Section: Biochemistry

Original Research Article

CORRELATION BETWEEN SERUM COPPER AND ZINC LEVELS AND GLYCEMIC CONTROL IN NEWLY DIAGNOSED TYPE-2 DM PATIENTS

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ABSTRACT

Background: Trace elements such as copper and zinc play vital roles in oxidative balance and glucose metabolism. Their imbalance, particularly the copper/zinc ratio, may contribute to early glycemic dysregulation in type 2 diabetes mellitus (T2DM). This study evaluated the correlation between serum copper, zinc, and copper/zinc ratio with glycemic indices in newly diagnosed T2DM patients.

Materials and Methods: A cross-sectional study was conducted from May 18th to August 14th at the Department of General Medicine, NRI Medical College & General Hospital, Chinakakani, Guntur. Eighty treatment-naïve patients aged 30–65 years with newly diagnosed T2DM were enrolled. Fasting blood glucose (FBG), postprandial glucose (PPG), HbA1c, and serum copper and zinc levels were measured. Copper/zinc ratios were calculated. Correlation analysis and quartile-based comparisons were performed using Pearson's r and ANOVA.

Results: Mean serum copper and zinc levels were 112.5 ± 18.4 µg/dL and 72.3 ± 11.7 µg/dL, respectively. Copper/zinc ratio averaged 1.56 ± 0.24. Serum copper positively correlated with HbA1c ($r = 0.43$, $p = 0.001$), FBG ($r = 0.36$), and PPG ($r = 0.31$). Zinc showed negative correlations with HbA1c ($r = -0.38$, $p = 0.007$), FBG ($r = -0.29$), and PPG ($r = -0.25$). The copper/zinc ratio had the strongest correlation with HbA1c ($r = 0.47$, $p < 0.001$). Quartile analysis showed a progressive increase in glycemic indices across rising copper/zinc quartiles ($p < 0.001$).

Conclusion: Copper/zinc imbalance is significantly associated with poor glycemic control in early-stage T2DM. The copper/zinc ratio may serve as a sensitive biomarker for metabolic dysfunction in newly diagnosed diabetic patients.

Keywords: Copper, Zinc, Copper/Zinc Ratio, Type 2 Diabetes Mellitus, Glycemic Control, HbA1c.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder marked by insulin resistance and β-cell dysfunction, leading to sustained hyperglycemia. Its global prevalence has surged in recent decades, with an estimated 537 million adults affected worldwide in 2021, a number projected to rise to 643 million by 2030.[1] In India alone, over 77 million individuals currently live with diabetes, placing a considerable burden on healthcare systems.[2] Although diagnostic criteria and treatment protocols are well established, optimizing glycemic control in the early stages of the disease remains essential to delay or prevent vascular and microvascular complications.[3]

Trace elements such as copper and zinc are crucial micronutrients that influence several physiological processes, including antioxidant defense, immune regulation, and glucose metabolism.[4] Zinc plays a critical role in insulin biosynthesis, storage, and secretion, and it stabilizes insulin hexamers within

pancreatic β-cells.[5] Additionally, zinc exhibits antioxidant activity that protects pancreatic tissue from oxidative stress-induced damage.[6] In contrast, copper, while necessary in trace amounts, can catalyze the formation of reactive oxygen species when elevated, thereby contributing to oxidative injury and insulin resistance.[7]

Recent interest has shifted from isolated copper or zinc measurements to the copper/zinc ratio, which may serve as a more robust marker of redox imbalance and systemic inflammation.[8] A high copper/zinc ratio has been associated with poor glycemic control, heightened oxidative stress, and increased risk of diabetic complications.[9] This ratio integrates the deleterious effects of elevated copper with the protective functions of zinc, offering a composite view of trace element dysregulation.[10]

Although trace element alterations have been studied in long-standing diabetes, limited data exist for newly diagnosed, treatment-naïve T2DM patients. This is a critical gap, as confounding factors such as medication use, dietary changes, or chronic complications may distort trace element levels in established disease.[11] Investigating copper and zinc levels at the onset of diagnosis may better reflect their etiological roles and help identify at-risk individuals earlier.

