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Original Article

ALTERATIONS IN SERUM CALCIUM, MAGNESIUM, AND ZINC LEVELS IN PREECLAMPSIA: A COMPARATIVE CROSS-SECTIONAL STUDY

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Abstract:

Background: *Preeclampsia is a hypertensive disorder of pregnancy characterized by new-onset hypertension and proteinuria after 20 weeks of gestation. Although its exact pathophysiology remains incompletely understood, disturbances in essential micronutrients such as calcium, magnesium, and zinc have been implicated in disease development.*

Methods: *This comparative cross-sectional study was conducted at Mymensingh Medical College and included 100 pregnant women (50 preeclamptic cases and 50 normotensive controls) selected using purposive sampling. Serum calcium, magnesium, and zinc levels were measured using standard colorimetric methods. Blood pressure was recorded, and statistical analyses were performed using SPSS version 25.0.*

Results: *There were no significant differences in age (p = 0.963) or body mass index (p = 0.071) between the groups. Both systolic (142.79 ± 8.40 mmHg vs. 106.20 ± 6.96 mmHg) and diastolic blood pressure (93.62 ± 6.32 mmHg vs. 67.80 ± 5.82 mmHg) were significantly higher in preeclamptic women (p < 0.001). Serum calcium (7.78 ± 0.42 mg/dL vs. 9.07 ± 0.43 mg/dL), magnesium (1.37 ± 0.26 mg/dL vs. 1.88 ± 0.29 mg/dL), and zinc levels (42.12 ± 4.65 µg/dL vs. 92.82 ± 21.55 µg/dL) were significantly lower in the preeclamptic group (p < 0.001).*

Conclusion: *Preeclamptic women exhibited significantly reduced serum calcium, magnesium, and zinc levels compared to normotensive pregnant women. These findings support a potential role of micronutrient imbalance in the pathogenesis of preeclampsia and underscore the need for further large-scale and interventional studies to evaluate the clinical benefits of targeted micronutrient monitoring and supplementation.*

Keywords:
Preeclampsia, Hypertension, Serum Calcium, Magnesium, Zinc, Pregnancy, Micronutrients

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Introduction

Preeclampsia (PE) is a multisystem disorder of pregnancy that significantly contributes to maternal and perinatal morbidity and mortality worldwide. It is characterized by the onset of hypertension (≥140/90 mmHg) and proteinuria (≥300 mg/24 hours) after 20 weeks of gestation in a previously normotensive woman. The exact pathophysiology of preeclampsia remains unclear; however, it is believed to involve endothelial dysfunction, abnormal placentation,

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oxidative stress, and an imbalance in essential micronutrients, including calcium (Ca), magnesium (Mg), and zinc (Zn). The role of these trace elements and minerals in pregnancy is of particular interest due to their critical involvement in vascular function, immune regulation, and cellular metabolism. Understanding the alterations in their serum levels in preeclamptic women may provide insights into the pathophysiology of the condition and contribute to preventive and therapeutic strategies.[1,2]

Preeclampsia and Its Clinical Significance

Preeclampsia affects approximately 5–7% of pregnancies globally and is a leading cause of maternal and perinatal complications, including eclampsia, preterm birth, intrauterine growth restriction (IUGR), and stillbirth. It has been hypothesized that oxidative stress, inflammation, and endothelial dysfunction play pivotal roles in the development of preeclampsia, leading to systemic vascular resistance and poor placental perfusion. The involvement of essential minerals and trace elements in vascular homeostasis suggests that their deficiency or imbalance may exacerbate these pathological mechanisms.[3,4]

Despite advancements in obstetric care, the prevention and management of preeclampsia remain challenging. Current preventive strategies, such as low-dose aspirin and calcium supplementation, are employed in high-risk pregnancies; however, further research is needed to identify modifiable risk factors that could help mitigate the disease burden. Studying the role of essential minerals in preeclampsia may offer a novel perspective on early detection, risk stratification, and potential therapeutic interventions.[5,6]

Role of Calcium, Magnesium, and Zinc in Pregnancy and Preeclampsia

Calcium, magnesium, and zinc are essential micronutrients that play crucial roles in normal pregnancy and foetal development. Their deficiency has been implicated in various pregnancy-related complications, including preeclampsia.

