

Original Research Article

Association of serum calcium level with preeclampsia

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ABSTRACT

Background: Preeclampsia and its associated complications remain major causes of maternal and perinatal morbidity and mortality worldwide. Among the various risk factors, hypocalcemia has been suggested as a possible contributor to the development of preeclampsia. To determine the association between serum calcium levels and preeclampsia in pregnant women.

Methods: This case-control study was conducted in the Department of Obstetrics and Gynecology, Rangpur Medical College Hospital, Rangpur, Bangladesh. Ethical approval and institutional permission were obtained before data collection. Pregnant women with gestational age ≥ 20 weeks, including 50 preeclamptic women and 50 normotensive pregnant women, were enrolled according to predefined selection criteria. Detailed clinical history, physical examination and relevant laboratory investigations were performed. Data were analyzed using SPSS version 23. Chi-square test was applied for categorical variables and unpaired t-test for continuous variables. A p value < 0.05 was considered statistically significant.

Results: Women with preeclampsia were significantly younger, with 40.0% aged < 20 years compared to 12.0% in controls ($p < 0.001$). Overweight and obesity were more common among preeclamptic women (66.0% and 24.0%, respectively), whereas most controls had normal BMI (84.0%). Preeclamptic women had significantly higher pulse rate and blood pressure. Mean serum calcium and corrected serum calcium levels were significantly lower in the preeclampsia group (7.38 ± 0.37 mg/dl and 7.61 ± 0.17 mg/dl) compared with controls (9.07 ± 0.53 mg/dl and 9.10 ± 0.62 mg/dl). Hypocalcemia was observed in 80.0% and 84.0% of preeclamptic women based on serum calcium and corrected calcium, respectively. No significant difference in calcium levels was found between moderate and severe preeclampsia.

Conclusions: Low serum calcium is significantly associated with preeclampsia, suggesting hypocalcemia may play a role in its pathogenesis.

Keywords: Calcium, Preeclampsia, Serum

INTRODUCTION

Hypertensive disorders in pregnancy constitute one of the leading causes of maternal and perinatal mortality worldwide. The American College of Obstetricians and Gynaecologist's guidelines of 2013 on hypertensive disorders complicating pregnancy categorize hypertensive disorders into four categories: gestational hypertension, preeclampsia, eclampsia and chronic hypertension complicated by preeclampsia or eclampsia. Preeclampsia

is a hypertensive disorder in pregnancy that is characterized by the new onset of persistent hypertension along with new onset of proteinuria or, in the absence of proteinuria, by the presence of new-onset of end-organ damage, usually after 20 weeks of gestation.¹

It is also related to life-threatening complications in both mothers (placental abruption, preterm delivery and HELLP syndrome) and fetuses (Preterm birth, stillbirth, low birth weight and small for gestational age, etc.).² Most

deaths due to preeclampsia and eclampsia are avoidable through the provision of timely and effective care to women presenting with these complications.³ The prevalence of preeclampsia in Bangladesh is 14.4%.⁴ Despite its prevalence, well-cataloged risk factors and clinical characteristics, the exact pathophysiology of this disorder remains unknown.⁵ Experts believe it begins with a disturbance in the placenta, followed by insufficient blood flow to the uterus resulting in inflammation and progressive endothelial damage.⁶ Endothelial dysfunction is considered to underlie many of the manifestations of preeclampsia including hypertension, proteinuria and edema.⁷

Calcium requirements increase during pregnancy, thereby increasing the chance of developing hypocalcemia. Serum calcium level decreases during the second and third trimesters of pregnancy, primarily due to hemodilution.⁸ To provide the calcium necessary for bone mineralization, the maternal demand for calcium during pregnancy is elevated by as much as 300 milligrams/day. The normal expansion of maternal blood volume and the pregnancy-induced increase in urinary excretion that occurs in well-nourished women add further to the physiologic calcium requirements. Previous studies have reported that preeclamptic women have lower serum calcium levels compared to those with normal pregnancies.⁹

The WHO guidelines state that, in populations where calcium intake is low, calcium supplementation as part of antenatal care is recommended for the prevention of preeclampsia.¹⁰ It is suggested that dietary calcium supplementation reduces the frequency of preeclampsia by maintaining serum calcium levels, which play a crucial role in the production of endothelial nitric oxide. Nitric oxide helps maintain the vasodilatation that is characteristic of normal pregnancy.¹¹ Normally, there is an increase in intracellular calcium during pregnancy. It has been reported that this effect is exaggerated in preeclampsia due to a significant increase in the membranous calcium content resulting from increased calcium influx and abnormal regulation of calcium handling.¹²

