

Original Research Article

COMPARATIVE ANALYSIS OF SERUM ZINC, COPPER, IRON, AND MAGNESIUM LEVELS IN PREGNANT WOMEN WITH AND WITHOUT PREECLAMPSIA: AN ANALYTICAL CROSS-SECTIONAL STUDY

Balaji B R¹, Mayuri Madhukarrao Palmate², Mahesh Bhanudasrao Phad³

¹Assistant Professor, Department of Biochemistry, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh, India.

²Assistant Professor, Department of Biochemistry, MIMSR Medical College Latur, Maharashtra, India.

³Assistant Professor, Department of Biochemistry, Government medical college, Baramati, Maharashtra, India.

Received : 21/07/2025
Received in revised form : 10/09/2025
Accepted : 29/09/2025

Corresponding Author:

Dr. Mayuri Madhukarrao Palmate,
Assistant Professor, Department of
Biochemistry, MIMSR Medical College
Latur, Maharashtra, India.
Email: mayurimpalmate@gmail.com

DOI: 10.70034/ijmedph.2025.4.224

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (4); 1246-1250

ABSTRACT

Background: Preeclampsia is a hypertensive disorder of pregnancy characterized by new-onset hypertension and proteinuria after 20 weeks of gestation. It remains a leading cause of maternal and perinatal morbidity and mortality worldwide. Emerging evidence implicates trace element imbalances—particularly of zinc, copper, iron, and magnesium—in the pathogenesis of preeclampsia, potentially through mechanisms involving oxidative stress, endothelial dysfunction, and vascular dysregulation. This study aimed to assess and compare serum levels of these trace elements in pregnant women with and without preeclampsia, and to explore their potential pathophysiological role.

Materials and Methods: This analytical cross-sectional study was conducted at a tertiary care hospital over two years. A total of 276 pregnant women beyond 20 weeks of gestation were enrolled, comprising 138 preeclamptic cases and 138 age-matched normotensive controls. Inclusion and exclusion criteria were applied rigorously. Venous blood samples were collected, centrifuged, and analyzed using validated colorimetric methods. Serum levels of zinc, copper, iron, and magnesium were measured. Statistical analysis was performed using the independent samples t-test; p-values <0.05 were considered statistically significant.

Results: Mean serum zinc, copper, and magnesium levels were significantly lower in preeclamptic women ($37.75 \pm 3.86 \mu\text{g/dL}$, $47.23 \pm 4.16 \mu\text{g/dL}$, and $0.96 \pm 0.27 \text{ mg/dL}$ respectively) compared to controls ($87.37 \pm 7.37 \mu\text{g/dL}$, $94.41 \pm 8.09 \mu\text{g/dL}$, and $2.03 \pm 0.48 \text{ mg/dL}$) ($p < 0.0001$ for all). In contrast, serum iron levels were significantly elevated in the preeclampsia group ($184.29 \pm 5.53 \mu\text{g/dL}$ vs. $96.30 \pm 8.54 \mu\text{g/dL}$; $p < 0.0001$).

Conclusion: Preeclamptic pregnancies are associated with significant alterations in trace element status. Depletion of zinc, copper, and magnesium, along with elevated iron levels, may contribute to the disease's pathophysiology. These elements warrant further investigation as potential biomarkers for early detection and as targets for preventive interventions.

Keywords: Preeclampsia, Trace Elements, Zinc, Magnesium, Oxidative Stress.

INTRODUCTION

Preeclampsia is a multisystem hypertensive disorder unique to pregnancy, typically defined by new-onset hypertension ($\geq 140/90 \text{ mmHg}$) and proteinuria after 20 weeks of gestation in a previously normotensive

woman. It affects approximately 5–10% of pregnancies globally and remains a leading cause of maternal and perinatal morbidity and mortality, especially in low-resource settings¹.

The exact pathogenesis of preeclampsia is not fully understood, but growing evidence supports a

multifactorial model involving abnormal placental development, systemic endothelial dysfunction, oxidative stress, and a heightened inflammatory response². A prominent biochemical hallmark of preeclampsia is oxidative stress, resulting from an imbalance between reactive oxygen species (ROS) production and antioxidant defense mechanisms. Trace elements such as zinc, copper, iron, and magnesium play vital roles in maintaining redox balance, vascular tone, and immune modulation, suggesting that their alteration could contribute to the disease mechanism^{3–5}.

