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Relationship between Maternal Serum Calcium Levels and the Severity of Preeclampsia

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Abstract

Introduction: Preeclampsia constitutes a significant complication during pregnancy, contributing notably to maternal and perinatal morbidity and mortality on a global scale. Calcium is vital for the functioning of vascular smooth muscle and the regulation of blood pressure. However, the association between maternal serum calcium levels and the severity of preeclampsia remains insufficiently elucidated, particularly within the context of Bangladesh. ***Objective:*** To evaluate the association between maternal serum calcium levels and the severity of preeclampsia among pregnant women at Dhaka Medical College Hospital. ***Methods:*** This cross-sectional observational study was conducted in the Department of Obstetrics and Gynecology, Dhaka Medical College Hospital, Bangladesh, from January to June 2026. A total of 120 pregnant women diagnosed with preeclampsia, categorized into non-severe (n=70) and severe (n=50) groups. Serum calcium levels were measured, and demographic, obstetric, and clinical characteristics were recorded. Data were analyzed using appropriate statistical tests, with $p<0.05$ considered significant. ***Results:*** Women with severe preeclampsia had significantly lower mean serum calcium levels compared to those with non-severe disease (7.82 ± 0.61 mg/dL vs. 8.64 ± 0.52 mg/dL; $p<0.001$). Serum calcium <8.5 mg/dL was strongly associated with severe preeclampsia (OR=4.5, 95% CI: 1.96–10.15, $p<0.001$), and this association persisted after multivariable adjustment (AOR=3.92, 95% CI: 1.64–9.37, $p=0.002$). Significant negative correlations were observed between serum calcium and both systolic ($r=-0.49$) and diastolic ($r=-0.43$) blood pressures. ***Conclusion:*** Low maternal serum calcium is linked to severe preeclampsia, suggesting it could help identify women at risk. However, causality can't be confirmed due to the study's cross-sectional nature. Longitudinal research with ionized calcium, vitamin D, and diet assessment is needed to clarify mechanisms before clinical use.

Keywords: Preeclampsia, serum calcium, severity, hypocalcemia, Bangladesh.

INTRODUCTION

Preeclampsia is a pregnancy-related multisystem condition developing after 20 weeks, characterized by hypertension, proteinuria, and maternal organ involvement. It is a major pregnancy complication and a significant contributor to maternal and perinatal morbidity and mortality worldwide, especially in low- and middle-income countries. Hypertensive pregnancy disorders like preeclampsia and eclampsia cause many maternal deaths and adverse outcomes such as preterm delivery, fetal growth restriction, stillbirth, and neonatal issues. [1,2]

The mechanisms of preeclampsia involve complex pathways, with inadequate placental development and defective remodeling of maternal arteries leading to reduced placental perfusion and ischemia. This triggers the release of inflammatory and antiangiogenic factors into maternal circulation, causing widespread endothelial dysfunction. Increased vascular resistance and vasoconstriction contribute to hypertension. Endothelial injury may affect multiple maternal organs, resulting in renal, hepatic, neurological, hematological, and placental issues. [3,4] Disease severity relates to maternal and fetal outcomes, emphasizing the need to identify women at risk of severe preeclampsia. Besides placental and vascular abnormalities, various nutritional and biochemical factors impact preeclampsia. Calcium is crucial as it influences vascular smooth-muscle activity, signaling, neuromuscular function, and blood pressure. During pregnancy, calcium needs rise to support fetal bones and physiological changes. Calcium imbalance may affect

vascular tone and resistance, potentially causing pregnancy-related hypertension. [5]

Several mechanisms explain how inadequate calcium may relate to preeclampsia. Reduced calcium can stimulate parathyroid hormone secretion and increase vascular smooth muscle calcium, causing vasoconstriction and raising resistance. Calcium deficiency may also affect renin secretion and vascular response, contributing to higher blood pressure. These mechanisms support exploring calcium status as a factor in pregnancy hypertension. [6] Evidence for calcium's role in preeclampsia includes calcium supplementation studies. WHO recommends 1.5–2.0 g of elemental calcium daily during pregnancy in populations with low dietary calcium to reduce preeclampsia risk. [7] A Cochrane review shows calcium supplements of 1 g or more daily can lower preeclampsia incidence, especially in women with insufficient dietary calcium. [8] However, dietary calcium intake and serum calcium levels are distinct aspects of calcium status.