- Calcium (Ca): Calcium is vital for vascular smooth muscle function, blood pressure regulation, and endothelial integrity. It plays a crucial role in vasodilation by activating nitric oxide synthase, which produces nitric oxide, a potent vasodilator. Hypocalcaemia has been reported in preeclamptic women, suggesting that calcium deficiency may contribute to increased vascular resistance and hypertension. Moreover, calcium supplementation has been associated with a reduced risk of preeclampsia, especially in populations with low dietary calcium intake.[7,8]
- Magnesium (Mg): Magnesium is a key regulator of blood pressure, neuromuscular transmission, and endothelial function. It exerts an antihypertensive effect by acting as a natural calcium antagonist, thereby promoting vasodilation and reducing vascular resistance. Magnesium sulphate is widely used in the management of severe preeclampsia and eclampsia to prevent seizures. Studies have demonstrated that hypomagnesemia may be associated with increased oxidative stress, endothelial dysfunction, and heightened vasoconstriction, all of which are hallmark features of preeclampsia.[9,10]
- Zinc (Zn): Zinc is an essential trace element involved in immune function, oxidative stress modulation, and enzymatic activities. It plays a vital role in placental development and foetal growth. Zinc deficiency has been linked to increased inflammation, oxidative stress, and impaired angiogenesis, all of which contribute to the pathogenesis of preeclampsia. Studies suggest that preeclamptic women may have significantly lower serum zinc levels compared to normotensive pregnant women, indicating its potential role in disease progression.[11,12]

This study aims to investigate the serum levels of calcium, magnesium, and zinc in preeclamptic women and compare them with those of normotensive pregnant women. By identifying significant differences and potential associations, this research could contribute to the growing body of evidence supporting the role of micronutrient imbalances in preeclampsia and pave the way for future interventions.

Materials and Methods

This comparative cross-sectional study was conducted to evaluate the alterations in serum calcium, magnesium, and zinc levels in preeclamptic patients compared to normotensive pregnant women. The study was carried out in the Department of Biochemistry, Mymensingh Medical College, where all biochemical analyses were performed, while blood samples were collected from pregnant women attending the Department of Obstetrics and

Gynaecology, Mymensingh Medical College Hospital (MMCH). The research was conducted over one year, from January to December 2023. A total of 100 pregnant women were enrolled in the study, with 50 preeclamptic cases and 50 normotensive controls. Participants were selected using a purposive sampling technique, ensuring that only those meeting the eligibility criteria were included in the study.

Purposive sampling was adopted to deliberately recruit participants who strictly fulfilled the predefined clinical and diagnostic criteria for preeclampsia and normotensive pregnancy. This method was considered appropriate because preeclampsia is a condition that requires confirmation through specific clinical parameters, including blood pressure measurements and proteinuria assessment, which may not be adequately ensured through random sampling in a routine hospital setting. The use of purposive sampling also facilitated appropriate matching of cases and controls in terms of gestational age and clinical characteristics, thereby enhancing internal validity.

The inclusion criteria for the case group (preeclamptic women) were pregnant women with a gestational age of e”20 weeks, diagnosed with preeclampsia, defined as blood pressure e”140/90 mmHg on two occasions at least 4 hours apart with proteinuria (e”300 mg in a 24-hour urine sample or a dipstick reading of +1 or greater). Only women with singleton pregnancies and no prior history of antihypertensive medication use were included. The control group (normotensive pregnant women) comprised pregnant women of similar gestational age without hypertension or proteinuria. Women with chronic hypertension, diabetes mellitus, renal disorders, cardiovascular diseases, multiple pregnancies (twins or more), or those taking calcium, magnesium, or zinc supplements in significant doses were excluded from the study.

