# **Original** Article

# Serum Calcium and Its Association with Preeclampsia

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## <u>Abstract</u>

Background: The purpose of the study was to evaluate association of serum calcium concentration with preeclampsia. Method: This study was carried out in the Department of Obstetrics and Gynaecology of Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from January 2016 to December 2016 including 120 antenatal patients in their second half of pregnancy. All the included patients were classified as 40 mild preeclampsia (Group A) 40 severe preeclampsia (Group B) and 40 normal pregnant women (Group C). Serum calcium was estimated in the Department of Biochemistry and correlated with preeclampsia. **Result:** In results the mean serum calcium concentration was found 8.2±0.2mg /dl in Group A, 7.6  $\pm$  0.3 mg/dl in Group B and 9.0 $\pm$ 0.5 mg/dl in Group C (p=0.001). Low serum calcium was found 53.7% and 12.5% in case and control respectively. The difference was statistically significant (p = < 0.05) between case and control groups having OR=8.1 with 95% CI (2.7 - 26.5) %. Pearson's correlation test revealed that both systolic and diastolic blood pressure had negative correlation with the serum calcium concentration (p = <0.05). Conclusion: In conclusion this study showed that low serum calcium is associated with preeclampsia and its concentration inversely proportional to the severity of preeclampsia and both systolic and diastolic blood pressure.

Keywords: Serum calcium; Preeclampsia; Systolic and diastolic blood pressure; Normal pregnant women.

Bangladesh Journal of Medical Science Vol. 20 No. 02 April'21. Page : 379-383 DOI: https://doi.org/10.3329/bjms.v20i2.51552

## **Introduction**

Preeclampsia is a hypertensive disorder in pregnancy which is characterized by the occurrence of new onset of persistent hypertension with new onset of proteinuria or in absence of proteinuria presence of new onset of end organ damage, usually after 20 weeks of gestation.<sup>1</sup> Around 40,000 women, mostly from developing countries, die each year due to preeclampsia or eclampsia. Preeclampsia alone is estimated to account for about 40% to 60% of maternal deaths in developing countries.<sup>2</sup> The prevalence of preeclampsia in developing countries ranges from 1.8% to 16.7%.<sup>2-3</sup> Despite active research for many years, the etiology of this disorder remains unknown. 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 cellular calcium can cause an elevation of blood pressure

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in preeclamptic women. The increase of cellular calcium concentration when serum calcium went lower led to constriction of smooth muscles in blood vessels and increase of vascular resistance.<sup>4</sup> Serum calcium concentration measurement is relatively easy, minimally invasive test and not very much costly. Therefore, considering the above mentioned facts, the present study was designed for evaluation of serum calcium concentration in pregnant women with preeclampsia and comparing them with those of the control group to verify the possible association between low serum calcium and preeclampsia.

#### **Materials and Methods**

This case control study was carried out at the Obstetrics and Gynaecology Department Bangabandhu Sheikh Mujib Medical University (BSMMU) from January 2016 to December 2016. A total number of 120 women were included in this study, of whom 40 were with mild Preeclampsia (Group A) 40 with severe preeclampsia (Group B) and the other 40 were normal pregnant women without preeclampsia taken as controls (Group C). All subjects were selected according to the eligibility criteria by purposive sampling. Case and control were matched for gestational age, parity, anthropometric and socioeconomic status. Age of the subjects were within 18 to 38 years, gestational age within >20 weeks to 40 weeks, subjects who gave informed written consent, singleton pregnancy, systolic blood pressure (SBP)  $\geq$  140 mm of Hg and/ or Diastolic blood pressure (DBP)  $\geq$  90 mm of Hg, proteinuria  $\geq$  1+ in Dipstick method were enrolled as case and Blood pressure < 140/90 mm of Hg, Proteinuria- nil/ trace were enrolled as control. However, pregnant women with multiple pregnancy, diabetes, renal disease, cardiac disease, gestational hypertension, chronic hypertension, hemorrhagic disorder were excluded from this study. Detailed socio-demographic data, obstetric history, gestational age, family history and medical history were recorded in a predesigned data sheet. Then physical examination was performed and recorded.

After 10 minutes' rest, blood was measured following standard procedure. Korotkoff phase 1(first beat heard) and phase V (disappearance of sound) were used to determine systolic pressure (SBP) and diastolic blood pressure (DBP). When blood pressure found elevated on initial assessment, the measurement was repeated at least 4 to 6 hours apart to confirm hypertension. Proteinuria was measured by dipstick method. After selecting case and control, with all aseptic precaution 05ml antecubital venous blood sample was collected from each subject for measurement of serum calcium. Blood was immediately transferred into a clean dry test tube and sent to Biochemistry laboratory of BSMMU. Serum calcium was estimated by Arsenazol-III. It is recommended that each laboratory determine its own reference range based upon its particular locale and population characteristics. Where was our reference value of serum calcium 8.5 - 10.5 mg/dl considered as normal.

#### Statistical analysis

Statistical analysis of the results was obtained by using window based computer software devised with Statistical Packages for Social Sciences (SPSS-20). Mean comparison among three groups were done by ANOVA test. Chi square test was done to see the significance of difference between case and control. Strength of association was determined by estimating odds ratios (OR) and their 95% confidence intervals (CI). To understand the relationship between two variables Pearson's correlation coefficient (r) was done. Probability of <0.05 was considered as statistically significant.