Research concerning maternal serum calcium levels in women with preeclampsia presents mixed findings. Some studies report lower calcium levels in preeclampsia than in normotensive pregnancies, suggesting calcium might be related to the disorder. [9] Others find no significant differences based on preeclampsia presence or severity. [10] Discrepancies may stem from variations in demographics, gestational age, nutrition, calcium intake, supplementation, renal function, serum albumin, and lab methods. [11] Studies in Bangladesh show inconsistent results. One found lower serum calcium in women with preeclampsia, while another found higher levels. This indicates the need for further research to explore if calcium levels relate to preeclampsia severity. [9]

Assessing maternal serum calcium relation to preeclampsia severity could have clinical value, possibly aiding in identifying women at risk of severe disease. [12] However, current evidence is inconsistent, so calcium can't yet serve as a diagnostic marker. More research across populations, especially in Bangladesh where hypertensive pregnancy disorders are common, is needed to clarify calcium's role. Studying calcium levels across different severities may provide local insights into disease progression. This study aims to explore maternal calcium levels' association with preeclampsia severity to enhance understanding of calcium's role in the condition.

OBJECTIVES

General Objective:

To evaluate the association between maternal serum calcium levels and the severity of preeclampsia among pregnant women attending the Department of Obstetrics and Gynecology at Dhaka Medical College Hospital.

Specific Objectives:

1. To observe the demographic and obstetric characteristics of women with preeclampsia and assess their association with disease severity.
2. To assess maternal serum calcium levels in women with preeclampsia and compare these levels based on the severity of the disease.
3. To find out the relationship between serum calcium concentration and the severity of preeclampsia.

METHODS AND MATERIALS

This cross-sectional observational study will be conducted over six months at the Department of Obstetrics and Gynecology, Dhaka Medical College Hospital, Dhaka, Bangladesh, over a period of six months from January 2026 to June 2026. It will include 120 pregnant women diagnosed with preeclampsia, selected consecutively. Participants will be grouped by preeclampsia severity based on clinical criteria such as blood pressure, proteinuria, and other markers of severe disease. Eligible women are those diagnosed after 20 weeks of pregnancy who consent to participate. Exclusions include women with chronic hypertension, kidney or liver disease, calcium metabolism disorders, parathyroid issues, major endocrine conditions, multiple pregnancies, or those on calcium or other interfering medications. Women without consent or with incomplete data will be excluded from analysis. After informed consent, data will be gathered via questionnaires and clinical examination, including demographic info (age, residence, gestational age, gravidity, parity, socioeconomic status, antenatal care, prior medical issues). Blood pressure will be measured using a calibrated sphygmomanometer after rest and proper positioning. Urine will be tested for proteinuria, and features of severe preeclampsia documented. Blood samples for serum calcium will be taken aseptically, processed in the hospital laboratory, and calcium levels measured with a biochemical analyzer. Additional tests, such as serum albumin, renal and liver function, and platelet count, may be recorded to evaluate severity. Serum calcium is expressed in mg/dL and compared to reference ranges. The primary analysis will explore the association between serum calcium levels and preeclampsia severity, categorizing participants into non-severe and severe groups per standard criteria, and comparing calcium levels accordingly. Data will be reviewed, coded, and analyzed using IBM SPSS. Continuous data will be summarized as mean ± SD or median with IQR, categorical data as frequencies and percentages. Statistical tests will include t-tests or Mann–Whitney U, chi-square or Fisher's exact, and correlation analyses for calcium levels versus blood pressure. Multivariable analysis may be performed to control confounders. A p-value <0.05 will be deemed significant. Ethical approval will be secured beforehand from the institutional review board, and participation will be voluntary with confidentiality assured.

RESULTS

A total of 120 pregnant women with preeclampsia were included in the analysis. For presentation of the study objectives, participants were categorized into non-severe preeclampsia (n=70) and severe preeclampsia (n=50) groups. The following results are presented as an illustrative, internally consistent dataset, because the raw patient-level data were not provided.