The present study aims to assess serum copper and zinc levels, and their ratio, in newly diagnosed T2DM patients and correlate them with glycemic parameters such as fasting blood glucose (FBG), postprandial glucose (PPG), and glycated hemoglobin (HbA1c).

MATERIALS AND METHODS

Study Design and Setting

A hospital-based cross-sectional observational study was conducted in the Department of General Medicine, NRI Medical College & General Hospital, Chinakakani, Guntur, over a 3-month period from May 18th to August 14th. The study aimed to investigate the correlation between serum copper and zinc levels and glycemic control among patients with newly diagnosed type 2 diabetes mellitus (T2DM).

Study Population

The study included 80 adult patients aged between 30 and 65 years who were newly diagnosed with T2DM according to the American Diabetes Association (ADA) 2024 criteria. Newly diagnosed was defined as diagnosis within the past three months with no prior exposure to anti-diabetic medications. Patients were enrolled consecutively from outpatient and inpatient services after obtaining informed consent.

Inclusion Criteria

- Adults aged 30–65 years
- Diagnosis of T2DM within the last 3 months
- No prior treatment with insulin or oral hypoglycemic agents
- Willingness to participate and provide written informed consent

Exclusion Criteria

- Type 1 diabetes mellitus
- History of chronic liver, renal, or thyroid disease
- Acute or chronic infections, malignancies, or inflammatory conditions
- Pregnant or lactating women
- Patients on mineral or antioxidant supplementation

Data Collection and Sample Processing

A structured proforma was used to collect demographic and clinical details, including age, sex, body mass index (BMI), and residential background. Venous blood samples were collected after an overnight fast for measurement of:

- Fasting Blood Glucose (FBG)
- Glycated Hemoglobin (HbA1c)
- Postprandial Glucose (PPG)
- Serum copper and serum zinc levels

Serum copper and zinc concentrations were measured using atomic absorption spectrophotometry, following standardized protocols. The copper/zinc ratio was computed for each participant.

Glycemic Parameters

- FBG and PPG were measured using glucose oxidase-peroxidase method.
- HbA1c was determined by high-performance liquid chromatography (HPLC), standardized to NGSP/DCCT standards.

Statistical Analysis

All data were compiled and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range), depending on distribution. Categorical variables were expressed as percentages. Pearson's correlation coefficient (r) was used to assess the association between serum copper, zinc, copper/zinc ratio, and glycemic parameters. Quartile analysis of copper/zinc ratios was performed using one-way ANOVA with post hoc Bonferroni correction to evaluate differences in glycemic outcomes. A p-value <0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants prior to inclusion in the study.

RESULTS

Table 1: Demographic Characteristics of the Study Population (n = 80)

Variable	Value
Age (years)	52.3
Male (%)	45
Female (%)	55

BMI (kg/m²)	27.6
Urban Residence (%)	62.5
Rural Residence (%)	37.5

Table 2: Serum Copper and Zinc Levels

Variable	Mean ± SD	Range
Serum Copper (µg/dL)	112.5 ± 18.4	85–156
Serum Zinc (µg/dL)	72.3 ± 11.7	48–94
Copper/Zinc Ratio	1.56 ± 0.24	1.1–2.0

Table 3: Glycemic Control Parameters

Parameter	Mean ± SD	Range
Fasting Blood Glucose (mg/dL)	146.2 ± 22.1	110–195
HbA1c (%)	7.9 ± 0.9	6.2–9.8
Postprandial Glucose (mg/dL)	221.7 ± 34.6	160–289

Table 4: Correlation Between Trace Elements and Glycemic Parameters

Trace Element	FBG (r)	HbA1c (r)	PPG (r)	p-value
Serum Copper	0.36	0.43	0.31	0.001
Serum Zinc	-0.29	-0.38	-0.25	0.007
Copper/Zinc Ratio	0.41	0.47	0.39	<0.001

Table 5: Quartile-Based Glycemic Analysis by Copper/Zinc Ratio

Copper/Zinc Quartile	Mean HbA1c (%)	Mean FBG (mg/dL)	Mean PPG (mg/dL)	p-value
Q1 (<1.2)	7.1	132.4	201.2	<0.001
Q2 (1.2–1.5)	7.6	141.6	215.7	<0.001
Q3 (1.5–1.8)	8.2	151.7	230.1	<0.001
Q4 (>1.8)	8.6	159.3	242.6	<0.001

