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Research Article

Serum Calcium and Magnesium Levels in Preeclampsia and Normotensive Pregnancy: A Comparative Study

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ABSTRACT

Background: Preeclampsia is a leading cause of maternal and fetal morbidity and mortality, particularly in developing regions. Micronutrient deficiencies, especially of calcium and magnesium, are implicated in its pathogenesis. However, limited data exist for tribal populations in India.

Aim: To compare serum calcium and magnesium levels in preeclamptic and normotensive pregnant women and evaluate their association with disease severity and pregnancy outcomes in South Rajasthan.

Methods: This hospital-based comparative cross-sectional study included 240 pregnant women (120 preeclamptic, 120 normotensive) between 28–36 weeks of gestation at Pacific Medical College and Hospital, Udaipur. After obtaining ethical approval and consent, clinical and obstetric data were recorded. Serum calcium and magnesium were measured using atomic absorption spectrophotometry. Statistical analysis involved t-tests, Pearson correlation, ANOVA, and ROC curve analysis (SPSS v24), with significance set at p<0.05.

Results: Preeclamptic women had significantly lower serum calcium $(7.4 \pm 1.38 \text{ mg/dl})$ and magnesium $(1.71 \pm 0.45 \text{ mg/dl})$ compared to normotensive women $(9.45 \pm 0.62 \text{ mg/dl})$ and $1.98 \pm 0.38 \text{ mg/dl}$, respectively; p<0.0001). Levels were further reduced in severe preeclampsia. Serum calcium and magnesium showed negative correlations with systolic and diastolic blood pressure. Lower mineral levels were associated with adverse outcomes, including higher cesarean rates, low birth weight, low APGAR scores, and NICU admissions. ROC analysis showed serum calcium had better diagnostic utility (AUC = 0.782) than magnesium (AUC = 0.694).

Conclusion: Calcium and magnesium deficiencies are associated with preeclampsia severity and poor pregnancy outcomes. Serum calcium may serve as a useful predictive biomarker, particularly in resource-limited settings.

Keywords: Preeclampsia, Calcium, Magnesium, Maternal outcomes, Fetal outcomes, Biomarkers.

INTRODUCTION

Hypertensive disorders in pregnancy, including preeclampsia (PE), continue to be significant contributors to maternal and fetal morbidity and mortality worldwide. These disorders affect 5–10% of pregnancies and form a critical part of the triad responsible for adverse obstetric outcomes, alongside hemorrhage and infection [1–3]. Preeclampsia, a multisystem condition characterized by new-onset hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman, accounts for a large share of complications and deaths, especially in developing countries where it contributes to 20–80% of maternal deaths [3].

Although the exact etiology of PE remains unclear, abnormal placentation, oxidative stress, immune dysregulation, and endothelial dysfunction are recognized contributors. Defective trophoblastic invasion leads to poor remodeling of the

maternal spiral arteries, resulting in increased vascular resistance and placental hypoperfusion. This ischemia induces systemic endothelial dysfunction and vasoconstriction via the release of antiangiogenic factors [4].

Nutritional deficiencies, particularly of calcium and magnesium, have emerged as modifiable risk factors for PE [5]. In low-resource settings, inadequate dietary intake, food insecurity, and poor prenatal supplementation increase the likelihood of micronutrient deficiencies, which can exacerbate vascular dysfunction and oxidative stress [6].

Calcium plays a critical role in vascular smooth muscle contraction and blood pressure regulation. It modulates vasoconstriction via angiotensin II and noradrenaline and decreases vasodilator prostacyclin levels. Low serum calcium levels in PE are linked to heightened vascular tone and elevated blood pressure. Many studies have demonstrated significantly reduced calcium levels in preeclamptic women compared to normotensive controls, although others found no significant differences, suggesting potential roles for genetic and environmental modifiers [7-8] In view of these findings, the WHO recommends calcium supplementation (1.5–2.0 g/day) for pregnant women in regions with high prevalence of calcium deficiency [2].

