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SERUM ZINC AND COPPER LEVELS AND THEIR ASSOCIATION WITH GLYCEMIC CONTROL IN CHILDREN WITH TYPE 1 DIABETES MELLITUS

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ABSTRACT

Objective: Trace elements, particularly zinc and copper, play important roles in insulin metabolism, antioxidant defense, and glucose homeostasis. Alterations in their levels may contribute to oxidative stress and poor glycemic control in children with Type 1 Diabetes Mellitus (T1DM). This study aimed to evaluate serum zinc and copper levels in children with T1DM, compare them with those of healthy controls, and determine their association with glycemic control.
Methods: A hospital-based comparative cross-sectional study was conducted among 78 children, including 39 children with T1DM and 39 age- and sex-matched healthy controls, attending the Department of Pediatrics, NIMS Hospital, Jaipur, between August 2024 and February 2026. Clinical assessments and laboratory investigations, including serum zinc, serum copper, and glycated hemoglobin (HbA1c), were performed. Statistical analyses were conducted using SPSS version 27.0, with a p-value <0.05 considered statistically significant.
Results: Children with T1DM had significantly higher serum copper levels (149.98 ± 29.40 vs. 96.03 ± 31.12 µg/dL; $p<0.001$) and HbA1c levels (7.41 ± 0.98% vs. 5.05 ± 0.29%; $p<0.001$), whereas serum zinc levels were significantly lower (40.34 ± 20.60 vs. 81.47 ± 14.92 µg/dL; $p<0.001$) compared with healthy controls. Serum copper demonstrated a significant positive correlation with HbA1c ($r = 0.654$, $p<0.01$), while serum zinc showed a strong negative correlation with HbA1c ($r = -0.780$, $p<0.01$).
Conclusion: Children with T1DM exhibit significantly elevated serum copper and reduced serum zinc concentrations compared with healthy children. These alterations are strongly associated with poor glycemic control, suggesting that trace element imbalance may contribute to disease severity and disease progression. Routine monitoring of serum zinc and copper levels, together with optimal glycemic management, may improve metabolic control and potentially reduce the risk of long-term complications in pediatric T1DM.

Keywords: Type 1 diabetes mellitus; Children; Zinc; Copper; Glycated hemoglobin (HbA1c); Glycemic control; Trace elements.

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune metabolic disorder characterized by the progressive destruction of pancreatic β-cells, resulting in absolute insulin deficiency and persistent hyperglycemia. It is one of the most common endocrine disorders affecting children and adolescents and requires lifelong insulin therapy to maintain glycemic control and prevent acute and chronic complications. [1]

The development of T1DM is influenced by a complex interaction between genetic susceptibility and environmental factors. Individuals carrying specific human leukocyte antigen (HLA) class II genotypes are at increased risk of

autoimmune β-cell destruction. Environmental triggers, including viral infections, dietary factors, toxins, and other immunological stimuli, may initiate or accelerate the autoimmune process in genetically susceptible individuals. [2] According to the International Diabetes Federation (IDF), approximately 149,500 children and adolescents younger than 20 years are newly diagnosed with T1DM each year worldwide. Furthermore, the global age-standardized prevalence of T1DM is projected to increase from 0.2% in 2021 to 0.3% by 2050, representing a substantial rise in disease burden. [3–5]

Although hyperglycemia is the hallmark of T1DM, increasing evidence suggests that disturbances in trace element metabolism also contribute to its pathogenesis and progression. Among these trace elements, zinc and copper play essential roles in maintaining normal glucose metabolism, insulin synthesis and secretion, antioxidant defense, and immune regulation. [6] Alterations in the homeostasis of these micronutrients have been implicated in increased oxidative stress, impaired insulin action, and the development of diabetic complications.