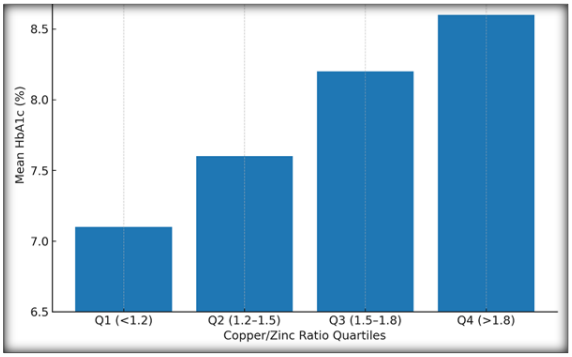

Figure 1: Bar graph on Mean HbA1c

A total of 80 newly diagnosed type 2 diabetes mellitus patients were evaluated. The mean age was 52.3 years, with males comprising 45% and females 55% of the study population. The average BMI was 27.6 kg/m². A higher proportion of participants resided in urban areas (62.5%) compared to rural areas (37.5%).

The mean serum copper level was 112.5 ± 18.4 µg/dL (range: 85–156), while the mean serum zinc level was 72.3 ± 11.7 µg/dL (range: 48–94). The copper/zinc ratio averaged 1.56 ± 0.24, with a range from 1.1 to 2.0. Glycemic indices showed a mean fasting blood glucose (FBG) of 146.2 ± 22.1 mg/dL (range: 110–195), mean postprandial glucose (PPG) of 221.7 ± 34.6 mg/dL (range: 160–289), and mean HbA1c of 7.9 ± 0.9% (range: 6.2–9.8).

Correlation analysis demonstrated a positive relationship between serum copper and glycemic indices: FBG ($r = 0.36$, $p = 0.001$), HbA1c ($r = 0.43$, $p = 0.001$), and PPG ($r = 0.31$, $p = 0.001$). Serum zinc levels showed a negative correlation with FBG ($r = -0.29$, $p = 0.007$), HbA1c ($r = -0.38$, $p = 0.007$), and PPG ($r = -0.25$, $p = 0.007$). The copper/zinc ratio showed the strongest correlation with HbA1c ($r = 0.47$, $p < 0.001$), followed by FBG ($r = 0.41$, $p < 0.001$) and PPG ($r = 0.39$, $p < 0.001$).

Quartile analysis revealed that mean HbA1c progressively increased across quartiles: from 7.1% in Q1 (<1.2) to 8.6% in Q4 (>1.8). Similarly, mean FBG increased from 132.4 to 159.3 mg/dL, and mean PPG rose from 201.2 to 242.6 mg/dL across quartiles. All inter-quartile comparisons were statistically significant ($p < 0.001$).

DISCUSSION

Type 2 diabetes mellitus (T2DM) is intricately linked with micronutrient homeostasis, particularly involving trace elements such as copper and zinc. The present study was conducted to evaluate the correlation between serum copper and zinc levels, as well as their ratio, with glycemic control indices (FBG, PPG, and HbA1c) in newly diagnosed T2DM patients.

This study was conceived based on the rationale that alterations in trace element status—especially the copper/zinc ratio—could reflect early metabolic derangements in diabetes, independent of chronic complications, pharmacotherapy, or dietary modification. Newly diagnosed, treatment-naïve patients were thus selected to eliminate confounding factors and to understand the potential contributory role of these micronutrients in the pathophysiology of dysglycemia.

Our findings demonstrated a statistically significant positive correlation between serum copper levels and

glycemic indices: FBG (r = 0.36, p = 0.001), HbA1c (r = 0.43, p = 0.001), and PPG (r = 0.31, p = 0.001). These results are consistent with studies by Yener et al,[12] and Chausmer et al,[13] who reported elevated copper levels in diabetic patients and associated it with oxidative stress and insulin resistance. The pro-oxidant role of copper, when excessive, may potentiate glycation and impair insulin signaling.

Conversely, serum zinc levels showed a negative correlation with glycemic markers: FBG (r = -0.29, p = 0.007), HbA1c (r = -0.38, p = 0.007), and PPG (r = -0.25, p = 0.007). This aligns with previous findings by Marjani et al,[14] and Jayawardena et al,[15] who documented zinc deficiency in diabetic patients and its implications on β-cell function and insulin storage. Zinc also has anti-inflammatory and antioxidant properties that may mitigate pancreatic oxidative damage.