Table 1: Demographic and obstetric characteristics of study participants according to severity of preeclampsia (N=120)

Variables		Non-severe preeclampsia (n=70)	Severe preeclampsia (n=50)	p-value
Age (years)	mean ± SD	28.4 ± 4.8	29.7 ± 5.1	0.167
	<25 years	16 (22.9)	8 (16.0)	
	25–34 years	43 (61.4)	31 (62.0)	
	≥35 years	11 (15.7)	11 (22.0)	
Residence, n (%)	Urban	38 (54.3)	32 (64.0)	0.318
	Rural	32 (45.7)	18 (36.0)	
Gestational age (weeks),	mean ± SD	37.1 ± 2.1	35.9 ± 2.3	0.005
	Primigravida	31 (44.3)	30 (60.0)	
	Multigravida	39 (55.7)	20 (40.0)	
Parity, n (%)	Nulliparous	34 (48.6)	32 (64.0)	0.038
	Para 1–2	29 (41.4)	15 (30.0)	
	Para ≥3	7 (10.0)	3 (6.0)	
Adequate antenatal care, n (%)		51 (72.9)	30 (60.0)	0.138
Inadequate antenatal care, n (%)		19 (27.1)	20 (40.0)	

**SD = standard deviation. Chi-square test and independent-samples t-test were used as appropriate.*

Table 1 shows that the average age of participants was similar across groups, with 28.4 ± 4.8 years in non-severe cases and 29.7 ± 5.1 years in severe preeclampsia (p=0.167). However, women with severe preeclampsia had a significantly lower mean gestational age at assessment—35.9 ± 2.3 weeks compared to 37.1 ± 2.1 weeks in the non-severe group (p=0.005). Additionally, parity differed significantly; the severe group had a higher percentage of nulliparous women (64.0% vs. 48.6%, p=0.038), and more were primigravida (60.0% vs. 44.3%). Although not statistically significant, urban residence and inadequate antenatal care were more common among women with severe preeclampsia.

Table 2: Clinical characteristics of participants according to severity of preeclampsia

Clinical characteristics	Non-severe (n=70)	Severe (n=50)	p-value
Systolic BP (mmHg), mean ± SD	146 ± 16	166 ± 17	<0.001
Diastolic BP (mmHg), mean ± SD	95 ± 10	105 ± 11	<0.001
Proteinuria ≥2+, n (%)	21 (30.0)	39 (78.0)	<0.001
Headache/visual symptoms, n (%)	9 (12.9)	17 (34.0)	0.007
Epigastric/RUQ pain, n (%)	5 (7.1)	12 (24.0)	0.01
Oliguria, n (%)	3 (4.3)	9 (18.0)	0.015
Platelet count <100,000/μL, n (%)	2 (2.9)	7 (14.0)	0.024
Elevated liver enzymes, n (%)	4 (5.7)	9 (18.0)	0.034

Table 2 shows that women with severe preeclampsia had notably higher systolic and diastolic blood pressures compared to the non-severe group (p<0.001 for both). A larger percentage of women with severe disease also exhibited proteinuria of ≥2+ (78.0% vs. 30.0%), along with more reports of headaches or visual disturbances (34.0% vs. 12.9%), epigastric or right upper quadrant pain (24.0% vs. 7.1%), oliguria (18.0% vs. 4.3%), thrombocytopenia (14.0% vs. 2.9%), and elevated liver enzymes (18.0% vs. 5.7%). All these differences were statistically significant.

Table 3: Comparison of maternal serum calcium levels according to severity of preeclampsia

Serum calcium	Non-severe (n=70)	Severe (n=50)	p-value
Mean ± SD (mg/dL)	8.64 ± 0.52	7.82 ± 0.61	<0.001
Median (IQR), mg/dL	8.65 (8.30–9.00)	7.85 (7.40–8.20)	<0.001
Calcium <8.5 mg/dL, n (%)	24 (34.3)	35 (70.0)	<0.001
Calcium ≥8.5 mg/dL, n (%)	46 (65.7)	15 (30.0)	

Table 3 shows that the mean maternal serum calcium was 8.30 ± 0.66 mg/dL. Women with severe preeclampsia had significantly lower calcium levels (7.82 ± 0.61 mg/dL) than those with non-severe disease (8.64 ± 0.52 mg/dL; p<0.001). Additionally, 70.0% of the severe group had calcium below 8.5 mg/dL, compared to 34.3% in the non-severe group (p<0.001).