Table I: Comparison of mean serum calcium in case and control groups

	Group A(n=40)	Group B(n=40)	Group C(n=40)	<i>p</i> value
	Mean±SD	Mean±SD	Mean±SD	
Serum calcium (mg/dl)	8.2±0.2	7.6±0.3	9.0±0.5	0.001 <sup>s</sup>

p-value reached from ANOVA test

F value:155.79 with df (2,117)

Table II: Result of serum calcium concentration in case and control groups

Serum calcium	Case (n=80)		Control (n=40)		OR 95 CI%	p Value
(mg/di) -	n	%	n	%	-	
Low <8.5 mg	43	53.7	5	12.5	8.1	0.0015
Norma (8.5-10.5) mg	37	46.3	35	87.5	(2.7 - 26.5)	0.0015

*p*-value reached from chi square test

Chi value 18.90 with df 1



**Figure 1:** Scatter diagram showing a significant negative Pearson's correlation coefficient of serum calcium concentration with systolic blood pressure r=-0.746 (p=0.001) and Diastolic blood pressure r=-0.688 (p=0.001) in preeclampsia group.

**Ethical clearance:** This study protocol was approved by the Institutional Review Board, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

### **Results**

In this present study the mean serum calcium was found  $8.2\pm0.2$  mg/dl in Group A,7.6±0.3 mg/dl in Group B and 9.0±0.5 mg/dl in Group C. The difference was statistically significant (p<0.05) among three groups. The mean serum calcium was significantly (p<0.05) lower in severe preeclampsia as compared to mild preeclampsia and normal pregnant women (Table I). It was found that low serum calcium level (<8.5mg/dl) 8.1 times significantly increased to developed preeclampsia with 95% CI (2.7 – 26.5) %; p=<0.05(Table II). Pearson's correlation test revealed that both systolic blood pressure (r= -0.746; p=0.001) and diastolic blood pressure (r= -0.688; p=0.001) had negative correlation with the serum calcium concentration (Figure 1).

### **Discussion**

In this present study, it was observed that 53.7% of pregnant women with preeclampsia was associated with low serum calcium, where as it was just 12.5% among the normal pregnancy. The mean serum calcium was significantly lower (*p*=0.001) in the cases as compared to controls.

Baruah and Biju Choudhury<sup>5</sup> obtained in his study that serum calcium level was significantly lower in preeclampsia group in comparison to those of control group (p<0.05). Kanagal et al.<sup>6</sup> obtained in their study that the serum calcium concentration was significantly lower in the preeclamptic cases as compared to the normotensive controls, where the mean serum calcium concentration were 7.84±0.87 mg/dl and 8.97± 0.69 mg/dl, (p<0.05) respectively, which support with the present study.

In India Sharma, <sup>7</sup> observed the mean serum calcium was  $7.20\pm0.44$  mg/dl in normal pregnancy women,  $7.13\pm0.26$  mg/dl in mild preeclampsia women and  $6.89\pm0.31$  mg/dl in severe preeclampsia women. The serum calcium concentration in severe preeclamptic pregnant women was significantly lower than that in normal pregnant women and mild preeclamptic women.

Many investigators Adewolu,<sup>8-9</sup> showed serum calcium level in severe preeclamptic women had significantly lower than normal pregnant women and mild preeclamptic women. The above findings were closely resembled with the current study.

The present study result was contradictory to some studies that the mean serum calcium levels in preeclampsia were not different from normal pregnancy like.<sup>10-12</sup>

Levine et al.<sup>13</sup> in a prospective study in American population showed that calcium supplementation during pregnancy did not prevent preeclampsia in healthy nulliparous women. Conversely, Crowther et al.<sup>14</sup> in Colombia reported in their own studies lowering of blood pressure with calcium supplementation in primigravid women.

In this study it was observed that a significant negative Pearson's correlation between serum calcium concentration with systolic and diastolic blood pressure. Similarly, Suryono et al.<sup>15</sup> obtained in their study that there was a significant correlation between blood calcium levels with systolic blood pressure (p<0.001), with a negative correlation coefficient of 0.62 which indicates a very strong relationship between the decrease in blood calcium levels and increase in systolic blood pressure, which is consistent with the current study. The authors reported that there was a significant correlation between blood calcium level with diastolic blood pressure (p<0.05), with a negative correlation coefficient of 0.65, which indicates a very strong

correlation between the decrease in blood calcium level and the increase in diastolic blood pressure.

## Conclusion

In this study, it has been revealed that low serum calcium is associated with preeclampsia. Both the mean and the percentage of serum calcium were significantly lower in preeclampsia cases as compared to their normal counterpart. Both the systolic and diastolic blood pressure had negative association with low serum calcium concentration.

# Conflict of interest: None declared

# **Authors' Contributions:**

Conceptual work: Sultana Parvin, Saleha Begum Chowdhury, K. N. Nahar, MD. Mozammel Hoque Data collection: Sultana Parvin

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Editing of final manuscript: Sultana Parvin, Saleha Begum Chowdhury, K. N. Nahar, MD. Mozammel Hoque

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