Magnesium, a natural calcium antagonist, is essential for vascular tone regulation and cellular stability. It prevents excessive calcium influx into cells, facilitates vasodilation, and reduces oxidative stress and platelet aggregation. During pregnancy, serum magnesium tends to decline due to hemodilution, increased renal excretion, and fetal demands. Hypomagnesemia has been associated with neuromuscular irritability, vasospasm, and higher blood pressure—features typical of PE [9].

Magnesium sulfate is the standard anticonvulsant for eclampsia prevention and treatment, highlighting its critical role in hypertensive disorders of pregnancy [20]. However, routine magnesium supplementation remains controversial due to inconsistent outcomes in clinical trials [10].

Given these physiological roles, deficiencies in calcium and magnesium may contribute significantly to the pathogenesis of PE. Although several studies report reduced serum levels of these minerals in preeclamptic women, findings remain inconsistent, necessitating further research [7-10]. Therefore, this study was undertaken to compare serum calcium and magnesium levels in preeclamptic and normotensive pregnant women in Rajasthan, India, to better understand their association with hypertensive disorders of pregnancy and to identify potential nutritional interventions.

MATERIAL AND METHODS

This hospital-based observational comparative cross-sectional study was conducted in the Department of Obstetrics and Gynaecology at Pacific Medical College and Hospital (PMCH), Udaipur, Rajasthan. The study population comprised pre-eclamptic and normotensive pregnant women with live singleton pregnancies between 28 and 36 weeks of gestation. Participants were recruited from both the outpatient and inpatient departments after obtaining approval from the Institutional Ethical Committee and informed written consent. The inclusion criteria were women aged 20–40 years with singleton pregnancies beyond 28 weeks of gestation who were willing to participate. Women with chronic hypertension, diabetes, renal, cardiovascular, or liver disorders, multiple gestation, hydatidiform mole, or a history of smoking or alcohol use were excluded.

A total of 240 participants were enrolled and divided equally into two groups: Group 1 included 120 pre-eclamptic women, while Group 2 consisted of 120 normotensive pregnant women. The sample size was calculated based on a 5% level of significance, 80% power, and an effect size of 0.364. After detailed history-taking, general, systemic, and obstetric examinations were performed. Blood pressure was measured, and proteinuria was assessed via dipstick to confirm pre-eclampsia, defined as systolic BP >140 mmHg and/or diastolic BP >90 mmHg with proteinuria >+1. Pre-eclamptic cases were further classified into mild and severe based on BP readings and associated symptoms.

Venous blood samples were collected under aseptic precautions and centrifuged at 3000 rpm to separate serum. Serum calcium and magnesium levels were measured using Atomic Absorption Spectrophotometry (Buck Scientific, Model AVG210), and packed cell volume (PCV) was determined via microhematocrit centrifugation. All biochemical measurements were performed with appropriate calibration and quality control. Data were compiled in Microsoft Excel and analyzed using SPSS version 24.0. Descriptive statistics, Chi-square/Fisher's exact tests, and unpaired t-tests were employed, with p < 0.05 considered statistically significant.

RESULTS

Demographic and clinical characteristics between preeclamptic and normotensive women, showing that preeclamptic women had higher BMI, and demonstrated the expected blood pressure differences that define preeclampsia.[table 1] The primary finding demonstrates that both serum calcium and magnesium levels are significantly lower in preeclamptic women compared to normotensive controls, establishing the key association between mineral deficiency and preeclampsia. [table 2]

A dose-response relationship is evident where severe preeclampsia cases have the lowest mineral levels, followed by mild preeclampsia, then normal controls, suggesting a gradient effect based on disease severity. [table 3]

Negative correlations between blood pressure measurements and mineral levels indicate that as calcium and magnesium decrease, blood pressure increases, supporting a potential causal relationship between mineral deficiency and hypertension. [table 4]

Pregnancy outcomes demonstrate that preeclamptic women experience significantly worse maternal and fetal outcomes including higher cesarean rates, lower birth weights, and more NICU admissions compared to normotensive controls. [table 5]

ROC analysis evaluates the clinical utility of measuring these minerals for predicting preeclampsia, showing that serum calcium has better diagnostic accuracy than magnesium, with moderate sensitivity and specificity for clinical screening purposes. [table 6]