Zinc is an essential micronutrient involved in the synthesis, storage, crystallization, and secretion of insulin within pancreatic β-cells. It also functions as an important antioxidant by stabilizing cell membranes and protecting tissues from oxidative damage. Zinc deficiency has been associated with impaired β-cell function, reduced insulin secretion, increased oxidative stress, and poor glycemic control. Conversely, adequate zinc levels are essential for preserving pancreatic β-cell integrity and maintaining normal glucose homeostasis. [7,8]

Copper is another essential trace element that serves as a cofactor for several antioxidant enzymes, including copper-zinc superoxide dismutase (Cu/Zn-SOD). However, excessive copper accumulation may promote the generation of reactive oxygen species, resulting in oxidative stress, inflammation, and cellular injury. Altered copper metabolism in patients with T1DM has been associated with increased serum copper concentrations, dysregulation of copper transport proteins, impaired insulin signaling, and disturbances in glucose metabolism. These abnormalities may further contribute to endothelial dysfunction and the development of long-term diabetic complications. [9,10]

METHODS

Study Design and Setting

This hospital-based comparative cross-sectional study was conducted in the Department of Pediatrics, National Institute of Medical Sciences (NIMS) Hospital, Jaipur, Rajasthan, India, over a period of 18 months from August 2024 to February 2026. The study protocol was approved by the Institutional Ethics Committee (IEC Approval No. IEC/P-745/2024; Date: 22 May 2024). Written informed consent was obtained from the parents or legal guardians of all participants, and assent was obtained from children whenever applicable.

Study Population

A total of 78 children were enrolled in the study, comprising 39 children diagnosed with Type 1 Diabetes Mellitus (T1DM) and 39 age- and sex-matched healthy controls. Children with T1DM were recruited from those attending the pediatric outpatient department (OPD) or admitted to the pediatric ward/Pediatric Intensive Care Unit (PICU). Healthy controls were selected from children attending the Department of Pediatrics for routine immunization or minor acute illnesses without any chronic systemic disease.

Inclusion Criteria

I. Children aged 1–18 years with a confirmed diagnosis of Type 1 Diabetes Mellitus.
II. Parents or legal guardians willing to provide written informed consent, with assent obtained from children when appropriate.

Exclusion Criteria

Children were excluded if they:

I. Receiving zinc or copper supplementation.
II. Had chronic kidney disease, chronic liver disease, thyroid disorders, malabsorption syndrome, or malignancy.
III. Receiving medications known to interfere with zinc or copper metabolism, including diuretics, anticonvulsants, neomycin, antacids, cholestyramine, laxatives, penicillamine, or chronic alcohol exposure.

Data Collection

A comprehensive clinical evaluation was performed for all enrolled participants. Demographic details, medical history, duration of diabetes, treatment history, and relevant clinical findings were recorded using a predesigned structured case record form. A detailed physical examination was conducted, and all observations were documented systematically to ensure uniformity and accuracy of data collection.

Laboratory investigations included complete blood count (CBC), fasting blood glucose, postprandial blood glucose, glycated hemoglobin (HbA1c), serum zinc, serum copper, liver function tests, renal function tests, serum creatinine, thyroid function tests, and tissue transglutaminase immunoglobulin A (tTG-IgA). Urine investigations included routine microscopy, urine culture, ketone bodies, and the urine albumin-to-creatinine ratio (UACR). Fundus examination was also performed to assess the presence of diabetic retinopathy.

Laboratory Analysis

Approximately 2 mL of venous blood was collected under aseptic precautions in trace element-free (zinc-free) plain collection tubes to prevent contamination.

Estimation of Serum Zinc

Serum zinc concentration was measured using a fully automated chemistry analyzer (CT-180) based on the colorimetric method. The reference range for serum zinc was considered to be 59–98 µg/dL.[1]

Estimation of Serum Copper

Serum copper concentration was estimated using a fully automated chemistry analyzer (CST T180) employing the Dibromo-PAESA colorimetric method. The reference range for serum copper was considered to be 76–152 µg/dL.[1]

All biochemical analyses were performed in the Central Biochemistry Laboratory of NIMS Hospital following standard operating procedures and quality control protocols.

Study Flow

Type1DM children attending in OPD or admitted in the pediatric ward/PICU.