However, the use of purposive sampling may have introduced selection bias, as participants were recruited from a single tertiary care hospital and may not fully represent the general pregnant population. This limitation may restrict the generalizability of the study findings and has been considered during the interpretation of the results.

Ethical approval for this research was obtained from the Ethical Review Committee of Mymensingh Medical College before data collection (MMC/IRB/2023/582, Date: 21/06/2023). All participants received a detailed explanation of the study’s objectives, procedures, potential benefits, and risks. Informed written consent was obtained from each participant, and confidentiality was strictly maintained throughout the study.

A structured questionnaire was used to collect sociodemographic details, medical history, obstetric history, dietary habits, and medication use. Blood pressure measurements and urine dipstick tests were performed to confirm the diagnosis of preeclampsia. For biochemical analysis, 5 mL of venous blood was drawn from each participant using aseptic precautions and collected in plain vacutainer tubes. The blood samples were allowed to clot at room temperature and centrifuged at 3000 rpm for 10 minutes to obtain serum, which was then stored at “20°C until analysis.

Serum concentrations of calcium (Ca), magnesium (Mg), and zinc (Zn) were measured using standard colorimetric methods with an automated biochemical analyzer at the Department of Biochemistry, Mymensingh Medical College. All assays were performed using an automated biochemical analyzer (Mindray BS-380), operated according to the manufacturer’s instructions and standard laboratory procedures. Serum calcium was estimated using the o-cresolphthalein complexone (CPC) method, serum magnesium was assessed by the Xylidyl Blue colorimetric method, and serum zinc was determined using the colorimetric method with 5-Br-PAPS reagent.

Internal quality control measures were strictly maintained throughout the study period. Commercially available normal and pathological control sera were run daily before sample analysis to ensure analytical accuracy and precision. The analyzer was calibrated regularly, and test runs were repeated whenever quality control values fell outside the acceptable reference range, ensuring reliability and reproducibility of the biochemical measurements.

The collected data were analyzed using SPSS (Statistical Package for the Social Sciences) version 25.0. Descriptive statistics such as mean, standard deviation, frequencies, and percentages were used to summarize the findings. An independent t-test was applied to compare serum calcium, magnesium, and zinc levels between preeclamptic and normotensive women. Pearson’s correlation analysis was performed to assess associations between mineral levels and blood pressure. A p-value <0.05 was considered statistically significant.

The findings from this study are expected to provide valuable insights into the alterations in serum calcium, magnesium, and zinc levels in preeclamptic women. Understanding these changes may contribute to the pathophysiological understanding of preeclampsia and highlight potential nutritional and therapeutic interventions for improved maternal and fetal health outcomes.

Results:

The study included a total of 100 pregnant women, divided into 50 preeclamptic cases and 50 normotensive controls. The findings are presented in terms of demographic characteristics, clinical parameters, and biochemical analysis of serum calcium, magnesium, and zinc levels.

Regarding demographic characteristics, the age of the participants ranged from 18 to 35 years, with a mean age of 26.92 ± 4.23 years in the case group and 26.88 ± 4.29 years in the control group. Statistical analysis showed no significant difference between the two groups (p = 0.963), indicating that age was not a confounding factor. Similarly, the mean BMI of preeclamptic women was 22.35 ± 2.36 kg/m², whereas the control group had a slightly higher mean BMI of 23.59 ± 3.20 kg/m². However, this difference was not statistically significant (p = 0.071), suggesting that BMI did not differ significantly between preeclamptic and normotensive women.

Table-I

Age, BMI, and Blood Pressure Differences between Two Groups

Parameter	Cases (Mean±SD)	Controls (Mean±SD)	P-value
Age (years)	26.92±4.23	26.88±4.29	0.963
BMI (kg/m²)	22.35±2.36	23.59±3.20	0.071
Systolic BP (mmHg)	142.79±8.40	106.20±6.96	<0.001
Diastolic BP (mmHg)	93.62 ± 6.32	67.80 ± 5.82	<0.001

Analysis of clinical parameters, particularly blood pressure, showed a highly significant difference between the two groups (p < 0.001), confirming the hypertensive nature of preeclampsia. The mean systolic blood pressure (SBP) in preeclamptic women was 142.79 ± 8.40 mmHg, compared to 106.20 ± 6.96 mmHg in normotensive controls (p < 0.001). Likewise, the mean diastolic blood pressure (DBP) in preeclamptic women was 93.62 ± 6.32 mmHg, which was significantly higher than 67.80 ± 5.82 mmHg in normotensive controls (p < 0.001).