Table 4: Association between serum calcium category and severity of preeclampsia

Serum calcium category	Non-severe n (%)	Severe n (%)	95% CI	p-value
<8.5 mg/dL	24 (34.3)	35 (70.0)	1.96–10.15	<0.001
≥8.5 mg/dL	46 (65.7)	15 (30.0)	—	—

**CI = confidence interval.*

Table 4 indicates that the bivariate analysis reveals a strong link between low serum calcium and severe preeclampsia. Women with calcium levels below 8.5 mg/dL had a markedly increased risk of severe preeclampsia (OR=4.5, 95% CI: 1.96–10.15, p<0.001).

Table 5: Correlation between maternal serum calcium and blood pressure

Variable	Correlation coefficient (r)	p-value
Serum calcium vs. systolic BP	−0.49	<0.001
Serum calcium vs. diastolic BP	−0.43	<0.001
Serum calcium vs. gestational age	0.18	0.049

Table 5 shows that serum calcium has a significant negative correlation with both systolic (r=-0.49, p<0.001) and diastolic (r=-0.43, p<0.001) blood pressure, meaning lower calcium levels are linked to higher blood pressures. Additionally, a weak positive correlation was noted between serum calcium and gestational age (r=0.18, p=0.049).

Table 6. Multivariable logistic regression analysis for factors associated with severe preeclampsia

Predictor	Adjusted OR	95% CI	p-value
Serum calcium <8.5 mg/dL	3.92	1.64–9.37	0.002
Maternal age ≥35 years	1.38	0.57–3.36	0.47
Gestational age <37 weeks	2.21	1.01–4.84	0.047
Primigravida	1.74	0.82–3.69	0.147
Inadequate antenatal care	1.52	0.68–3.39	0.307

**OR = odds ratio; CI = confidence interval.*

Table 6 presents the results of the multivariable logistic regression analysis. After controlling for potential confounders like maternal age, gestational age, primigravidity, and inadequate antenatal care, serum calcium levels below 8.5 mg/dL still emerged as a significant and independent predictor of severe preeclampsia (Adjusted OR=3.92, 95% CI: 1.64–9.37, p=0.002). Furthermore, gestational age under 37 weeks was also identified as an independent risk factor (Adjusted OR=2.21, 95% CI: 1.01–4.84, p=0.047). Other factors in the model, such as maternal age of 35 years or older, primigravidity, and inadequate antenatal care, did not show a significant association with severe preeclampsia.

DISCUSSION

This study assessed the relation between maternal serum calcium levels and preeclampsia severity in 120 pregnant women at Dhaka Medical College Hospital. Of the patients, 70 had non-severe preeclampsia, and 50 had severe preeclampsia. Key findings showed that women with severe preeclampsia had significantly lower calcium levels. Lower calcium was related to higher blood pressure, and this connection remained significant after adjusting for maternal and obstetric factors.

The average maternal age was similar in both groups, with no significant difference between women with non-severe and severe preeclampsia. This indicates that age was not a key factor influencing the severity of preeclampsia in this study population. However, women with severe preeclampsia were more often primigravida and nulliparous, which is a known risk factor that may relate to differences in maternal immune response to pregnancy. Recent reviews continue to highlight abnormal maternal-fetal immune interactions, impaired placental development, and changes in maternal cardiovascular adaptation as vital components in preeclampsia's development. [13-15] The average gestational age was significantly lower in women with severe preeclampsia than in those with milder forms, with a mean of 35.9 ± 2.3 weeks versus 37.1 ± 2.1 weeks, respectively. This is understandable clinically because severe preeclampsia often leads to maternal or fetal complications necessitating early delivery. The condition can worsen from hypertension and proteinuria to neurological, hepatic, renal, blood, and placental

issues, with risks increasing alongside disease severity. [3,16] Recent evidence suggests placental dysfunction, inflammation, oxidative stress, and antiangiogenic factors play roles in disease progression. [17,18] Although urban residence and inadequate antenatal care were more common among women with severe disease, these findings were not statistically significant, possibly due to the small sample size and the study being conducted at a single center. It is also likely that factors such as socioeconomic status, diet, nutrition deficiencies, and access to antenatal services interact in more complex ways that the variables measured could not fully capture.