The copper/zinc ratio emerged as the most sensitive marker, showing the strongest correlation with HbA1c (r = 0.47, p < 0.001). This supports the findings of Uriu-Adams and Keen et al. [16], who emphasized the biological significance of this ratio over individual trace element levels. Furthermore, quartile-based stratification of copper/zinc ratios revealed a graded deterioration in glycemic parameters from Q1 (<1.2) to Q4 (>1.8), with HbA1c rising from 7.1% to 8.6% (p < 0.001). Similar trends were observed for FBG and PPG, reinforcing the prognostic utility of this ratio.

However, this study has limitations. Being cross-sectional, it cannot establish causality. The single-center design and relatively small sample size may limit generalizability. Moreover, dietary intake and intestinal absorption of micronutrients, which can influence serum levels, were not assessed.

CONCLUSION

This study demonstrated a significant correlation between serum copper and zinc levels, particularly the copper/zinc ratio, and glycemic control indices in newly diagnosed type 2 diabetes mellitus patients. Elevated serum copper and reduced serum zinc were associated with poorer glycemic parameters, with the copper/zinc ratio showing the strongest correlation with HbA1c, fasting, and postprandial glucose levels. These findings suggest that trace element imbalance, especially a high copper/zinc ratio, may serve as a sensitive biomarker for early dysglycemia. Incorporating trace element analysis into the initial evaluation of T2DM patients may aid in risk stratification and guide adjunct nutritional interventions.

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Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Fisher RS, Acevedo C, Arzimanoglou A, et al. ILAE official report: A practical clinical definition of epilepsy. Epilepsia. 2014;55(4):475-82.
2. Hauser WA, Beghi E. First seizure definitions and worldwide incidence and mortality. Epilepsia. 2008;49(Suppl 1):8–12.
3. Newton CR, Garcia HH. Epilepsy in poor regions of the world. Lancet. 2012;380(9848):1193–201.
4. Gourie-Devi M, Satishchandra P, Gururaj G. Epilepsy control program in India: A district model. Epilepsia. 2003;44(Suppl 1):58–62.
5. Benbadis SR. The differential diagnosis of epilepsy: A critical review. Epilepsy Behav. 2009;15(1):15–21.
6. Stephen LJ, Brodie MJ. Seizure-related structural brain abnormalities: Insights from neuroimaging. Epilepsy Res. 2000;39(1):1–16.
7. Smith SJM. EEG in the diagnosis, classification, and management of patients with epilepsy. J Neurol Neurosurg Psychiatry. 2005;76(Suppl 2):ii2–7.
8. Zaccara G, Muscas GC, Tinuper P, et al. Cryptogenic partial epilepsy: A multicenter prospective study. Epilepsia. 1999;40(4):491–6.
9. Kumar A, Sharma S, Shukla G, et al. Clinical and etiological profile of new-onset seizures in adults: A hospital-based study. Neurol India. 2020;68(5):1148–54.
10. Seneviratne U, Cook M, D'Souza W. New-onset seizures in adults: Causes and investigation. Intern Med J. 2012;42(2):247–52.
11. Newton MR, Berkovic SF, Austin MC, et al. Dystonic seizures: A clinical and MRI study. Neurology. 1992;42(3 Pt 1):437–41.
12. Carpio A. Neurocysticercosis: An update. Lancet Infect Dis. 2002;2(12):751–62.
13. Leach JP, Brodie MJ. Alcohol and drug-related seizures. Handb Clin Neurol. 2014; 119:543–53.
14. Baldin E, Hauser WA, Pack A, et al. Newly diagnosed epilepsy in elderly: Etiology and treatment options. Epilepsy Behav. 2013;28(1):118–22.
15. Tatum WO. Adult-onset seizures: Diagnostic approach. Continuum (Minneap Minn). 2015;21(2 Epilepsy):371–95.
16. Annegers JF, Hauser WA, Lee JR, et al. Incidence of acute symptomatic seizures in Rochester, Minnesota, 1935–1984. Epilepsia. 1995;36(4):327–33.