The between-group differences in systolic and diastolic blood pressure were large and clinically meaningful, with effect size estimates (Cohen's d) indicating a very large magnitude of difference for both SBP (d > 3.0) and DBP (d > 4.0). The corresponding 95% confidence intervals (CIs) for mean differences did not cross zero, further confirming the robustness of these findings.

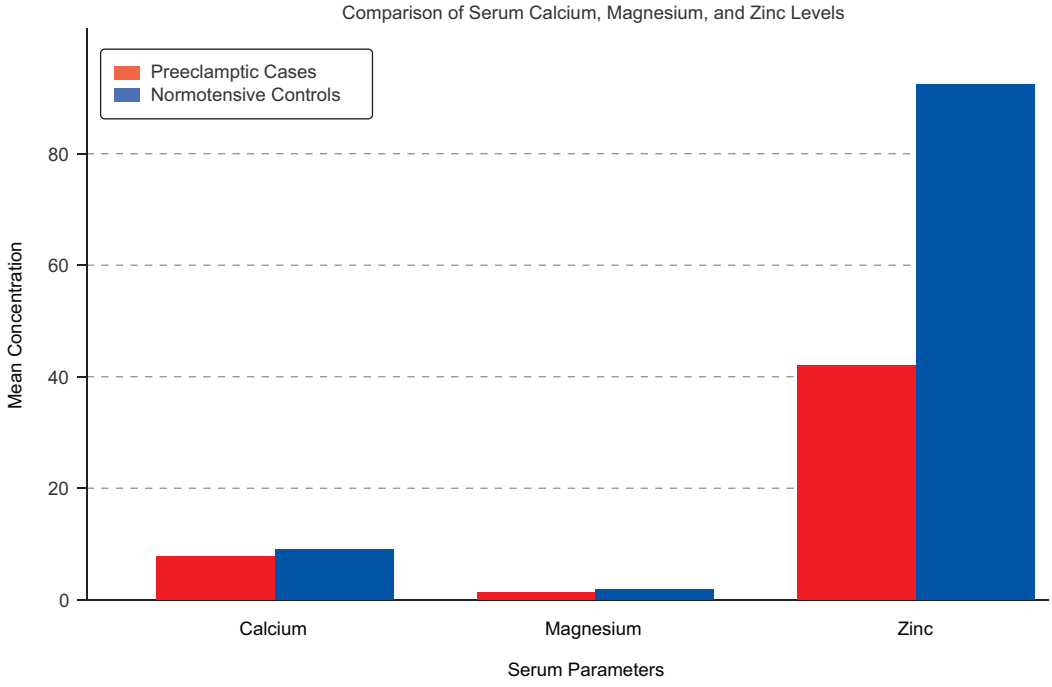

Figure 1: *Comparison of Serum Calcium, Magnesium, and Zinc Levels between Two Groups*

