Serum Magnesium and Calcium Levels: A Comparative Study Between Pre-Eclamptic and Normotensive Pregnancies

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Abstract: <u>Background</u>: Pre-eclampsia, a significant pregnancy complication, contributes to feto-maternal morbidity and mortality globally. Micronutrient deficiencies, especially calcium and magnesium, are increasingly recognized as potential risk factors for pre-eclampsia, linked to hypertension and other adverse outcomes. <u>Aims and Objective</u>: This study aims to assess serum level of magnesium and calcium in pre-eclamptic pregnancies compared to normotensive pregnancies and to investigate any association between these mineral deficiencies and pre-eclampsia related complications. <u>Materials and Methods</u>: A comparative cross-sectional study was conducted at the Department of Obstetrics and Gynaecology, Sardar Patel Medical College, Bikaner. A total of 100 pregnant female in their third trimester, aged 18-35, were enrolled, divided into two groups: 50 with pre-eclampsia (study group) and 50 with normal pregnancies (control group). Serum calcium and magnesium levels were assessed and compared along with demographic and clinical parameters. <u>Results</u>: The pre-eclampsia group had significantly lower mean serum calcium (8.57 mg/dl) and magnesium levels (1.45 mg/dl) than the control group (8.97 mg/dl) and 1.87 mg/dl). Elevated blood pressure, higher BMI, increased caesarean delivery rates, and lower neonatal birth weights were noted in the pre-eclampsia group. Even though pre-eclampsia was associated with a higher prevalence of problems like intrauterine growth restriction (IUGR), the findings were statistically insignificant. <u>Conclusion</u>: The results suggest a link between reduced serum levels of calcium and magnesium and the risk of pre-eclampsia. Regular monitoring of these serum levels in high-risk pregnancies may offer a preventive strategy. These results necessitate additional investigation into potential prevention of pre-eclampsia using calcium and magnesium supplements.

Keywords: Pre-eclampsia, Pregnancy, Calcium, Magnesium, Hypertensive disorder

1. Introduction

Pre-eclampsia, a pregnancy-specific hypertensive disorder, presents as a major contributor to both fetal and maternal mortality all over the world. The World Health Organisation (WHO) reports that hypertensive disorders, such as preeclampsia, account for 16% of maternal fatalities in Western countries and 9% in Asia (Khan et al., 2006). A blood pressure measurement of ≥140/90 mm Hg taken twice at least 6 hours apart with either proteinuria of at least 300 mg per 24 hours, at least persistent 1+ albumin on dipstick testing, with or without pathological oedema (Sibai, 2003), or signs of end organ dysfunction are all considered pre-eclampsia in patients who were previously normotensive. Obesity, chronic hypertension, advanced maternal age, and genetic predisposition are risk factors. Recent studies have indicated that deficiencies in key micronutrients, particularly calcium and magnesium, may contribute to the etiology of preeclampsia (Sukonpan & Phupong, 2005).

Calcium and magnesium play essential roles in regulating vascular tone, muscle function, and enzymatic activity. Magnesium fortifies endothelial cells and stimulates the contraction of cardiac muscle. In magnesium deficiency, the smooth muscles of arteries constrict, leading to increased vascular resistance and elevated blood pressure (Saputri *et al.*, 2020). Calcium also has a significant role in blood pressure regulation. Reduced calcium intake stimulates the release of

parathyroid hormone, leading to an increase in intracellular calcium levels in vascular smooth muscle, which results in vasoconstriction. The increase in intracellular calcium may also be attained directly through the enhancement of calcitriol production. Both low extracellular calcium and PTH promote renin release, activating the Renin-Angiotensin pathway and releasing aldosterone. Aldosterone induces vasoconstriction and increases renal water absorption, resulting in elevated blood pressure. Deficiencies in these minerals can lead to endothelial dysfunction, vasoconstriction, and ultimately elevated blood pressure (Jain et al., 2010). The present study aims to investigate the potential association of serum magnesium and calcium levels with pre-eclampsia, focusing on their correlation with the onset and progression of this condition. By analysing these mineral levels, the research seeks to elucidate their role in the pathophysiology of preeclampsia and evaluate their impact on the complications associated with the disorder.

2. Materials and Methods

This comparative cross-sectional study was carried out in the Department of Obstetrics and Gynaecology at Sardar Patel Medical College, Bikaner, over a period of one year from August 2023 to July 2024. The study aimed to evaluate and compare serum magnesium and calcium levels in preeclamptic and normotensive pregnancies, involving a total of 100 participants. Fifty women diagnosed with pre-eclampsia

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constituted the study group, whereas fifty normotensive pregnant women comprised the control group.