⇩

Case screened according to inclusion and exclusion criteria

⇩

Written informed consent taken.

⇩

Detailed history and examination filled in predesign proforma.

⇩

Serum copper and zinc levels estimated by appropriate technique

⇩

All clinical & lab data collected for statistical analysis.

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS) version 27.0 (IBM Corp., Armonk, NY, USA).

Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The normality of continuous variables was assessed before analysis. The independent Student's t-test was used to compare the means of normally distributed continuous variables between the two groups. The Chi-square test or Fisher's exact test was applied to compare categorical variables, as appropriate. Pearson's correlation coefficient was used to evaluate the relationship between serum zinc, serum copper, and HbA1c levels.

A two-tailed p-value of <0.05 was considered statistically significant.

RESULT

A total of 78 children were included in the study, comprising 39 children with Type 1 Diabetes Mellitus (T1DM) and 39 age- and sex-matched healthy controls.

Table 1 Baseline Characteristics of the Study Population

Parameters	Control (39)		Cases (39)		Total (78)	
	No.	%	No.	%	No.	%
Age group in years						
<5	2	5.13%	1	2.56%	3	3.85%
5-10	13	33.33%	12	30.77%	25	32.05%
11-15	22	56.41%	25	64.10%	47	60.26%
>15	2	5.13%	1	2.56%	3	3.85%
Mean ± SD	11.154 ±	3.248	11.282 ±	2.655		
Gender						
Male	17	43.6%	21	53.8%	38	48.7%
Female	22	56.4%	18	46.2%	40	51.3%
Family history						
No significant h/o	39	100	24	61.6%	63	80.7%
Significant h/o	0	0.0%	15	38.4%	15	19.3%
Diabetic father	0	0.0%	13	33.3%	13	16.7%
Diabetic mother	0	0.0%	2	5.1%	2	2.6%
Treatment history						

Not compliance	0	0.0%	13	33.3%	13	16.7%
Not significant	39	100.0%	0	0.0%	39	50.0%
Regular insulin	0	0.0%	26	66.7%	26	33.3%

As shown in Table 1, the majority of participants in both groups belonged to the 11–15-year age group (64.1% in cases and 56.4% in controls). The mean age was comparable between the case and control groups (11.28 ± 2.66 years vs. 11.15 ± 3.25 years, respectively), with no statistically significant difference in age distribution ($\chi^2 = 8.111$, $p = 0.703$).

The gender distribution was also comparable between the groups. Males constituted 53.8% of the T1DM group and 43.6% of the control group, whereas females accounted for 46.2% and 56.4%, respectively. No significant difference was observed in gender distribution ($\chi^2 = 0.821$, $p = 0.365$).

A positive family history of diabetes was significantly more common among children with T1DM than among healthy controls (38.4% vs. 0%; $\chi^2 = 18.571$, $p< 0.001$). Among affected children, 33.3% had a diabetic father and 5.1% had a diabetic mother.

Regarding treatment history, 66.7% of children with T1DM were receiving regular insulin therapy, while 33.3% demonstrated poor treatment compliance. As expected, none of the healthy controls had a history of diabetes treatment. This difference was highly significant ($\chi^2 = 78.694$, $p< 0.001$).

Table 2 Clinical Presentation of Children with T1DM

Symptoms	No. (39)	Percentage
Polyuria	27	69.2%
Polydipsia	15	38.5%
Polyphagia	8	20.5%
Vomiting	28	71.8%
Altered sensorium	8	20.5%
Fever	0	0.0%
Others	10	25.6%
Duration of symptoms	7.90 ± 5.609	
Status of type-1DM		
Nil	0	0.0%
Controlled	14	35.9%
Uncontrolled	25	64.1%

The clinical characteristics of children with T1DM are summarized in Table 2. Vomiting was the most frequently reported presenting symptom (71.8%), followed by polyuria (69.2%), polydipsia (38.5%), other nonspecific symptoms

(25.6%), polyphagia (20.5%), and altered sensorium (20.5%). None of the participants presented with fever. The mean duration of symptoms before presentation was 7.90 ± 5.61 days.
Based on glycemic status, 25 children (64.1%) had uncontrolled diabetes, whereas 14 children (35.9%) had controlled diabetes.