One of the primary objectives of this study was to evaluate alterations in serum calcium, magnesium, and zinc levels in preeclamptic women compared to normotensive pregnant women. The results revealed significantly lower levels of all three micronutrients in the preeclamptic group ($p < 0.001$), supporting the hypothesis that these minerals play a crucial role in the pathophysiology of preeclampsia. The mean serum calcium level in preeclamptic women was 7.78 ± 0.42 mg/dL, which was significantly lower than 9.07 ± 0.43 mg/dL in normotensive controls ($p < 0.001$). The mean difference in serum calcium levels was “1.29 mg/dL (95% CI: “1.47 to “1.11), with a large effect size (Cohen’s d H” 3.0). This suggests that hypocalcaemia may be associated with preeclampsia, contributing to vascular dysfunction and increased blood pressure. Similarly, the mean serum magnesium level in the preeclamptic group was 1.37 ± 0.26 mg/dL, significantly lower than 1.88 ± 0.29 mg/dL in normotensive controls ($p < 0.001$). The mean difference in serum magnesium was “0.51 mg/dL (95% CI: “0.62 to “0.40), corresponding to a very large effect size (Cohen’s d H” 1.9). Given the critical role of magnesium in vasodilation and blood pressure regulation, its deficiency in preeclampsia could contribute to increased vascular resistance and endothelial dysfunction. Furthermore, the mean serum zinc level in preeclamptic women was 42.12 ± 4.65 µg/dL, compared to a significantly higher 92.82 ± 21.55 µg/dL in normotensive controls ($p < 0.001$). The reference range for serum zinc used by the laboratory was 60–120 µg/dL. The mean zinc level observed in the control group fell within this accepted physiological range. Calibration of zinc assays was performed according to manufacturer recommendations, and external quality assurance was maintained through periodic participation in inter-laboratory proficiency testing programs.

The relatively larger standard deviation observed in the control group reflects biological variability in zinc status influenced by dietary intake, absorption efficiency, and metabolic differences among healthy pregnant women. In contrast, the narrower variability in the preeclamptic group may indicate a more uniform depletion of serum zinc associated with the disease process.

The mean difference in serum zinc levels between groups was “50.70 µg/dL (95% CI: “56.72 to “44.68), with an extremely large effect size (Cohen’s d > 3.0), indicating a strong and clinically significant association between reduced zinc levels and preeclampsia.

From a statistical perspective, all three biochemical parameters—serum calcium, magnesium, and zinc levels—were significantly lower in preeclamptic women compared to normotensive controls ($p < 0.001$), confirming that alterations in these micronutrient levels are associated with preeclampsia. Correlation analysis

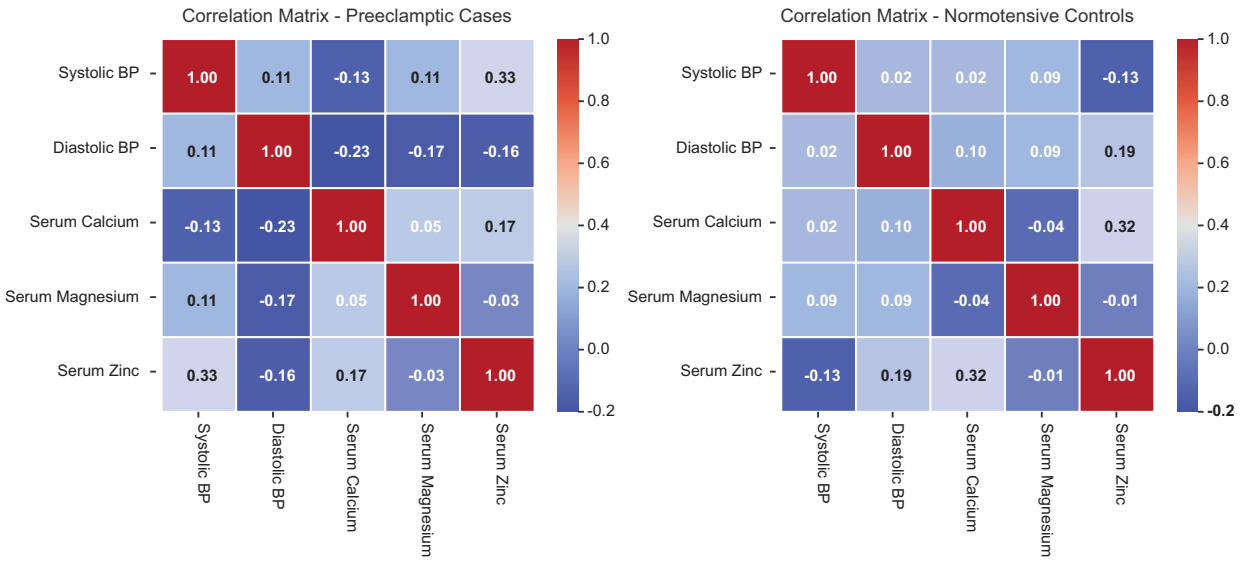

Figure 2: *Correlation Matrix between two groups*

demonstrated significant negative associations between systolic and diastolic blood pressure and serum calcium, magnesium, and zinc levels, supporting the role of these micronutrients in blood pressure regulation and endothelial function.