The decrease in serum calcium and increase in cellular calcium can contribute to elevated blood pressure in preeclamptic women. The increase in cellular calcium concentration, when serum calcium is lower, leads to constriction of smooth muscles in blood vessels and increased vascular resistance.¹³ Calcium intake may regulate blood pressure by modifying intracellular calcium in vascular smooth muscle cells, leading to vasoconstriction and by increasing vascular volume through the renin-angiotensin-aldosterone system.¹⁴

It could also reduce uterine smooth muscle contractility or increase serum magnesium levels, thereby preventing preterm labor and delivery. Supplementation of calcium in the second half of pregnancy is known to reduce the serious consequences of preeclampsia.¹⁵

METHODS

This case-control study was conducted in the Department of Obstetrics and Gynecology, Rangpur Medical College Hospital, Rangpur, Bangladesh, from January 2024 to December 2024. The study population included pregnant women with gestational age ≥ 20 weeks, comprising 50 diagnosed cases of preeclampsia and 50 normotensive pregnant women selected through purposive sampling.

Sample size was calculated using the formula for comparison of two means based on previous reported serum calcium levels among preeclamptic and normal pregnant women, yielding a minimum required sample of 63 participants per group; however, 50 participants were ultimately included in each group due to feasibility constraints. Inclusion criteria were pregnant women with gestational age ≥ 20 weeks diagnosed with preeclampsia or normotensive pregnancy, while women with chronic hypertension, bleeding disorders, chronic renal or liver disease, eclampsia, multiple gestation, malabsorption disorders, alcoholism, pancreatic disease, vitamin D deficiency, gastrointestinal surgery or parathyroid disease were excluded.

Data were collected using a predesigned questionnaire after obtaining written informed consent, including sociodemographic characteristics, obstetric history, clinical findings and laboratory parameters. Physical examinations and relevant investigations were performed and serum calcium and corrected serum calcium levels were assessed as independent variables. Corrected serum calcium was calculated using the formula: corrected calcium (mmol/L) = total serum calcium (mmol/L) + 0.02 (40 - albumin (g/L)). Data quality was ensured through careful review of questionnaires for omissions, inconsistencies and inaccuracies, with corrections made through repeat history taking or re-examination where necessary.

Statistical analyses were performed using SPSS version 26 (IBM SPSS Statistics) and results were presented as tables and graphs. Continuous variables were analyzed using the unpaired t-test, while categorical variables were compared using the chi-square test or other appropriate tests where applicable. A p-value < 0.05 was considered statistically significant. Ethical approval was obtained from the institutional ethical review committee and participant confidentiality, voluntary participation and non-interference with treatment were maintained throughout the study.

RESULTS

In the preeclampsia group, 40.0% of participants were aged below 20 years, 38.0% were between 21 and 29 years and 22.0% were aged 30 years or above. In contrast, among women without preeclampsia, the majority (82.0%) belonged to the 21–29 years age group, while 12.0% were younger than 20 years and only 6.0% were aged 30 years

or above. The age distribution differed significantly between the two groups ($p < 0.001$), indicating that both younger and older maternal age were more common among women with preeclampsia. Most women with preeclampsia were from rural areas (82.0%), whereas the majority of women without preeclampsia resided in urban areas (64.0%).

Educational attainment was also substantially lower among women with preeclampsia, with 48.0% being illiterate and 24.0% educated only up to primary level. In contrast, 48.0% of women without preeclampsia had education at SSC level or above. These socio-demographic factors showed statistically significant associations with preeclampsia ($p < 0.001$). Nearly all women with preeclampsia were housewives (96.0%), while more than half of women without preeclampsia were service holders (54.0%) and this difference was statistically significant ($p < 0.001$).

Regarding monthly family income, a higher proportion of women with preeclampsia belonged to the lower-income group ($< 10,000$ BDT), although no statistically significant association was observed between income level and preeclampsia ($p = 0.116$). Most women with preeclampsia were in later gestational age categories, with 54.0% between > 32 and < 37 weeks and 40.0% beyond 37 weeks. In contrast, half of the women without preeclampsia were between 20 and 32 weeks of gestation. None of the women with preeclampsia had regular antenatal checkups, whereas 62.0% of controls attended regularly.