Zinc is a crucial cofactor for numerous enzymes involved in antioxidant defense (e.g., superoxide dismutase), DNA repair, and cellular proliferation. Its deficiency has been associated with impaired placental growth, poor trophoblast invasion, and elevated oxidative stress — all central to preeclampsia pathogenesis⁶. Copper, although essential in moderate concentrations, is redox-active and can contribute to oxidative tissue injury when unbound, thereby potentially exacerbating endothelial dysfunction⁷. Iron is similarly a double-edged element; while it supports oxygen transport, excessive free iron can catalyze the Fenton reaction, generating harmful hydroxyl radicals⁸. Conversely, magnesium acts as a natural calcium antagonist, promoting vasodilation and inhibiting vascular smooth muscle contraction — a mechanism that underpins its clinical use in preventing eclamptic seizures⁹.

Numerous case-control and observational studies have reported that serum concentrations of these trace elements are significantly altered in preeclamptic women compared to healthy pregnant controls. A meta-analysis involving over 50 studies confirmed that zinc and magnesium levels are typically lower in preeclampsia, whereas serum iron levels tend to be elevated¹⁰. These alterations may not only reflect the systemic oxidative stress and inflammation characteristic of preeclampsia but could also play a causative role.

Despite considerable research, findings remain inconsistent across populations and methodologies. For instance, some studies observed significant deficiencies in zinc and copper among preeclamptic patients¹¹, while others found no significant difference between cases and controls¹². Similarly, the role of serum iron remains controversial, with some reports of elevation and others of no change¹³. Such inconsistencies underscore the need for well-structured, population-specific studies.

In the Indian context, where micronutrient deficiencies during pregnancy are common due to dietary habits, socioeconomic factors, and limited antenatal supplementation, studying trace element status in preeclampsia is particularly relevant. However, comprehensive local data on the simultaneous status of zinc, copper, iron, and magnesium in preeclampsia remain limited.

Understanding trace element imbalances in preeclampsia can enhance early risk prediction, guide targeted supplementation strategies, and improve maternal-fetal outcomes. The current study aims to fill this gap by analyzing and comparing the serum levels of zinc, copper, iron, and magnesium in pregnant women with and without preeclampsia in a tertiary care hospital setting.

MATERIALS AND METHODS

This analytical cross-sectional study was conducted in the Department of Biochemistry in collaboration with the Department of Obstetrics and Gynaecology at a tertiary care hospital over a period of two years. A total of 276 pregnant women were enrolled and categorized into two groups: 138 pregnant women clinically diagnosed with preeclampsia (cases), and 138 normotensive pregnant women (controls), matched for gestational age. Preeclampsia was defined according to standard diagnostic criteria as a systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg after 20 weeks of gestation, accompanied by proteinuria. Inclusion criteria for both groups were pregnant women aged between 20–40 years and beyond 20 weeks of gestation. Participants with pre-existing conditions such as diabetes mellitus, chronic hypertension, renal or thyroid disorders, cardiovascular diseases, severe anemia, infections, or those on medications like diuretics, corticosteroids, and antihypertensives were excluded. Written informed consent was obtained from all participants. Ethical clearance for the study was obtained from the Institutional Ethics Committee, and all procedures were carried out in accordance with the Declaration of Helsinki.

Venous blood samples were collected under aseptic conditions. For controls, leftover samples from routine antenatal testing were utilized after obtaining consent. All samples were allowed to clot at room temperature and then centrifuged at 3000 rpm for 10 minutes. The separated serum was analyzed for zinc, copper, iron, and magnesium using colorimetric methods with commercially available kits. Zinc estimation was based on the formation of a purple-colored complex with nitro-PAPS in alkaline medium, with absorbance read at 570 nm. Copper, iron, and magnesium were also determined by established spectrophotometric protocols specific to each element. All biochemical analyses were conducted in the central clinical biochemistry laboratory using a semi-automated photometric analyzer. Quality control was ensured by processing standards and controls with each batch of samples. Statistical analysis was performed using appropriate software; the data were expressed as mean $\pm$ standard deviation, and group comparisons were conducted using the independent samples t-test. A p-value <0.05 was considered statistically significant.

RESULTS

A total of 276 pregnant women were included in the study, with 138 in the preeclamptic group and 138 in the normotensive control group (Table 1). The participants were age-matched, and the groups were similar in terms of demographic distribution.