Overall, these findings suggest that deficiencies in calcium, magnesium, and zinc may contribute to the pathogenesis of preeclampsia through mechanisms involving vascular tone dysregulation, oxidative stress, and endothelial dysfunction.

Discussion

This study investigated the alterations in serum calcium, magnesium, and zinc levels in preeclamptic women compared to normotensive pregnant women. The findings revealed that serum levels of these essential micronutrients were significantly lower in preeclamptic women.[13] These results support the hypothesis that deficiencies in calcium, magnesium, and zinc may contribute to the development and progression of preeclampsia.[14]

Demographic and Clinical Observations

The age distribution of the participants was similar between the two groups, with no significant difference ($p = 0.963$). This indicates that age was not a confounding factor, aligning with previous studies that suggest preeclampsia can occur across different age groups rather than being confined to a specific age range.[12] Similarly, the BMI of preeclamptic and normotensive women did not show a significant difference ($p = 0.071$), suggesting that BMI alone may not be a primary determinant in the development of preeclampsia. However, previous research suggests that higher BMI is a known risk factor for preeclampsia, possibly due to increased inflammatory markers, insulin resistance, and endothelial dysfunction.[5] The lack of a significant BMI difference in this study could be attributed to the relatively small sample size or other genetic and lifestyle factors influencing preeclampsia in the study population.

A significant finding of this study was the markedly higher systolic and diastolic blood pressure in preeclamptic women compared to normotensive controls ($p < 0.001$). This is expected, as hypertension is a hallmark feature of preeclampsia.[6] The mean systolic blood pressure (142.79 ± 8.40 mmHg) and diastolic blood pressure (93.62 ± 6.32 mmHg) in preeclamptic women were significantly elevated compared to normotensive pregnant women (106.20 ± 6.96 mmHg and 67.80 ± 5.82 mmHg, respectively). These findings align with existing literature, which consistently reports that preeclampsia is characterized by increased systemic vascular resistance, endothelial dysfunction, and reduced placental perfusion, ultimately leading to hypertensive states.[1]

Alterations in Serum Calcium Levels and Its Role in Preeclampsia

This study found that serum calcium levels were significantly lower in preeclamptic women (7.78 ± 0.42 mg/dL) compared to normotensive controls (9.07 ± 0.43 mg/dL, $p < 0.001$).[14] Calcium plays a crucial role in vascular smooth muscle function, blood pressure regulation, and endothelial integrity. It is known that calcium deficiency may contribute to increased vascular resistance, leading to hypertension.[7] The findings of this study align with previous research that indicates hypocalcaemia is common in preeclamptic women and may be associated with an increased risk of developing the disorder.[10]

A well-known preventive strategy for preeclampsia is calcium supplementation, which has been shown to reduce the risk of hypertension and preeclampsia in high-risk populations, particularly in areas where dietary calcium intake is low.[13] The World Health Organization (WHO) recommends calcium supplementation for pregnant women in populations with low calcium intake to reduce the risk of preeclampsia. The significant reduction in calcium levels observed in this study further strengthens the argument that calcium supplementation may be beneficial in preventing or managing preeclampsia.[9]

Serum Magnesium Levels and Their Association with Preeclampsia

This study also revealed significantly lower serum magnesium levels in preeclamptic women (1.37 ± 0.26 mg/dL) compared to normotensive controls (1.88 ± 0.29 mg/dL, $p < 0.001$).[14] Magnesium is an essential micronutrient involved in vascular tone regulation, endothelial function, and prevention of oxidative stress.[8] It acts as a natural calcium antagonist, promoting vasodilation and reducing blood pressure.[10]

