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Association between serum calcium levels and severity of preeclampsia among pregnant women: A cross-sectional study in a tertiary care Hospital in India

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Abstract
Background: Preeclampsia is a hypertensive disorder of pregnancy that significantly contributes to maternal and perinatal morbidity and mortality, particularly in developing countries. Altered calcium metabolism has been suggested as a potential factor in the pathophysiology of preeclampsia, but findings remain inconsistent across populations.
Objectives: To estimate serum calcium levels among pregnant women diagnosed with preeclampsia and to assess the association between serum calcium levels and the severity of the condition.
Methods: A hospital-based cross-sectional study was conducted over 12 months at the Department of Obstetrics and Gynecology, Rajkiya Mahila Chikitsalaya, JLN Medical College, Ajmer. A total of 300 pregnant women with gestational age >28 weeks and clinically diagnosed preeclampsia were enrolled. Sociodemographic and obstetric data were collected using a pre-tested questionnaire. Serum calcium levels were measured using an enzymatic colorimetric method. Preeclampsia was classified as mild, moderate, or severe based on clinical criteria. Statistical analysis was performed using SPSS version 20.0, and a p-value <0.05 was considered statistically significant.
Results: The mean serum calcium level among participants was 9.56 ± 1.10 mg/dL. A significant inverse relationship was observed between serum calcium levels and the severity of preeclampsia. Women with mild preeclampsia had the highest mean calcium levels (9.58 ± 0.68 mg/dL), followed by those with moderate (8.67 ± 1.43 mg/dL), and severe preeclampsia (8.12 ± 1.54 mg/dL) ($p < 0.0001$). Additionally, the majority of participants belonged to rural areas and lower socioeconomic classes, with a high prevalence of overweight and obesity.
Conclusion: Lower serum calcium levels were significantly associated with increased severity of preeclampsia. Monitoring calcium levels during pregnancy may offer a simple and cost-effective strategy for early risk assessment and improved management of preeclampsia, especially in resource-limited settings.

Keywords: Preeclampsia, serum calcium, pregnancy, hypertensive disorders, maternal health

Introduction

Preeclampsia is a hypertensive disorder unique to pregnancy, affecting approximately 2% to 8% of pregnancies worldwide. It is a significant contributor to maternal morbidity and mortality, responsible for an estimated 9% to 26% of maternal deaths in low- and high-income countries, respectively [1]. Clinically, preeclampsia is defined as the new onset of hypertension—systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg on two separate occasions at least four hours apart—occurring after 20 weeks of gestation in previously normotensive women. Severe hypertension is considered at systolic ≥160 mmHg or diastolic ≥110 mmHg [2].

The clinical presentation of preeclampsia often occurs near term but may also present preterm or postpartum. Diagnostic criteria extend beyond hypertension and include proteinuria and signs of maternal organ dysfunction such as thrombocytopenia, impaired liver function, persistent right upper quadrant pain, renal insufficiency, pulmonary edema, or cerebral symptoms such as persistent headaches and visual disturbances [3]. Based on symptomatology and laboratory findings, preeclampsia is typically categorized as mild or severe [2, 3].

Despite a comprehensive understanding of its clinical manifestations and management, the exact etiology of preeclampsia remains unclear. However, abnormal placentation is widely regarded as a central mechanism. This involves defective remodeling of spiral arteries, leading to placental ischemia, hypoxia, and oxidative stress, which collectively trigger systemic maternal endothelial dysfunction [4].

Globally, hypertensive disorders of pregnancy—including pre-eclampsia and eclampsia—account for over 50,000 maternal deaths annually [2]. The incidence and outcomes of preeclampsia are influenced by various factors including race and ethnicity, with African American and Hispanic women showing disproportionately higher risks [2]. In India, the reported incidence of hypertensive disorders of pregnancy is approximately 6.9%, with hospital-based data showing preeclampsia in 5%–15% of pregnancies and eclampsia in about 1.5% [5]. The risk of eclampsia has ranged between 0.179% and 5% in India over several decades, averaging 1.5% [6].

Risk factors for preeclampsia include nulliparity, multiple gestation, maternal age >35 years, assisted reproductive technologies, and pre-existing conditions such as chronic hypertension, kidney disease, diabetes mellitus, thrombophilia, obstructive sleep apnea, and obesity (pre-pregnancy BMI >30). Additional risks include a family or personal history of preeclampsia or intrauterine growth restriction [7].