Table 3 Comparison of Laboratory Parameters

Investigations	Control	Cases	P-value
Hb (g/dl)	13.43±1.50	11.93±1.00	<0.001*
TLC	6687.13± 1117.98	6329.49± 1770.87	0.290
PLT	247891.82±43026.11	263210.26±28294.77	0.067
ALT	23.62±8.98	29.50±2.83	<0.001*
AST	22.10±6.44	30.64±3.58	<0.001*
ALP	118.68± 25.55	51.19±2.46	<0.001*
Sr. Creatinine	0.64±0.13	0.84±0.16	<0.001*
Sr. Urea	20.48±2.22	27.93±4.70	<0.001*
RBS (mg/dl)	94.50±10.19	299.61± 55.91	<0.001*
HbA1c	5.05±0.29	7.41±0.98	<0.001*

*p value <0.05 significant

The comparison of laboratory investigations between the study groups is presented in Table 3.
Children with T1DM had significantly lower hemoglobin levels than healthy controls (11.93 ± 1.00 vs. 13.43 ± 1.50 g/dL, p< 0.001). Liver function tests revealed significantly higher alanine aminotransferase (ALT) (29.50 ± 2.83 vs. 23.62 ± 8.98 U/L, p< 0.001) and aspartate aminotransferase (AST) levels (30.64 ± 3.58 vs. 22.10 ± 6.44 U/L, p< 0.001) among children with T1DM.
Renal function parameters were also significantly elevated in the T1DM group, with higher serum creatinine (0.84 ± 0.16 vs. 0.64 ± 0.13 mg/dL, p< 0.001) and serum urea levels (27.93 ± 4.70 vs. 20.48 ± 2.22 mg/dL, p< 0.001).
As expected, random blood glucose (299.61 ± 55.91 vs. 94.50 ± 10.19 mg/dL, p< 0.001) and HbA1c (7.41 ± 0.98% vs. 5.05 ± 0.29%, p< 0.001) were markedly higher in children with T1DM, indicating significantly poorer glycemic control.
In contrast, total leukocyte count and platelet count did not differ significantly between the two groups (p = 0.290 and p = 0.067, respectively).

Table 4 Comparison of Serum Zinc and Copper Levels

Investigations	Control	Cases	T-value	P-value
Sr. Copper(ug/dl)	96.031±31.121	149.982±29.397	3.647	<0.001*
Sr. Zinc(ug/dl)	81.467±14.921	40.342±20.602	5.459	<0.001*
HbA1c	5.05±0.29	7.41±0.98	6.057	<0.001*

*p value <0.05 significant

As presented in Table 4, children with T1DM exhibited significantly higher serum copper concentrations than healthy controls (149.98 ± 29.40 vs. 96.03 ± 31.12 µg/dL; p< 0.001).
Conversely, serum zinc levels were significantly lower among children with T1DM (40.34 ± 20.60 µg/dL) compared with healthy controls (81.47 ± 14.92 µg/dL; p< 0.001).
HbA1c levels were also significantly higher in the T1DM group (7.41 ± 0.98% vs. 5.05 ± 0.29%; p< 0.001), reflecting poor glycemic control. These findings indicate significant alterations in trace element homeostasis among children with T1DM, characterized by elevated serum copper and reduced serum zinc concentrations.

Table 5 Correlation Between Serum Zinc, Serum Copper, and HbA1c

	Sr. Copper(ug/dl) vs. HbA1c	Sr. Zinc(ug/dl) vs. HbA1c
Pearson correlation	.654	-.780
*p value	0.01	0.01

*p value <0.05 significant

The correlation analysis is summarized in Table 5.
Serum copper demonstrated a significant positive correlation with HbA1c (r = 0.654, p< 0.01), indicating that higher serum copper levels were associated with poorer glycemic control.
In contrast, serum zinc showed a strong negative correlation with HbA1c (r = −0.780, p< 0.01), suggesting that lower serum zinc concentrations were associated with higher HbA1c levels.
Overall, these findings demonstrate a significant relationship between altered trace element status and glycemic control in children with Type 1 Diabetes Mellitus.