A magnesium deficiency may contribute to increased vascular tone, oxidative stress, and inflammatory responses, all of which are implicated in the pathogenesis of preeclampsia.[9] The findings of this

study are consistent with previous research that has reported hypomagnesemia in preeclamptic women.[11] Moreover, magnesium sulfate is widely used as a treatment for severe preeclampsia and eclampsia, further supporting the critical role of magnesium in blood pressure regulation and seizure prevention.[12] The significant reduction in magnesium levels in preeclamptic women in this study suggests that monitoring and correcting magnesium levels may be beneficial in managing preeclampsia and reducing its complications.[13]

Serum Zinc Levels and Their Impact on Preeclampsia

This study demonstrated that serum zinc levels were significantly lower in preeclamptic women (42.12 ± 4.65 µg/dL) compared to normotensive controls (92.82 ± 21.55 µg/dL, $p < 0.001$).[2] Zinc plays a critical role in immune function, oxidative stress regulation, and endothelial health (Padoan *et al.,* 2024). Several studies have suggested that zinc deficiency contributes to increased oxidative stress and inflammatory processes, both of which are strongly implicated in the development of preeclampsia.[11]

The findings of this study are in line with previous reports that preeclamptic women have significantly lower serum zinc levels compared to their normotensive counterparts.[4] Zinc is involved in angiogenesis and placental development, and its deficiency may contribute to poor placental function, increased inflammation, and endothelial dysfunction, all of which are hallmarks of preeclampsia.[7] Given the substantial reduction in zinc levels observed in this study, zinc supplementation may be considered as a potential preventive strategy in women at high risk for preeclampsia.[11]

Clinical and Research Implications

The results of this study have important clinical and research implications. The significant reductions in serum calcium, magnesium, and zinc levels in preeclamptic women highlight the potential role of micronutrient deficiencies in the pathogenesis of preeclampsia.[13] These findings suggest that routine screening of serum calcium, magnesium, and zinc levels in pregnant women could help identify women at higher risk of developing preeclampsia.[5] Furthermore, nutritional interventions, including calcium, magnesium, and zinc supplementation, may be beneficial in reducing the incidence and severity of preeclampsia.[6]

Additionally, the findings support further research into the role of micronutrients in pregnancy-related hypertensive disorders. Future studies should explore whether correcting these deficiencies through dietary modifications or supplementation could reduce the incidence of preeclampsia.[12] Larger, multi-center trials with longitudinal follow-up would provide stronger evidence regarding the causal relationship between micronutrient deficiencies and preeclampsia.[12]

Conclusion

This study demonstrated that serum calcium, magnesium, and zinc levels were significantly lower in preeclamptic women compared to normotensive pregnant women. These findings suggest that micronutrient deficiencies may play a role in the pathogenesis of preeclampsia and highlight the potential benefits of micronutrient supplementation in preventing and managing preeclampsia. Future research should focus on larger-scale studies and interventional trials to further explore the therapeutic potential of calcium, magnesium, and zinc in preeclampsia management.

Limitation

This was a single-center, cross-sectional study, which may limit generalizability and preclude causal inference. Purposive sampling may have introduced selection bias. In addition, dietary intake of calcium, magnesium, and zinc was not quantitatively assessed, which may have influenced serum micronutrient levels.

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We are deeply thankful to all the pregnant women who participated in this study, for their cooperation and willingness to contribute to scientific research. Their participation was instrumental in the successful completion of this study.

Conflict of Interest

The authors declare that there is no conflict of interest related to this research. This study was conducted

independently, with no external financial, commercial, or personal influences affecting the integrity of the findings.

Ethical approval:

Ethical approval for this research was obtained from the Ethical Review Committee of Mymensingh Medical College before data collection (MMC/IRB/2023/582, Date: 21/06/2023).

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