The pathogenesis of pre-eclampsia involves an imbalance in angiogenic and antiangiogenic factors. Ischemic placental tissues release antiangiogenic and pro-inflammatory molecules into maternal circulation, disrupting vascular homeostasis and contributing to endothelial dysfunction in multiple organs, especially the cardiovascular, hepatic, and renal systems [8, 9]. Notably, preeclampsia can present with atypical symptoms, such as new-onset headaches or visual disturbances unresponsive to treatment, upper abdominal pain, and worsening edema or dyspnea, which may be mistaken for normal pregnancy-related discomforts.

Effective management of preeclampsia requires timely diagnosis and intervention. Blood pressure control can be achieved using labetalol or nifedipine, and magnesium sulfate is the drug of choice for seizure prophylaxis in severe cases [10]. Fetal surveillance through ultrasonography and antenatal testing (e.g., biophysical profiles, non-stress tests) is essential for monitoring fetal well-being. Ultimately, delivery remains the definitive treatment. The American College of Obstetricians and Gynecologists (ACOG) recommends delivery at 37 weeks of gestation in cases of preeclampsia without severe features [10].

It is important to distinguish preeclampsia from other hypertensive or systemic conditions in pregnancy, such as chronic hypertension, lupus, epilepsy, and renal or hepatic disorders [9]. Early identification and rigorous maternal-fetal monitoring significantly reduce complications, especially among high-risk populations including those in Asia, Africa, and Latin America [7].

Hyponatremia has been reported in preeclamptic patients, although its frequency and implications are still being investigated. In non-pregnant individuals, hyponatremia is associated with seizures and cerebral edema, which also occur in eclampsia [11].

During pregnancy, calcium requirements increase from 600 mg/day to 1,200 mg/day to support fetal skeletal development [11]. Serum calcium levels tend to decrease during the second and third trimesters due to hemodilution [12]. Several studies have suggested a correlation between low serum calcium levels and adverse pregnancy outcomes, including preeclampsia, preterm birth, and low birth weight [13, 14]. While many investigations report significantly reduced serum calcium levels in preeclamptic women [15, 16], others, such as the study by Gupta *et al*. in North India, found no significant association [17]. The inconsistency in findings, particularly in Indian populations, underscores the need for further research [18].

Given these observations, the present study was undertaken to assess the serum calcium levels in pregnant women and investigate their association with the incidence and severity of preeclampsia as well as delivery outcomes.

Methods

This was a hospital-based cross-sectional study conducted in the Department of Obstetrics and Gynecology at Rajkiya Mahila Chikitsalaya, JLN Medical College, Ajmer. The study was carried out over a duration of 12 months, from August 2022 to August 2023. Prior to initiation, the study protocol was submitted to and approved by the Institutional Ethics Committee of JLN Medical College, Ajmer. Informed written consent was obtained from each participant after explaining the nature and objectives of the study in the local language. The study included pregnant women with a gestational age of more than 28 weeks. Women who had a history of hypertension diagnosed before 20 weeks of gestation, those unable to comprehend the study questionnaire, and participants with missing pregnancy outcome data were excluded from the analysis.

Data Collection

Eligible participants were enrolled after providing consent. Data collection was performed using a pre-tested, semi-structured interview schedule. Information regarding sociodemographic factors, obstetric history, antenatal care, and dietary intake was collected. Dietary calcium intake was assessed using a 24-hour dietary recall method, and the calcium content of foods was calculated based on standard nutritive values of Indian foods. To ensure accuracy, the dietary recall was repeated on the second day when the blood report was shared with the participant. Venous blood (3 ml) was drawn from the antecubital vein using standard aseptic precautions. Serum was separated by centrifugation at 2000 rpm for 10 minutes and stored at 4°C until analysis. Serum calcium levels were measured using an enzymatic colorimetric method with an automated spectrophotometer (Biolis 24i, Carolina Liquid Chemistries Corporation, Winston-Salem, North Carolina, USA). Blood pressure was recorded at the first visit using a manual sphygmomanometer (Industrial Electronic & Allied Products, Pune, India) with the participant seated comfortably, following guidelines from the British Hypertension Society. A clean-catch midstream urine sample was obtained and tested using dipstick method to detect albuminuria.

Operational Definitions

Preeclampsia was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg on two occasions at least four hours apart, in a previously normotensive woman, along with proteinuria defined as ≥1+ on dipstick testing. Hypocalcemia was defined as serum calcium level <9 mg/dL. Preterm delivery was defined as delivery before 37 completed weeks of gestation, and low birth weight was defined as a birth weight of less than 2,500 grams.