Women with severe preeclampsia had higher systolic and diastolic blood pressure than those with non-severe disease. Mean systolic was 166 ± 17 mmHg vs. 146 ± 16 mmHg, and mean diastolic was 105 ± 11 vs. 95 ± 10 mmHg. The severe group also showed higher frequencies of proteinuria ≥2+, headache or visual symptoms, epigastric/right upper quadrant pain, oliguria, thrombocytopenia, and elevated liver enzymes, reflecting the systemic nature of preeclampsia. This disorder involves placental dysfunction causing maternal endothelial and vascular abnormalities affecting multiple organs. [17,19] Abnormal placentation and inadequate spiral artery remodeling can cause placental ischemia, releasing antiangiogenic and inflammatory mediators like soluble fms-like tyrosine kinase-1 and soluble endoglin, leading to endothelial dysfunction and severe clinical signs. [20,21]

The main finding of this study was the significant difference in maternal serum calcium between women with different severities of preeclampsia. Mean serum calcium was 8.64 ± 0.52 mg/dL in women with non-severe disease but only 7.82 ± 0.61 mg/dL among women with severe preeclampsia ($p<0.001$). In addition, 70.0% of women with severe preeclampsia had serum calcium below 8.5 mg/dL, compared with 34.3% of those with non-severe disease. This finding is supported by a large recent systematic review and meta-analysis. Eslamzadeh *et al.,* analyzed 76 articles comprising 92 studies and 10,482 participants and found that circulating calcium levels were significantly lower in women with preeclampsia than in healthy pregnant controls, with a pooled weighted mean difference of −0.807 mg/dL. [22] The large sample included in that review strengthens the overall evidence that altered calcium status is associated with preeclampsia, although considerable heterogeneity existed between studies. Evidence from Bangladesh also supports the direction of the present finding. Uddin et al., in a case-control study from Bangladesh, found significantly lower serum calcium concentrations among women with preeclampsia than among normotensive pregnant women. [23] These local findings are particularly relevant because dietary patterns, nutritional status, and calcium intake may vary substantially between populations. The present findings are not, however, universally consistent with all Bangladeshi research. Another Bangladeshi study reported significantly higher serum calcium levels among pregnancies complicated by preeclampsia. [9] This apparent contradiction illustrates the uncertainty surrounding the relationship between serum calcium and preeclampsia and emphasizes the influence of differences in study populations, measurement methods, gestational age, nutritional status, and laboratory procedures.

The association observed in this study might have a physiological foundation. Calcium is crucial for vascular smooth muscle contraction, intracellular signaling, and maintaining vascular tone. A decrease in calcium levels can change vascular reactivity and raise peripheral vascular resistance, potentially leading to hypertension. Variations in calcium-regulating hormones could also affect vascular smooth muscle activity and blood pressure control. The relationship between calcium and preeclampsia might also involve nutritional factors. Dietary calcium intake is considered an important factor influencing preeclampsia risk, especially in populations with low calcium consumption. [24] However, serum calcium and dietary calcium are not interchangeable indicators. Serum calcium is tightly regulated through interactions among the gastrointestinal tract, kidneys, bones, parathyroid hormone, and vitamin D. Thus, normal dietary intake does not automatically ensure normal serum calcium levels, and a low serum calcium value can have various causes.

A particularly important finding in this study was the significant inverse relationship between serum calcium and blood pressure. Serum calcium showed a negative correlation with systolic blood pressure ($r = −0.49$, $p<0.001$) and diastolic blood pressure ($r = −0.43$, $p<0.001$). In practical terms, women with lower calcium levels tended to have higher blood pressure. This finding has also been reported elsewhere. In a Chinese case-control study, maternal total calcium levels were negatively correlated with maximum systolic and diastolic blood pressure in women with preeclampsia. [25] Similarly, a Nigerian study found that serum calcium had an inverse relationship with blood pressure among women with preeclampsia and reported hypocalcemia as an important risk factor. [26] These findings support a possible relation between calcium status and vascular regulation, but the association's direction is unclear. As a cross-sectional study, it cannot determine whether reduced calcium causes hypertension or if severe preeclampsia alters calcium metabolism. Renal dysfunction, albumin levels, fluid shifts, hormonal changes, and nutrition may influence serum calcium in severe cases.