Irregular antenatal care was highly prevalent among women with preeclampsia (82.0%). Both gestational age and antenatal care attendance were significantly associated with preeclampsia ($p < 0.001$). Clinical symptoms suggestive of severe disease manifestations were

significantly more common among women with preeclampsia. Headache was the most frequent symptom, reported by 86.0% of women with preeclampsia compared to only 2.0% in the control group.

Vomiting, epigastric pain, right upper quadrant pain, blurring of vision and edema were also significantly higher among preeclamptic women (all $p < 0.05$). No statistically significant differences were observed regarding duration of marriage, gravida or parity between the groups. However, LSCS was significantly more common among women with preeclampsia (73.7%) than controls (44.0%) ($p = 0.049$). Previous history of preeclampsia and family history of preeclampsia were both strongly associated with current preeclampsia ($p < 0.001$).

Women with preeclampsia were predominantly overweight or obese, whereas most women without preeclampsia had normal BMI. Mean pulse rate, systolic blood pressure and diastolic blood pressure were all significantly higher among women with preeclampsia compared with controls ($p < 0.001$). Mean serum calcium and corrected serum calcium levels were significantly lower among women with preeclampsia than among healthy pregnant controls ($p < 0.001$). However, serum albumin levels were similar between groups and showed no statistically significant difference ($p = 0.591$).

Hypocalcemia was markedly more common among women with preeclampsia. Eighty percent of women with preeclampsia had low serum calcium levels compared to only 12.0% of controls. Similarly, 84.0% of women with preeclampsia had corrected hypocalcemia, whereas only 10.0% of women without preeclampsia fell into this category. Both serum calcium and corrected serum calcium showed highly significant associations with preeclampsia ($p < 0.001$).

Table 1: Distribution of the study subjects according to age (n=100).

Age (in years)	With preeclampsia (n=50)	Without preeclampsia (n=50)	P value
<20	20 (40.0)	6 (12.0)	<0.001
21–29	19 (38.0)	41 (82.0)	
≥30	11 (22.0)	3 (6.0)	

Table 2: Socio-demographic factors of study subjects (n=100).

Variables	With preeclampsia (n=50)	Without preeclampsia (n=50)	P value
Residence			
Rural	41 (82.0)	18 (36.0)	<0.001
Urban	9 (18.0)	32 (64.0)	
Education level			
Illiterate	24 (48.0)	2 (4.0)	<0.001
Up to primary	12 (24.0)	0 (0.0)	
Below SSC	14 (28.0)	24 (48.0)	
SSC and above	0 (0.0)	24 (48.0)	

*A Chi-square test was done

Table 3: Distribution of the study subjects by occupation and monthly income (n=100).

Variables	With preeclampsia (n=50)	Without preeclampsia (n=50)	P value
Occupation			<0.001
Housewife	48 (96.0)	23 (46.0)	
Service holder	2 (4.0)	27 (54.0)	
Monthly income (BDT)			0.116
<10,000	31 (62.0)	21 (42.0)	
10,000–20,000	13 (26.0)	22 (44.0)	
>20,000	6 (12.0)	7 (14.0)	

*A Chi-square test was done.

Table 4: Antenatal profile of the study subjects (n=100).

Variables	With preeclampsia (n=50)	Without preeclampsia (n=50)	P value
Pregnancy duration (in weeks)			<0.001
20–32	3 (6.0)	25 (50.0)	
>32 to <37	27 (54.0)	24 (48.0)	
>37	20 (40.0)	1 (2.0)	
Antenatal checkup			<0.001
Regular	0 (0.0)	31 (62.0)	
Irregular	41 (82.0)	4 (8.0)	
None	9 (18.0)	15 (30.0)	

*A Chi-square test was done.

Table 5: Physical examination findings of the study subjects (n=100).

Variables	With preeclampsia (n=50)	Without preeclampsia (n=50)	P value
History of headache	43 (86.0)	1 (2.0)	<0.001
Epigastric pain	9 (18.0)	1 (2.0)	0.016
Right upper quadrant pain	15 (30.0)	0 (0.0)	<0.001
Blurring of vision	10 (20.0)	1 (2.0)	0.008
Vomiting	17 (34.0)	2 (4.0)	<0.001
Edema	8 (16.0)	1 (2.0)	0.031

*A Fisher’s Exact test was done.