Pregnancy Outcome Assessment

Pregnancy outcomes were assessed telephonically by a trained investigator (AG), at least three months after study enrollment. The participants were asked about the place, mode, and date of delivery; sex and birth weight of the newborn; and neonatal survival status at birth and on day 28. When possible, responses were verified with hospital records; otherwise, participants were asked to recall the details.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics for Windows, Version 20.0 (Armonk, NY: IBM Corp). Continuous variables were expressed as mean with standard deviation (SD), and categorical variables were described using proportions. The independent t-test was used to assess mean differences in serum calcium levels between groups. A p-value of less than 0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 300 pregnant women were included in the study. The mean age of the participants was 28.65 ± 5.26 years. The majority of women (29.33%) were in the age group of 21–25 years, followed by 26.33% in the 26–30-year group, and 23.33% were aged above 35 years. Only 10.33% of the participants were aged ≤20 years, while 10.67% fell into the 31–35-year age group. Regarding parity, more than half of the participants (58.67%) were nulliparous, and the remaining 41.33% were multiparous. Most women (64.33%) were in the 37–40-week gestational age range at the time of recruitment, while 22.00% had crossed 40 weeks, and 13.67% were between 32 and 36 weeks of gestation. A significant proportion of the study population (82.00%) resided in rural areas, while only 18.00% came from urban settings. In terms of socioeconomic status, the majority (66.00%) belonged to the lower socioeconomic class, followed by 20.67% in the middle class and 13.33% in the upper class. Analysis of body mass index (BMI) revealed that 45.00% of the participants were overweight, 37.33% had a normal BMI, and 17.67% were categorized as obese. The mean BMI among the study group was 28.15 ± 4.58 kg/m². Blood pressure measurements showed that the mean systolic blood pressure (SBP) was 153.2 ± 11.37 mmHg, while the mean diastolic blood pressure (DBP) was 97.5 ± 7.16 mmHg. The mean arterial pressure (MAP) calculated for the group was 116.05 ± 7.68 mmHg.

Type and Duration of Delivery

Out of the 300 pregnant women included in the study, the majority (60%) underwent lower segment cesarean section (LSCS), while 40% had a normal vaginal delivery. In terms of gestational age at delivery, 93% of the women delivered at term (≥37 weeks), whereas only 7% had preterm deliveries (<37 weeks).

Serum Calcium Levels

The mean serum calcium level among the study participants was found to be 9.56 ± 1.10 mg/dL, indicating that most women had calcium levels within the normal physiological range during the third trimester of pregnancy.

Severity of Preeclampsia

Among the 300 participants diagnosed with preeclampsia, nearly half (46.67%) presented with severe preeclampsia, making it the most common category observed. Moderate preeclampsia was reported in 40.00% of the cases, while only 13.33% of participants had mild preeclampsia. This distribution highlights the predominance of moderate to severe disease in the study population.

Association Between Serum Calcium and Severity of Preeclampsia

A statistically significant inverse association was observed between serum calcium levels and the severity of preeclampsia. Women with mild preeclampsia had the highest mean serum calcium level (9.58 ± 0.68 mg/dL), followed by those with moderate preeclampsia (8.67 ± 1.43 mg/dL). The lowest levels were recorded in participants with severe preeclampsia, with a mean serum calcium of 8.12 ± 1.54 mg/dL. The difference in serum calcium levels across severity categories was found to be highly significant ($p < 0.0001$).

Discussion

This study evaluated the serum calcium levels in pregnant women with preeclampsia and explored the association between calcium levels and the severity of the condition. The findings demonstrate a significant inverse relationship between serum calcium levels and the severity of preeclampsia, with progressively lower calcium levels observed in moderate and severe cases.

The mean serum calcium level among the study population was 9.56 ± 1.10 mg/dL, which falls within the normal reference range. However, when stratified by severity, a clear declining trend was noted: women with severe preeclampsia had the lowest mean calcium levels (8.12 ± 1.54 mg/dL), whereas those with mild preeclampsia had the highest (9.58 ± 0.68 mg/dL). This association was statistically significant ($p < 0.0001$), suggesting a potential role of calcium in the pathophysiology of preeclampsia.