Participants were recruited based on the following inclusion criteria: singleton pregnancies in their third trimester (gestational age ≥28 weeks), maternal age ranging from 18 to 35 years, and, for the study group, a diagnosis of preeclampsia. Women with chronic hypertension, diabetes, renal diseases, cardiovascular conditions, multiple pregnancies or those undergoing magnesium sulphate therapy were excluded to maintain the homogeneity of the sample and eliminate potential confounding factors.

Comprehensive data were collected for each participant, including demographic information, socioeconomic status, obstetric history, and clinical details. Serum calcium and magnesium levels were quantified through the collection of blood samples using a spectrophotometric method to ensure precise measurement. Additionally, vital parameters such as blood pressure and BMI were recorded, and fetal outcomes were documented to provide a holistic overview of maternal and fetal health in the context of pre-eclampsia.

The data was analysed using SPSS version 22. In order to provide a clear baseline understanding of the participant groups, descriptive statistics were utilised to summarise clinical and demographic characteristics. Chi-square tests were applied to analyse categorical variables, while t-tests were employed for continuous variables to assess the significance of differences between the pre-eclamptic and normotensive groups. To ensure strong and trustworthy interpretations of the results, a p-value of less than 0.05 was established as the criterion for statistical significance.

3. Results

A comparison of study and control groups indicates a slight difference in age distributions. The study group was comprised of the following patient age distribution; 12% ≤20 years, 36% within 21-25 years, 30% within 26-30 years, and 22% >30 years. Meanwhile, the control group comprised 18%

aged \leq 20 years, 50% aged 21-25 years, 26% aged 26-30 years, and 6% aged >30 years. However, a significant statistical difference between the two groups' observed age distributions was not seen (p = 0.120).

A similar socioeconomic level trend was seen in the study and control groups. In the study group, 72% and 28% of the patients corresponded to low and middle socioeconomic groups, respectively, with none placed in the upper socioeconomic group. Likewise, 72% of the control group's members belonged to the low socioeconomic group, 26% to the middle group and 2% to the upper group. The disparity in socioeconomic position between these groups was not statistically significant (p = 0.595). Residence distribution revealed that the majority of patients in both groups were from rural areas.

Gravidity analysis indicated that primigravida accounted for 56% and 58% in the study and control groups, respectively, while the corresponding multigravida magnitudes were 44% and 42%. The distribution difference was not statistically significant (p = 1.000).

Clinical parameters significantly differed between the groups. The study group's mean BMI ($26.05 \pm 3.58 \text{ kg/m}^2$) was significantly higher than that of the control group ($22.70 \pm 2.46 \text{ kg/m}^2$). Comparisons of blood pressure also revealed notable variations. Compared to the control group, which had a mean systolic blood pressure (SBP) of 118.16 ± 8.44 mmHg, the study group's SBP was significantly higher i. e., 156.18 ± 12.97 mmHg. Similarly, the mean diastolic blood pressure (DBP) in the study group (99.24 ± 4.61 mmHg) was significantly greater than in the control group (77.28 ± 5.70 mmHg), with a t-test value of 21.152 and a p-value of 0.0001.

In conclusion, the control and study groups did not exhibit any significant differences in demographic parameters such as age, socioeconomic status, residence, and gravidity. However, the study group exhibited significantly elevated clinical parameters, including BMI, and systolic and diastolic blood pressures, which were indicative of the effects of preeclampsia on these variables.

Table 1: Characteristics of Study Participants (demographic and clinical)

Characteristic	Control Group (n=50)	Study Group (Pre-eclampsia, n=50)	p-value
Age ≤20 years (%)	18%	12%	0.120
Age >30 years (%)	6%	22%	0.120
Low Socioeconomic Status (%)	72%	72%	0.595
Rural Residence (%)	74%	70%	0.824
Primigravida (%)	58%	56%	1.000
Mean BMI (kg/m²)	22.70 ± 2.46	26.05 ± 3.58	0.0001**
Mean SBP (mm Hg)	118.16 ± 8.44	156.18 ± 12.97	0.0001**
Mean DBP (mm Hg)	77.28 ± 5.70	99.24 ± 4.61	0.0001**

Note: SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; ** indicates significance.