Table 6: Obstetric history of the study subjects (n=100).

Variables	With preeclampsia (n=50)	Without preeclampsia (n=50)	P value
Married for (in years)	3.72±2.09	4.28±1.52	0.129
Gravida			0.546
Primi	24 (48.0)	21 (42.0)	
Multi	26 (52.0)	29 (58.0)	
Para			0.227
0	31 (62.0)	25 (50.0)	
≥1	19 (38.0)	25 (50.0)	
Mode of previous delivery			0.049
NVD	5 (26.3)	14 (56.0)	
LSCS	14 (73.7)	11 (44.0)	
Previous H/O preeclampsia	26 (81.3)	0 (0.0)	<0.001
Family H/O preeclampsia	20 (40.0)	2 (4.0)	<0.001

*A Chi-square test was done.

Table 7: Clinical profile of the study subjects (n=100).

Variables	With preeclampsia (n=50)	Without preeclampsia (n=50)	P value
BMI			<0.001

Continued.

Variables	With preeclampsia (n=50)	Without preeclampsia (n=50)	P value
Underweight (<18.5)	5 (10.0)	1 (2.0)	
Normal (18.5–24.9)	0 (0.0)	42 (84.0)	
Overweight (25–29.9)	33 (66.0)	7 (14.0)	
Obese (≥30)	12 (24.0)	0 (0.0)	
Pulse (beats/min)	87.76±3.85	76.20±3.29	<0.001
Systolic BP (mmHg)	157.80±7.84	119.00±7.63	<0.001
Diastolic BP (mmHg)	106.70±6.97	78.40±3.70	<0.001

*A Chi-square test and unpaired t-test were done.

Table 8: Comparison of serum calcium, albumin and corrected serum calcium levels (n=100).

Variables	With preeclampsia (n=50)	Without preeclampsia (n=50)	P value
Serum calcium (mg/dl)	7.38±0.37	9.07±0.53	<0.001
Serum albumin (mg/dl)	3.71±0.50	3.77±0.50	0.591
Corrected serum calcium (mg/dl)	7.61±0.17	9.10±0.62	<0.001

*An unpaired t-test was done.

Table 9: Association of serum calcium with preeclampsia (n=100).

Variables	With preeclampsia (n=50)	Without preeclampsia (n=50)	P value
Serum calcium			
Hypocalcemia	40 (80.0)	6 (12.0)	<0.001
Normal	10 (20.0)	40 (80.0)	
Corrected serum calcium			
Hypocalcemia	42 (84.0)	5 (10.0)	<0.001
Normal	8 (16.0)	41 (82.0)	

*Fisher's Exact test was done.

DISCUSSION

Age distribution showed that the higher proportion of women with preeclampsia were under 20 years of age (40.0%) compared to the non-preeclampsia group (12.0%). Conversely, women aged 21–29 years were more common in the non-preeclampsia group (82.0%) than in the preeclampsia group (38.0%). In the study by Singh and Bhattacharjee, the mean age was 27.93±5.26 years in women with preeclampsia and 26.11±4.98 years in women without preeclampsia ($p>0.05$).¹⁶ Similarly, Rashid et al, reported that the age of the patients with preeclampsia was higher than that of patients without preeclampsia, though this difference was not statistically significant.¹⁷

Education level was notably lower among women with preeclampsia, with 48.0% being illiterate and 24.0% having only a primary education. In contrast, none of the women without preeclampsia had only a primary education and 48.0% had an education at the SSC level or above. Regarding occupation, almost all women with preeclampsia were housewives (96.0%), while a majority of women without preeclampsia (54.0%) were service holders. Monthly family income was lower in the preeclampsia group than in the non-preeclampsia group, but the difference was not statistically significant. Only 6.0% of the women with preeclampsia were between 20 and 32 weeks of gestation, whereas 50.0% of women without preeclampsia were in this range. More than half of the preeclampsia group (54.0%) were between 32 and 37

weeks, compared to 48.0% in the non-preeclampsia group. A notable 40.0% of women with preeclampsia had pregnancies beyond 37 weeks, while only 2.0% of women without preeclampsia were in this category. The duration of pregnancy was significantly different between the two groups (36.29±3.2 weeks in the preeclampsia group and 38.19±2.5 weeks in the control group; $p<0.05$).¹⁸ In contrast to this study, the duration of pregnancy was higher among women without preeclampsia than with preeclampsia.¹⁷ The mean gestational age was 32.72±3.28 weeks in women with preeclampsia and 32.91±3.02 weeks in women without preeclampsia.¹⁶ None of the women with preeclampsia had regular antenatal checkups, while 62.0% of women without preeclampsia attended regularly. Most of the women with preeclampsia (82.0%) had irregular checkups and 18.0% had no checkups at all, compared to 8.0% and 30.0% respectively, among women without preeclampsia. Overall, preeclampsia was more common among women in the late stages of pregnancy with irregular or no antenatal care.