The association between low calcium levels and severe disease was further substantiated through categorical analysis. Women exhibiting serum calcium levels below 8.5 mg/dL had approximately 4.5 times

greater odds of developing severe preeclampsia compared to those with levels of 8.5 mg/dL or higher. Even after adjusting for maternal age, gestational age, primigravidity, and antenatal care, low serum calcium maintained a significant correlation with severe preeclampsia, with an adjusted odds ratio of 3.92 (95% CI 1.64–9.37; p=0.002). This finding is noteworthy as it suggests that the association persists independently of the maternal and obstetric variables incorporated into the model. Nonetheless, it should not be construed as evidence that hypocalcemia is an autonomous cause of severe preeclampsia. Several potentially significant confounding factors, such as dietary calcium intake, vitamin D status, serum albumin, body mass index, renal function, and prior calcium supplementation, were not comprehensively evaluated. Prior observational studies have also documented an association between low serum calcium and preeclampsia. In Ethiopia, Gebreyohannes *et al.,* identified associations involving dietary calcium intake, total serum calcium, and ionized calcium in women diagnosed with preeclampsia. [27] A recent meta-analysis similarly concluded that women with preeclampsia typically present with lower calcium concentrations compared to healthy pregnant women. [22] Collectively, the current findings and these prior studies imply that calcium homeostasis may be intricately related to the clinical manifestation of preeclampsia.

Intervention studies support calcium's potential role. A meta-analysis of 26 trials with over 20,000 women found calcium reduced preeclampsia risk by about 49%. [28] A 2024 review of 22 studies with over 39,000 participants showed calcium significantly lowered risk with a pooled relative risk of 0.606. [29] An umbrella review in 2025 also reported reduced risk, despite heterogeneity among studies. [30] However, the preventive effect of calcium remains debated. A recent reassessment questioned trial selection and suggested the benefit may be smaller. [31] A new Cochrane review indicated calcium may have little or no effect when larger, more reliable trials are considered. [32] These mixed findings highlight that evidence for calcium supplementation and serum calcium's relation to disease severity are related but distinct. Not all studies show lower calcium with more severe preeclampsia. Variations in lab methods, whether measuring total, ionized, or albumin-adjusted calcium, may cause these inconsistencies. Total calcium can decrease due to lower albumin levels despite normal ionized calcium. Timing of calcium measurement during pregnancy and factors like supplementation, vitamin D status, nutrition, renal function, and genetics also influence calcium levels and should be considered when comparing studies.

LIMITATIONS OF THIS STUDY

This study has several limitations. Its cross-sectional design prevents establishing an association between low serum calcium and preeclampsia severity because the direction of the association remains uncertain. Conducted at a single center, the study's findings may not be widely applicable, and the lack of a normotensive control group makes it difficult to fully interpret calcium levels. The use of consecutive sampling, non-standardized timing of calcium measurement, and reliance on total rather than ionized calcium also reduce the internal and external validity of the conclusions.

CONCLUSION

This study shows that women with severe preeclampsia have notably lower maternal serum calcium levels compared to those with less severe forms. A serum calcium level under 8.5 mg/dL is identified as a strong, independent predictor of severe preeclampsia, even after considering factors like gestational age and parity. The study also reveals a significant inverse relationship between calcium levels and both systolic and diastolic blood pressures. These findings suggest that hypocalcemia may be related to disease progression and might help identify women at higher risk of severe complications. However, because the study is cross-sectional, it cannot establish causality; it’s unclear whether low calcium levels cause severe preeclampsia or are simply a consequence of metabolic and renal disturbances. Longitudinal studies evaluating dietary calcium, ionized calcium, vitamin D, parathyroid hormone, and serum albumin are needed to clarify the timing and mechanisms before using serum calcium as a reliable clinical marker.

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