Table 1: Distribution of Study Participants into Case and Control Groups

Group	Number of Participants (n)	Percentage (%)
Preeclampsia Cases	138	50.0%
Normotensive Controls	138	50.0%
Total	276	100%

Age-wise distribution revealed that the majority of participants in both groups were between 21 and 25 years of age, accounting for 49.3% of cases and 50.7% of controls. The youngest age group (18–20 years) comprised 26.8% of the cases and 31.2% of the controls, while women aged above 30 years were

least represented in both groups (Table 2). The mean age of preeclamptic women was slightly higher (23.64 ± 4.07 years) compared to the control group (22.88 ± 3.49 years); however, the difference was not statistically significant (Table 3).

Table 2: Age-wise Distribution of Study Participants

Age Group (Years)	Preeclampsia Cases (n = 138)	%	Controls (n = 138)	%
18 – 20	37	26.8	43	31.2
21 – 25	68	49.3	70	50.7
26 – 30	20	14.5	20	14.5
> 30	13	9.4	5	3.6
Total	138	100%	138	100%

Table 3: Comparison of Mean Age Between Preeclampsia Cases and Controls

Group	Mean Age (Years)	Standard Deviation ($\pm$ SD)
Preeclampsia Cases	23.64	± 4.07
Normotensive Controls	22.88	± 3.49

Table 4: Comparison of Serum Trace Element Levels Between Preeclampsia and Control Groups

Biochemical Parameter	Unit	Preeclampsia Cases (n = 138)	Controls (n = 138)	t-value	p-value
Serum Zinc	$\mu\text{g/dL}$	37.75 ± 3.86	87.37 ± 7.37	70.017	$< 0.0001^{**}$
Serum Copper	$\mu\text{g/dL}$	47.23 ± 4.16	94.41 ± 8.09	60.942	$< 0.0001^{**}$
Serum Iron	$\mu\text{g/dL}$	184.29 ± 5.53	96.30 ± 8.54	-101.619	$< 0.0001^{**}$
Serum Magnesium	mg/dL	0.96 ± 0.27	2.03 ± 0.48	22.931	$< 0.0001^{**}$

A significant difference in serum trace element levels was observed between the two groups. Mean serum zinc levels were markedly lower in the preeclamptic group ($37.75 \pm 3.86 \mu\text{g/dL}$) compared to controls ($87.37 \pm 7.37 \mu\text{g/dL}$), with a highly significant p-value (< 0.0001). Similarly, serum copper levels were significantly reduced in preeclamptic women ($47.23 \pm 4.16 \mu\text{g/dL}$) relative to the control group ($94.41 \pm 8.09 \mu\text{g/dL}$) (Table 4). Conversely, serum iron levels were significantly elevated in the preeclamptic group ($184.29 \pm 5.53 \mu\text{g/dL}$) compared to controls ($96.30 \pm 8.54 \mu\text{g/dL}$), with a highly significant negative t-value, indicating an inverse trend. Serum magnesium levels were also notably lower among preeclamptic women ($0.96 \pm 0.27 \text{mg/dL}$) than in healthy pregnant controls ($2.03 \pm 0.48 \text{mg/dL}$), and the difference was statistically significant ($p < 0.0001$).

All trace elements demonstrated statistically significant differences between the groups, with serum zinc, copper, and magnesium being reduced, and iron being elevated in preeclampsia compared to normotensive pregnancy.

DISCUSSION

The present study demonstrates significant alterations in serum trace element levels in preeclamptic women compared to normotensive pregnant controls. Specifically, serum zinc, copper, and magnesium were significantly reduced, whereas serum iron was elevated in the preeclamptic group. These findings align with the hypothesis that oxidative stress and endothelial dysfunction—key features of preeclampsia—may be modulated by trace element imbalances.

In our study, the mean serum zinc level in preeclamptic women was $37.75 \pm 3.86 \mu\text{g/dL}$, significantly lower than the $87.37 \pm 7.37 \mu\text{g/dL}$ observed in controls. This represents a more than 56% reduction, consistent with findings from Balaji and Pujari, who reported zinc levels of $40.6 \pm 9.3 \mu\text{g/dL}$ in preeclamptic women versus $87.9 \pm 11.2 \mu\text{g/dL}$ in controls, noting a statistically significant difference ($p < 0.001$).^[14] Similarly, Mohamed et al. observed zinc levels of $60.8 \pm 13.7 \mu\text{g/dL}$ in preeclamptic women compared to $95.7 \pm 14.6 \mu\text{g/dL}$ in normotensive pregnant women, reinforcing the

inverse relationship between serum zinc and preeclampsia severity.^[15]

