels of calcium between preeclampsia and healthy pregnant individuals. they explained, decrease mobility may be the cause of normal level of serum calcium in preeclampsia. When the bones have less work to do, they can weaken and release more calcium into the bloodstream. So serum calcium level did not decrease. A conflicting study observed that there was increased in serum calcium level in preeclampsia than normal pregnant. The increased level of serum calcium in preeclampsia may be due to increased maternal bone resorption associated with a reduced fetoplacental demand for calcium in preeclampsia due to intrauterine growth restriction.

In the present study, mean $\pm$ SD of serum magnesium levels were found 2.17 $\pm$ 0.11 mg/dl and 1.24 $\pm$ 0.28 mg/dl in Group-I (control) and Group-II (case), respectively. There was a significant (P<0.001) decrease in serum magnesium

in preeclamptic patients when compared to that of the control group. Many studies showed that during pregnancy, the hemodilutional effect of estrogen and increased fetal demand decrease the serum magnesium level, and in preeclampsia, urinary excretion of magnesium also increases.

According to some studies, the decreased level of magnesium in women with preeclampsia could be due to decreased dietary intake, increased clearance by the kidneys, hemodilution due to expansion of extracellular space and increased consumption of minerals by the growing fetus. A few studies suggested that, an increase in the renal clearance during pregnancy may contribute to the reduction in serum magnesium, since the kidney is the main regulator of the body's magnesium. Another study showed that serum magnesium level was significantly reduced in preeclamptic mothers compared with the healthy group. Their study also revealed that the level of magnesium in preeclamptic women was not only significantly low when the diagnosis was confirmed, but also the initial level from early in the pregnancy was lower than the healthy pregnant group.

Their observation suggested that hypomagnesaemia may be one of the etiologies of preeclampsia. Magnesium is one of the essential intracellular cations and an important cofactor for activation of many enzymes. Magnesium has a significant role in pathophysiological regulation of blood pressure because it affects contractility and tone of blood vessels. These results show the relationship between the levels of elements in serum of mothers and fetus in Preeclampsia¹³⁻¹⁶.

However, some controversial studies found that no significant change in serum magnesium in preeclamptic patients compared to normal pregnancy. Magnesium may act by opposing calcium-dependent arterial constriction and may also antagonize the increase in intracellular calcium concentration¹⁷⁻¹⁸.

Conclusion

Preeclampsia is a disorder of widespread vascular endothelial dysfunction. Like other developing countries, in pregnancy. Analyzing the findings of the present study, significant alterations in serum calcium and magnesium levels were observed in preeclamptic patients. Therefore, it may be recommended that routine investigations of these biochemical parameters be included for pregnant women who attended the antenatal clinic, as this may help in the establishment of the diagnosis of preeclampsia before the appearance of its clinical manifestations and also produce a beneficial impact on the management of preeclampsia, which is still an important cause of maternal mortality and

adverse perinatal outcomes.

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Conflict of Interest: We do not have any conflict of interest.

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