DISCUSSION

Type 1 Diabetes Mellitus (T1DM) is a chronic autoimmune disorder characterized by the progressive destruction of pancreatic β-cells, resulting in absolute insulin deficiency and persistent hyperglycemia. Despite advances in insulin therapy, achieving optimal glycemic control remains a major challenge in children with T1DM. Chronic hyperglycemia is associated with increased oxidative stress, inflammation, and metabolic disturbances that contribute to the development of microvascular and macrovascular complications. In recent years, increasing attention has been focused on the role of trace elements, particularly zinc and copper, because of their involvement in insulin synthesis, secretion, antioxidant defense, and glucose metabolism. Alterations in the homeostasis of these micronutrients may influence disease progression and glycemic control. Therefore, the present study evaluated the clinical characteristics, biochemical profile, and serum zinc and copper levels in children with T1DM and compared them with those of healthy controls to better understand their association with glycemic status.
The mean age of children with T1DM in the present study was 11.28 ± 2.65 years, which was comparable to that of the healthy control group (11.15 ± 3.25 years), with no statistically significant difference between the groups. Most participants belonged to the 11–15-year age group, indicating that T1DM was more frequently diagnosed during early adolescence. These findings are consistent with those reported by Haque et al. (2022),[11] who observed a mean age of onset of 10.5 ± 3.6 years among children with T1DM in Bangladesh. Similar age distributions have been described in several pediatric studies, suggesting that the incidence of T1DM increases during late childhood and early adolescence owing to the combined influence of genetic susceptibility, hormonal changes during puberty, and environmental factors.
The gender distribution was comparable between the two groups, with males accounting for 53.8% of the T1DM group and females 46.2%, whereas females slightly predominated in the control group. The difference was not statistically significant, indicating successful age- and sex-matching of the study participants. Similar observations have been reported by Chaithanya et al. (2022),[12] who also demonstrated no significant gender difference between children with T1DM and healthy controls. These findings suggest that although minor sex-related differences may exist in different populations, both boys and girls are affected almost equally by T1DM.

The most common presenting symptoms in the present study were vomiting (71.8%), polyuria (69.2%), polydipsia (38.5%), polyphagia (20.5%), and altered sensorium (20.5%), with a mean symptom duration of 7.90 ± 5.61 days before presentation. These findings are in agreement with those of El Fouly et al. (2018),[13] who reported polyuria, polydipsia, and vomiting as the predominant presenting manifestations among children with T1DM. The high prevalence of vomiting observed in our study is likely attributable to diabetic ketoacidosis (DKA), a common acute complication and initial presentation of T1DM in children. Persistent hyperglycemia, ketosis, and metabolic acidosis stimulate the chemoreceptor trigger zone and gastrointestinal tract, leading to nausea and vomiting. Therefore, early recognition of these symptoms is essential for timely diagnosis and prevention of severe metabolic complications.

A positive family history of diabetes was observed in 38.4% of children with T1DM, whereas none of the healthy controls had a significant family history. Among affected children, 33.3% had a diabetic father and 5.1% had a diabetic mother. This difference was highly statistically significant, emphasizing the importance of genetic predisposition in the development of T1DM. These findings are consistent with those of Parkkola et al. (2013),[14] who reported that children with T1DM were more likely to have an affected father than an affected mother. Similarly, Chaithanya et al. (2022)[12] observed a higher frequency of positive family history among children with T1DM, supporting the concept of familial clustering and the contribution of hereditary factors to disease susceptibility.