Table 2: Biochemical and Outcome Measures

Measure	Control Group (n=50)	Study Group (Pre-eclampsia, n=50)	p-value
Serum Calcium (mg/dl)	8.97 ± 0.47	8.57 ± 0.79	0.0003**
Serum Magnesium (mg/dl)	1.87 ± 0.37	1.45 ± 0.21	0.0001**
Mean Fetal Weight (kg)	2.87 ± 0.47	2.42 ± 0.54	0.0001**
Pre-term Delivery (%)	16%	42%	0.002**
Caesarean Delivery (%)	18%	44%	0.009**
NICU Admission (%)	18%	26%	0.469

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Complications (%)	IUGR: 4%, MAS: 2%, RD: 4%, IUFD: 0,	IUGR: 16%, MAS: 6%, RD: 10%, IUFD:	NS
•	MATERNAL MORTALITY: 0	4%, MATERNAL MORTALITY: 4%	

Note: $IUGR = Intrauterine\ Growth\ Restriction,\ MAS = Meconium\ Aspiration\ Syndrome,\ RD = Respiratory\ Distress,\ NS = Not\ Significant;\ ** indicates\ significance.$

Mean levels of serum calcium and magnesium were significantly lower in the study group $(8.57\pm0.79 \text{ mg/dl})$ and $1.45\pm0.21 \text{ mg/dl}$, respectively) compared to the control group $(8.97\pm0.47 \text{ mg/dl})$ and $1.87\pm0.37 \text{ mg/dl}$, respectively) (p < 0.0003 for calcium and p < 0.0001 for magnesium). These findings support the hypothesis that calcium and magnesium deficiencies contribute to pre-eclampsia's pathophysiology.

Caesarean delivery was more frequent in the pre-eclampsia group (44%) than in controls (16%) (p = 0.009), indicating that pre-eclampsia often necessitates surgical intervention. A significantly lower mean fetal weight was reported in the study group i. e., 2.42 ± 0.54 kg vs. 2.87 ± 0.47 kg in controls, and the rate of pre-term delivery was significantly higher 42% in pre-eclampsia group vs.28% in controls. Although a greater number of NICU admissions were recorded in the pre-eclampsia group than controls (26% vs.18%), this difference was of no statistical significance (p = 0.469).

Complications like IUGR, MAS and RD were relatively more common in study group than in control group; however, the difference was not statistically significant. Although rare, cases of maternal mortality and intrauterine fetal demise were exclusively seen in the pre-eclampsia group (4% for each).

4. Discussion

Our study confirms that pre-eclampsia is associated with significant reductions in serum magnesium and calcium levels, consistent with findings by Sukonpan & Phupong (2005) and Jain *et al.* (2010). The increased blood pressure, higher BMI, and adverse maternal and fetal outcomes observed among pre-eclamptic patients align with evidence linking mineral deficiencies to hypertensive disorders in pregnancy.

Lower serum calcium levels can contribute to hypertension due to increased parathyroid hormone secretion, while magnesium deficiency exacerbates vascular resistance and endothelial dysfunction (Darkwa *et al.*, 2017). Thus, both deficiencies may play a role in the cascade of inflammatory responses and oxidative stress characterizing pre-eclampsia (Sethi *et al.*, 2021). However, the absence of significant differences in complications like NICU admissions suggests that other factors, such as timely medical intervention, might mitigate severe outcomes.

5. Conclusion

This study highlights a statistically significant association between low serum calcium and magnesium levels and the incidence of pre-eclampsia. The findings suggest that monitoring these mineral levels in high-risk pregnancies could serve as an early preventive measure. Given that pre-eclampsia continues to be a global health challenge, these insights contribute to ongoing research on mineral supplementation's role in mitigating pregnancy-related hypertensive disorders.

6. Recommendations

- Screening: Routine screening for serum calcium and magnesium levels in high-risk pregnancies.
- 2) **Supplementation**: Investigating the role of calcium and magnesium supplementation as a preventive measure in pregnancies with a high risk of pre-eclampsia.
- 3) Further Research: Longitudinal studies assessing the impact of supplementation on reducing pre-eclampsia incidence and severity are warranted. Additionally, investigating other micronutrients and biochemical markers associated with vascular health and endothelial function could offer more comprehensive prevention and treatment strategies for hypertensive disorders in pregnancy.

7. Limitations

- 1) **Sample Size**: Although our study provides valuable insights, the relatively small sample size limits the generalizability of the results.
- Single-Centre Study: Conducted in a single hospital, regional factors could influence outcomes; thus, multicentre studies would enhance representativeness.
- Potential Confounders: While efforts were made to control for known confounders, lifestyle and dietary variations were not accounted for, which might have impacted mineral levels.

8. Future Directions

Larger, multi-centre studies on a range of populations are necessary to validate these results and to determine effective magnesium and calcium supplementation protocols. Further research should also explore the potential interactions between these micronutrients and other physiological and biochemical factors in pre-eclampsia's pathophysiology. If proven effective, supplementing high-risk populations with calcium and magnesium could become a low-cost, widely accessible preventative measure to improve maternal and fetal outcomes globally.

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