Serum copper levels were also significantly reduced in our preeclamptic participants ($47.23 \pm 4.16 \mu\text{g/dL}$) compared to controls ($94.41 \pm 8.09 \mu\text{g/dL}$). This mirrors the findings of Jamal et al., who found copper levels of $47.9 \pm 20.0 \mu\text{g/dL}$ in cases and $91.7 \pm 23.2 \mu\text{g/dL}$ in controls, indicating a substantial decline in copper during preeclampsia ($p < 0.001$).^[16]

Mohamed et al. similarly noted a copper concentration of $62.9 \pm 15.3 \mu\text{g/dL}$ in preeclamptic women versus $96.7 \pm 14.8 \mu\text{g/dL}$ in healthy pregnancies¹⁵. These decreases in copper, while paradoxical given copper's pro-oxidant potential, may reflect impaired ceruloplasmin activity or altered hepatic metabolism under preeclamptic stress. The most striking finding in our study was the elevation in serum iron among preeclamptic women ($184.29 \pm 5.53 \mu\text{g/dL}$) compared to controls ($96.30 \pm 8.54 \mu\text{g/dL}$), representing a nearly two-fold increase. This is in agreement with findings by Al-Shalah et al., who reported significantly higher serum iron levels in preeclamptic patients ($138.6 \pm 20.1 \mu\text{g/dL}$) compared to healthy controls ($93.4 \pm 18.5 \mu\text{g/dL}$) ($p < 0.01$).^[17] The elevation in serum iron may be attributed to increased hemolysis, altered transferrin saturation, or oxidative damage releasing free iron into circulation—thus contributing to endothelial injury through Fenton chemistry.

Magnesium levels in our study were significantly lower in preeclamptic women ($0.96 \pm 0.27 \text{ mg/dL}$) compared to controls ($2.03 \pm 0.48 \text{ mg/dL}$). This aligns closely with the study by Hassan et al., who reported magnesium concentrations of $1.23 \pm 0.38 \text{ mg/dL}$ in preeclamptic women versus $2.04 \pm 0.22 \text{ mg/dL}$ in controls ($p < 0.05$), suggesting that magnesium depletion may exacerbate vasoconstriction and neuromuscular excitability.^[18] Similarly, Adam et al. found significantly reduced erythrocyte magnesium levels in preeclamptic women ($0.98 \pm 0.15 \text{ mmol/L}$) compared to controls ($1.35 \pm 0.30 \text{ mmol/L}$) ($p < 0.001$), indicating that intracellular magnesium deficits may precede or worsen hypertensive complications.^[19]

Notably, a 2022 meta-analysis by Hapsari and Putra incorporating 54 studies confirmed that serum zinc (SMD = -2.4), magnesium (SMD = -1.28), and calcium (SMD = -1.66) were significantly lower in preeclamptic women, whereas serum iron (SMD = +1.71) was significantly higher compared to controls. Copper levels, however, showed no consistent difference across all studies.^[20] This meta-analytic evidence supports the robustness of our findings and highlights the potential of these biomarkers for early risk prediction in preeclampsia.

A small subset of studies, however, reported no statistically significant differences in trace element levels between preeclamptic and healthy pregnancies. For instance, Lou et al. found no significant change in zinc, copper, magnesium, or calcium levels among third-trimester preeclamptic women when compared to controls.^[21] Discrepancies

may stem from methodological differences, sample sizes, geographic variability in nutrition, or differences in the severity of preeclampsia at the time of sampling.

The findings of our study confirm that serum levels of zinc, copper, and magnesium are significantly lower, while iron levels are significantly elevated in preeclamptic pregnancies. These results are consistent with several large-scale and region-specific studies and reinforce the hypothesis that trace element imbalances contribute to the pathophysiology of preeclampsia via oxidative stress, endothelial dysfunction, and impaired vascular regulation. Further longitudinal studies and clinical trials are warranted to explore the utility of trace element supplementation in reducing the incidence or severity of preeclampsia.

CONCLUSION

This study demonstrates significant alterations in serum trace element levels among preeclamptic women, with notably decreased concentrations of zinc, copper, and magnesium, and elevated serum iron compared to normotensive pregnant controls. These findings support the role of micronutrient imbalances in the pathophysiology of preeclampsia and highlight the potential value of monitoring trace elements as early biochemical markers for identifying at-risk pregnancies. Further research is recommended to evaluate the clinical benefits of targeted supplementation and to explore causal relationships in diverse populations.