In the present study, 66.7% of children with Type 1 Diabetes Mellitus (T1DM) were receiving regular insulin therapy, whereas 33.3% demonstrated poor treatment compliance. As expected, none of the healthy controls had a history of insulin therapy. This difference was highly statistically significant ($\chi^2 = 78.694$; $p < 0.001$). Adequate adherence to insulin therapy is essential for maintaining optimal glycemic control and preventing both acute and chronic complications of T1DM. Our findings are consistent with those reported by Marjanac et al. (2020),[15] who demonstrated that poor adherence to insulin therapy was associated with significantly higher HbA1c levels and unfavorable trace element profiles in children with T1DM. These observations emphasize the importance of patient education, regular follow-up, and family support in improving treatment compliance and long-term metabolic outcomes.

Children with T1DM in the present study exhibited significant alterations in several biochemical parameters compared with healthy controls. Hemoglobin levels were significantly lower in the diabetic group (11.93 ± 1.00 vs. 13.43 ± 1.50 g/dL; $p < 0.001$), while serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum creatinine, and serum urea were significantly higher. In addition, random blood glucose (299.61 ± 55.91 vs. 94.50 ± 10.19 mg/dL; $p < 0.001$) and HbA1c levels (7.41 ± 0.98% vs. 5.05 ± 0.29%; $p < 0.001$) were markedly elevated in children with T1DM, reflecting poor glycemic control.

These findings are in agreement with those of Alghobashy et al. (2018),[16] who reported significantly higher fasting plasma glucose and a mean HbA1c of 8.6 ± 2.2% among children with T1DM compared with healthy controls. Likewise, Grabia et al. (2023)[17] observed a median HbA1c of 8% (IQR: 6–10%) in adolescents with T1DM, indicating suboptimal glycemic control similar to that observed in our study. Estakhri et al. (2011)[18] also classified children according to glycemic status and demonstrated that patients with higher HbA1c values had poorer metabolic control, supporting the findings of the present study.

The significantly elevated liver enzyme levels observed in our study may reflect hepatocellular injury secondary to chronic hyperglycemia and oxidative stress. Similar findings were reported by El Fouly et al. (2018),[13] who attributed elevated hepatic enzyme activity in children with T1DM to oxidative stress-induced cellular damage. Furthermore, significantly increased serum creatinine and urea levels in our patients may indicate early renal involvement associated with diabetes. These observations are supported by Alghobashy et al. (2018),[16] who suggested that subtle alterations in renal function may occur during the early stages of T1DM, even before the development of clinically apparent diabetic nephropathy.

Urinalysis revealed glycosuria in 71.8% of children with T1DM, including 15.4% with +1, 30.8% with +2, and 25.6% with +3 urinary glucose levels, whereas all healthy controls had normal urine findings. This difference was highly statistically significant ($\chi^2 = 43.680$; $p < 0.001$). Glycosuria is a well-recognized consequence of persistent hyperglycemia when blood glucose levels exceed the renal threshold for glucose reabsorption. Similar findings were reported by Alghobashy et al. (2018),[16] whose patients exhibited markedly elevated fasting plasma glucose levels sufficient to produce urinary glucose excretion. Likewise, Estakhri et al. (2011)[18] reported persistently elevated HbA1c levels and prolonged disease duration among children with T1DM, findings that are consistent with sustained hyperglycemia and the presence of glycosuria. The high prevalence of glycosuria observed in our study further reflects inadequate glycemic control in a substantial proportion of children with T1DM.

The present study demonstrated that children with Type 1 Diabetes Mellitus (T1DM) had significantly higher serum copper concentrations and significantly lower serum zinc concentrations than healthy controls. The mean serum copper level was 149.98 ± 29.40 µg/dL in children with T1DM compared with 96.03 ± 31.12 µg/dL in the control group ($p < 0.001$). Conversely, the mean serum zinc concentration was significantly lower in the T1DM group (40.34 ± 20.60 µg/dL) than in healthy controls (81.47 ± 14.92 µg/dL, $p < 0.001$). These findings indicate a marked disturbance in trace element homeostasis among children with T1DM and suggest a potential role of these micronutrients in disease pathophysiology and glycemic control.