These findings are in line with several previous studies. Sukonpan and Phupong (2005) [16] reported significantly lower serum calcium levels in women with preeclampsia compared to normotensive pregnant women, supporting the hypothesis that hypocalcemia may contribute to vascular dysfunction, a hallmark of preeclampsia [16]. Similarly, Jain *et al*. (2010) [15] also found reduced calcium levels in preeclamptic patients, particularly those with severe disease [15]. A meta-analysis by Hofmeyr *et al*. further indicated that calcium supplementation during pregnancy could reduce the risk of preeclampsia, especially in women with low dietary calcium intake [14].

Calcium plays a vital role in vascular smooth muscle contraction, and a deficiency may lead to increased intracellular calcium concentrations in vascular cells, resulting in heightened vascular reactivity and hypertension [4]. Furthermore, low serum calcium may stimulate parathyroid hormone and renin release, contributing to vasoconstriction and increased blood pressure [19].

Our findings also mirror the results of Sabour *et al*. (2006) [13], who suggested that calcium imbalance might not only affect maternal vascular tone but also fetal outcomes, including preterm delivery and low birth weight [13]. In the present study, although the focus was on maternal calcium levels and disease severity, future work should also explore fetal outcomes in relation to maternal calcium status.

However, not all studies have found such associations. Gupta *et al*. (2016) [17], in a study conducted in North India, found no significant difference in serum calcium levels between preeclamptic and normotensive women [17]. The discrepancy may be attributed to variations in dietary calcium intake, genetic predisposition, socioeconomic factors, and methodological differences.

The high proportion of women from rural areas and lower socioeconomic backgrounds in our study may also influence baseline calcium intake and overall nutritional status, reinforcing the importance of dietary assessments alongside biochemical evaluation.

This study is limited by its cross-sectional design, which prevents the establishment of a causal relationship. Additionally, the absence of a normotensive control group restricts comparison. Despite these limitations, the large sample size and standardized measurement methods strengthen the reliability of our findings.

Table 1: Baseline Characteristics of Study Participants

Baseline Characteristics	Frequency (n)	Percentage (%)
Age Group (years)		
≤ 20	31	10.33
21–25	88	29.33
26–30	79	26.33
31–35	32	10.67
> 35	70	23.33
Mean age	28.65±5.26 years	
Parity		
Nulliparous	176	58.67
Multiparous	124	41.33
Gestational Age (weeks)		
32–36	41	13.67
37–40	193	64.33
> 40	66	22.00
Residence		
Urban	54	18.00
Rural	246	82.00
Socioeconomic Status		
Lower Class	198	66.00
Middle Class	62	20.67
Upper Class	40	13.33
BMI Category		
Normal	112	37.33
Overweight	135	45.00
Obese	53	17.67
Mean BMI	28.15 ± 4.58 kg/m^2	
Blood Pressure		
SBP (Mean ± SD, mmHg)	153.2 ± 11.37	
DBP (Mean ± SD, mmHg)	97.5 ± 7.16	
MAP (Mean ± SD, mmHg)	116.05 ± 7.68	

Table 2: Type and Duration of Delivery

Category	Frequency (n)	Percentage (%)
Type of Delivery		
Normal	120	40%
LSCS	180	60%
Duration		
Pre-term	21	7%
Term	279	93%

Table 3: Serum Calcium Levels of Participants

Parameter	Mean ± SD (mg/dL)
Serum Calcium Level	9.56 ± 1.10

Table 4: Severity of Preeclampsia

Severity Category	Frequency (n)	Percentage (%)
Mild	40	13.33%
Moderate	120	40.00%
Severe	140	46.67%

Table 5: Association Between Serum Calcium and Severity of Preeclampsia

Severity of Preeclampsia	Mean Serum Calcium (mg/dL)	P-value
Mild	9.58 ± 0.68	< 0.0001
Moderate	8.67 ± 1.43	
Severe	8.12 ± 1.54	

Conclusion

The present study demonstrates a significant inverse association between serum calcium levels and the severity of preeclampsia among pregnant women. Women with severe preeclampsia exhibited significantly lower serum calcium levels compared to those with mild or moderate disease. These findings support the hypothesis that hypocalcemia may play a contributory role in the pathophysiology and progression of preeclampsia. Given the simplicity and affordability of serum calcium estimation, routine monitoring of calcium levels during antenatal care could serve as a useful tool for early risk identification and intervention, especially in resource-limited settings. Further longitudinal and interventional studies are warranted to establish causality and to evaluate the potential benefits of calcium supplementation in reducing the incidence and severity of preeclampsia.

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