Table 1: Baseline characteristics of study participants

Characteristics	Preeclamptic women (n=120)	Normotensive women (n=120)	p-value	
Age (years)				
$Mean \pm SD$	27.65 ± 4.21	25.20 ± 3.48	0.026*	
BMI (kg/m²)				
<25	32 (26.7%)	70 (58.3%)	<0.001*	
25-30	65 (54.2%)	44 (36.7%)		
>30	23 (19.2%)	6 (5.0%)		
$Mean \pm SD$	27.2 ± 3.1	24.5 ± 2.4	<0.001*	
Blood pressure				
Systolic BP (mmHg)	155.8 ± 14.2	114.3 ± 7.8	<0.0001*	
Diastolic BP (mmHg)	98.7 ± 9.1	74.2 ± 6.3	<0.0001*	

Table 2: Serum calcium and magnesium levels by study groups

Parameters	Preeclamptic women (n=120)	Normotensive women (n=120)	p-value
Serum total calcium (mg/dl)	7.4 ± 1.38	9.45 ± 0.62	<0.0001*
Serum magnesium (mg/dl)	1.71 ± 0.45	1.98 ± 0.38	<0.0001*

Table 3: Serum calcium and magnesium levels by preeclampsia severity

Parameters	Mild preeclampsia (n=72)	Severe preeclampsia (n=48)	Normotensive women (n=120)	p-value
Serum total calcium (mg/dl)	8.32 ± 1.08	6.77 ± 1.52	9.45 ± 0.62	<0.0001*
Serum magnesium (mg/dl)	1.82 ± 0.36	1.53 ± 0.48	1.98 ± 0.38	<0.0001*

Table 4: Correlation between blood pressure and serum mineral levels

Parameters	r-value with Calcium	p-value	r-value with Magnesium	p-value
Systolic BP (mmHg)	-0.552	<0.0001*	-0.312	0.0015*
Diastolic BP (mmHg)	-0.526	<0.0001*	-0.335	0.0008*

Table 5: Maternal and fetal outcomes

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Outcomes	Preeclamptic women (n=120)	Normotensive women (n=120)	p-value		
Cesarean section	52 (43.3%)	26 (21.7%)	0.0003*		
Mean birth weight (kg)	2.56 ± 0.62	2.94 ± 0.48	<0.0001*		
Birth weight <2.5 kg	48 (40.0%)	22 (18.3%)	0.0002*		
APGAR at 1 min <7	22 (18.3%)	8 (6.7%)	0.006*		
NICU admission	26 (21.7%)	10 (8.3%)	0.004*		

Table 6: Diagnostic performance of serum calcium and magnesium

Parameters	AUC	95% CI	Cut-off value	Sensitivity	Specificity	p-value
Serum calcium (mg/dl)	0.782	0.724-0.840	3.8	76.7%	72.5%	<0.0001*
Serum magnesium (mg/dl)	0.694	0.628-0.760	1.8	68.3%	65.0%	<0.0001*

^{*}Statistically significant (p<0.05)

DISCUSSION

In this study, demographic analysis revealed that preeclamptic women had a significantly higher mean age $(27.65 \pm 4.21 \text{ years})$ than normotensive women $(25.20 \pm 3.48 \text{ years})$, with most preeclamptic cases falling within the 26-30

age group. This supports previous studies, such as those by Sethi et al. [11] and Sridevi et al. [12], who found similar age trends, though Allagoa et al. [13] reported no significant difference. Most participants in both groups resided in rural areas and belonged to lower socioeconomic classes, with no significant differences. This reflects the regional demographic of South Rajasthan and underscores the need for better healthcare access in underserved communities.

Illiteracy was marginally higher among preeclamptic women, though not statistically significant, and no notable differences in religion were observed. While these findings were not emphasized in other comparative studies, they provide insight into the broader sociodemographic context in tribal regions.

Clinically, BMI was significantly higher in preeclamptic women (mean 27.2 vs. 24.5, p<0.001), with more cases of obesity observed in the affected group. This is consistent with prior research, including findings by Sethi et al. [11] and Allagoa et al. [13], reinforcing obesity as a risk factor. Importantly, our study also noted a significant inverse correlation between BMI and both serum calcium (p=0.028) and magnesium (p=0.036), suggesting that obesity may be linked to micronutrient deficiencies contributing to preeclampsia.