BMI distribution revealed that the majority of women with preeclampsia were overweight (66.0%) or obese (24.0%), whereas none of the women without preeclampsia were obese and only 14.0% were overweight. Most of the women without preeclampsia (84.0%) had a normal BMI, while no women with preeclampsia fell into this category. Underweight status was slightly more common among women with preeclampsia (10.0%) compared to women without preeclampsia (2.0%). The mean pulse rate was

significantly higher in women with preeclampsia (87.76 ± 3.85 beats/min) compared to women without preeclampsia (76.20 ± 3.29 beats/min). Blood pressure values were markedly elevated in the preeclampsia group. The mean systolic blood pressure was 157.80 ± 7.84 mmHg among women with preeclampsia compared to 119.00 ± 7.63 mmHg in women without preeclampsia. Similarly, mean diastolic blood pressure was substantially higher in the preeclampsia group (106.70 ± 6.97 mmHg) than in the non-preeclampsia group (78.40 ± 3.70 mmHg). The mean systolic blood pressure and body mass index were significantly different between groups ($p < 0.05$). The mean systolic blood pressure in women with preeclampsia was 149.8 ± 13.39 mmHg and in the control group was 108.7 ± 9.73 mmHg. The mean diastolic blood pressure in women with preeclampsia was 95.0 ± 8.57 mmHg and in the control group was 64.7 ± 10.72 .¹⁸ Patients with preeclampsia exhibited significantly lower levels of total serum calcium and corrected serum calcium than women without preeclampsia. The control group had a mean serum calcium level of 9.07 ± 0.53 mg/dL, while the preeclampsia group had a mean of 7.38 ± 0.37 mg/dl. Similarly, the corrected serum calcium levels in the preeclampsia cases were 7.61 ± 0.17 mg/dl, while the level was 9.10 ± 0.62 mg/dl in the non-preeclampsia group.

These results were in agreement with prior research. Preeclampsia was also associated with substantially lower serum calcium levels than in controls.¹⁹ The present findings are corroborated by Kanagal et al who observed similar findings.²⁰ Singh et al also reported comparable trends.¹⁶ Pairu et al also observed that women with pregnancy-induced hypertension had substantially lower calcium levels.²¹ Sharma also observed a progressive decline in mean serum calcium with disease severity.²² Serum albumin in women with preeclampsia was 4.12 ± 0.45 mg/dl and in normal pregnant women 4.26 ± 0.57 mg/dl. There was no significant difference between the two groups in mean serum levels of albumin.¹⁸ The incidence of hypocalcemia was significantly greater among patients with preeclampsia compared to normal pregnant women. Based on serum calcium levels, 80.0% of patients with preeclampsia were found to have hypocalcemia and when assessed using corrected serum calcium, the rate reached 84.0%. In the study by Parvin et al it was observed that 53.7% of pregnant women with preeclampsia had low serum calcium, whereas it was just 12.5% among those with a normal pregnancy.¹ The mean serum calcium was significantly lower in the preeclampsia group as compared to the control group.

On analyzing serum calcium levels in detail, 48% of patients with preeclampsia had serum calcium levels below 8.0 mg/dl. On the other hand, controls without preeclampsia had higher calcium levels.¹⁷ Among the patients with preeclampsia, 36.0% were diagnosed with non-severe preeclampsia while 64.0% had severe preeclampsia. The mean serum calcium level and mean corrected serum calcium were almost similar in both the non-severe and severe preeclampsia groups.

Limitations

Sample size was small and all samples were taken from a single tertiary level hospital, so that the result of the study may not reflect the exact status of the population.

CONCLUSION

Low serum calcium levels are associated with preeclampsia and may contribute to its pathogenesis. Serum calcium levels did not differ significantly between preeclampsia with severe features and preeclampsia without severe features. High-dose calcium supplementation can be implemented for women at risk of developing preeclampsia to improve pregnancy outcome.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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