Conflict of Interest: None declared

REFERENCES

1. American College of Obstetricians and Gynecologists (ACOG). Hypertension in Pregnancy. *Obstet Gynecol*. 2013;122(5):1122–31.
2. Redman CW, Sargent IL. Placental stress and pre-eclampsia: a revised view. *Placenta*. 2009;30 Suppl A:S38–42.
3. Muna F, Sirazi A, Majumder M, Serajuddin K, Debnath B, Hossain H. Status of serum copper and zinc in pre-eclampsia. *Bangladesh J Med Biochem*. 2015;8(2):49–54.
4. Kumru S, Aydin S, Şimşek M, Şahin K, Yaman M, Ay G. Comparison of serum copper, zinc, calcium, and magnesium levels in preeclamptic and healthy pregnant women. *Biol Trace Elem Res*. 2003;94(2):105–12.
5. Lambe S, Mahajan B, Muddeshwar M. Comparative study of serum calcium, magnesium and zinc levels in preeclampsia and normal pregnancy. *Int J Med Biochem*. 2014;3(2):22–7.
6. Al-Shalah HH, Al-Hilli N, Hasan MA. The association of serum iron, zinc, and copper levels with preeclampsia. *Int J Adv Res*. 2016;4(11):1794–801.
7. Kumru S, Aydin S, Şimşek M, Şahin K, Yaman M. Copper and zinc levels in normotensive and preeclamptic pregnancies. *Biol Trace Elem Res*. 2003;94(2):105–12.
8. Hapsari W, Putra AJE. Maternal blood trace element levels in preeclampsia: comprehensive systematic review and meta-analysis. *Asian J Health Res*. 2022;1(3):1–15.
9. Adam B, Malatyahoglu E, Alvrur M, Talu C. Magnesium, zinc and iron levels in pre-eclampsia. *J Matern Fetal Med*. 2001;10(4):246–50.
10. Elmugabil A, Hamdan H, Elsheikh AE, Rayis DA, Adam I, Gasim GI. Serum calcium, magnesium, zinc and copper levels

- in Sudanese women with preeclampsia. *PLoS One*. 2016;11(12):e0167495.
11. Hassan EE, Elhhatim WS, Bakhit S, Shrif NM, Huneif M. Assessment of trace elements in Sudanese preeclamptic pregnant women. *Sudan Med J*. 2014;50(1):23–8.
 12. Lou SG, Amirabi A, Yazdian M, Pashapour N. Evaluation of serum calcium, magnesium, copper, and zinc levels in women with pre-eclampsia. *Iran J Med Sci*. 2008;33(4):231–4.
 13. Vafaei H, Dalili M, Hashemi S. Serum concentration of calcium, magnesium and zinc in normotensive versus preeclampsia pregnant women: a descriptive study in women of Kerman province of Iran. *Iran J Reprod Med*. 2015;13(1):23–6.
 14. Balaji BR, Pujari KN. Cross-sectional study of zinc, copper and magnesium levels in preeclampsia and normal pregnancy. *Int J Res Rev*. 2021;8(10):43–7.
 15. Mohamed A, El-Omda FA, Abdelfatah AT, Hashish M. Comparative study for serum zinc and copper levels in cases with normal pregnancy versus preeclampsia. *Egypt J Hosp Med*. 2019;77(2):5265–9.
 16. Jamal B, Shaikh F, Memon MY. To determine the effects of copper, zinc and magnesium in patients with pre-eclampsia. *J Liaquat Univ Med Health Sci*. 2017;16(1):53–7.
 17. Al-Shalah HH, Al-Hilli N, Hasan MA. The association of serum iron, zinc, and copper levels with preeclampsia. *Int J Adv Res*. 2016;4(11):1794–801.
 18. Hassan EE, Elhhatim WS, Bakhit S, Shrif NM, Huneif M. Assessment of trace elements in Sudanese preeclamptic pregnant women. *Sudan Med J*. 2014;50(1):23–8.
 19. Adam B, Malatyahoğlu E, Alvir M, Talu C. Magnesium, zinc and iron levels in pre-eclampsia. *J Matern Fetal Med*. 2001;10(4):246–50.
 20. Hapsari W, Putra AJE. Maternal blood trace element levels in preeclampsia: comprehensive systematic review and meta-analysis. *Asian J Health Res*. 2022;1(3):1–15.
 21. Lou SG, Amirabi A, Yazdian M, Pashapour N. Evaluation of serum calcium, magnesium, copper, and zinc levels in women with pre-eclampsia. *Iran J Med Sci*. 2008;33(4):231–4.