Although primigravidity was more common in preeclamptic women (55.8% vs. 48.3%), this was not statistically significant (p=0.245). This aligns with previous studies that identify primigravidity as a known but not universally consistent risk factor [11,13]. Blood pressure values, as expected, were significantly elevated in the preeclamptic group, serving more as diagnostic confirmation than a comparative parameter.

The key finding of our study was the significantly lower serum calcium and magnesium levels in preeclamptic women compared to normotensive controls. Calcium levels were 7.4 ± 1.38 mg/dl in the preeclamptic group vs. 9.45 ± 0.62 mg/dl in controls (p<0.0001), while magnesium levels were 1.71 ± 0.45 mg/dl vs. 1.98 ± 0.38 mg/dl, respectively (p<0.0001). These results are in agreement with several studies [11,13,14,15], suggesting a consistent trend across populations. However, a few studies, including those by Darkwa et al. [16] and Sah et al. [17], did not find significant differences, indicating variability possibly due to nutritional, genetic, or methodological differences.

Further analysis revealed a clear gradient between mineral levels and preeclampsia severity. Women with severe preeclampsia had significantly lower serum calcium and magnesium than those with mild cases or normotensive pregnancies. This dose-response relationship is supported by Sethi et al. [11] and Seedipally et al. [15], and strengthens the hypothesis that mineral deficiencies may contribute to disease progression.

There was a strong inverse correlation between serum calcium and both systolic and diastolic blood pressure (r = -0.552 and -0.526), and a moderate inverse correlation between magnesium and blood pressure (r = -0.312 and -0.335), all statistically significant (p<0.0001). These results mirror findings by Allagoa et al. [13] and Sethi et al. [11], highlighting the potential mechanistic role of these minerals in blood pressure regulation through effects on vascular tone and endothelial function.

In terms of outcomes, preeclamptic women had significantly higher rates of cesarean delivery, low birth weight, NICU admissions, and low APGAR scores. These findings reaffirm the known adverse impact of preeclampsia on maternal and neonatal outcomes [60,62,66]. Importantly, lower maternal serum calcium and magnesium levels were significantly associated with these adverse outcomes, suggesting that micronutrient deficiency not only contributes to disease onset but may also affect prognosis.

Our ROC analysis demonstrated that serum calcium (AUC = 0.782) had superior predictive value compared to magnesium (AUC = 0.694) in identifying preeclampsia. This supports conclusions by Sethi et al. [11] and Allagoa et al. [13], indicating calcium as a potentially more reliable biomarker.

Mechanistically, hypocalcemia may increase intracellular calcium in vascular smooth muscle cells, promoting vasoconstriction and hypertension, while also affecting endothelial function and coagulation pathways. Magnesium, as a calcium antagonist, modulates vascular reactivity and serves anti-inflammatory and anticonvulsant roles. These mechanisms are supported by several studies [11-13,16], reinforcing the biological plausibility of our findings.

Given the significant associations between serum calcium and magnesium with preeclampsia risk, severity, and outcomes, our study highlights the potential value of micronutrient assessment and supplementation. The WHO already recommends calcium supplementation in populations with low dietary intake to prevent preeclampsia. Our findings in the tribal population of South Rajasthan—where dietary deficiencies are common—support this guideline and suggest a need for targeted public health interventions to improve maternal nutrition and reduce preeclampsia burden.

CONCLUSION

This study found significantly lower serum calcium and magnesium levels in preeclamptic women compared to normotensive pregnant women in South Rajasthan. These deficiencies were associated with higher blood pressure, greater disease severity, and adverse maternal and fetal outcomes. Calcium showed a stronger and more consistent

association with preeclampsia, supporting the potential role of supplementation, especially in nutritionally vulnerable populations. While magnesium's role showed more variability, it remains relevant. The negative correlation of these minerals with blood pressure and outcomes highlights their possible pathophysiological role and diagnostic utility in preeclampsia, particularly in resource-limited settings.

Declaration:

Conflicts of interests: The authors declare no conflicts of interest. Author contribution: All authors have contributed in the manuscript.

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