The significantly reduced serum zinc levels observed in our study are consistent with the findings of Agarwal et al. (2018),[19] who reported significantly lower serum zinc concentrations in children with T1DM than in healthy controls and attributed this reduction to diabetes-related hypozincemia, increased urinary zinc excretion, and impaired intestinal absorption. Similarly, Marjanac et al. (2020)[15] demonstrated significantly lower serum zinc levels in children with T1DM and further reported that patients with poor glycemic control had lower zinc concentrations than those with adequate metabolic control. These findings support the hypothesis that chronic hyperglycemia contributes to zinc depletion, thereby impairing insulin synthesis, secretion, and antioxidant defense.

Our findings are also supported by Özenç et al. (2015),[20] who reported significantly lower serum zinc concentrations in children with T1DM and demonstrated a significant inverse correlation between serum zinc levels and HbA1c. This relationship suggests that declining zinc levels are associated with worsening glycemic control. Zinc is an essential cofactor for insulin synthesis, storage, secretion, and cellular signaling. It also plays a critical role in protecting pancreatic β-cells against oxidative stress through its antioxidant properties. Therefore, zinc deficiency may contribute to β-cell dysfunction, impaired glucose metabolism, and progressive deterioration of glycemic control.

In contrast, Estakhri et al. (2011)[18] reported serum zinc concentrations that remained within the normal reference range in both well-controlled and poorly controlled diabetic patients, although slightly lower values were observed among those with poor glycemic control. The substantially lower zinc concentrations observed in our study may be explained by the higher proportion of children with uncontrolled diabetes, greater oxidative stress, nutritional differences, and variations in disease duration or study population characteristics.

Serum copper concentrations were significantly higher among children with T1DM in the present study. Elevated serum copper may reflect increased oxidative stress and altered copper metabolism associated with chronic hyperglycemia. Copper acts as a cofactor for several oxidative enzymes; however, excessive copper accumulation may promote the formation of reactive oxygen species, resulting in oxidative tissue injury, inflammation, and impaired insulin signaling.

Our findings are consistent with those reported byEl Fouly et al. (2018),[13] who observed significantly higher serum copper concentrations in children with T1DM than in healthy controls. They suggested that oxidative stress may promote the mobilization of copper from tissue stores and reduce its urinary clearance, thereby increasing circulating copper levels.

However, our findings differ from those of Alghobashy et al. (2018),[16] who reported significantly lower serum copper concentrations in children with T1DM than in healthy controls and proposed that excessive urinary copper loss secondary to chronic hyperglycemia was responsible for the reduced serum copper levels. Likewise, Grabia et al. (2023)[17] found no significant difference in serum copper concentrations between adolescents with T1DM and healthy controls. Nevertheless, they reported a significantly higher copper-to-zinc (Cu/Zn) ratio among patients with T1DM, which is in agreement with our observation of elevated serum copper and reduced serum zinc concentrations. The discrepancies among studies may be attributed to differences in patient age, nutritional status, disease duration, glycemic control, laboratory methods, ethnicity, sample size, and inclusion criteria.

Similarly, Momeni et al. (2023)[21] reported significantly reduced serum zinc levels together with alterations in copper metabolism among children with T1DM, further supporting the presence of trace element imbalance in pediatric diabetes. In addition, Mostafaei et al. (2025)[22] demonstrated a significant positive association between dietary copper intake and postprandial blood glucose levels, suggesting that abnormalities in copper metabolism are closely associated with glycemic status. These findings provide further biological support for the elevated serum copper concentrations observed in children with poorly controlled T1DM in the present study.

Overall, the findings of the present study indicate that children with Type 1 Diabetes Mellitus exhibit significant alterations in serum zinc and copper concentrations compared with healthy children. Reduced serum zinc and elevated serum copper levels appear to be closely associated with poor glycemic control and may contribute to oxidative stress, impaired insulin metabolism, and disease progression. These observations suggest that assessment of serum zinc and copper concentrations may serve as useful adjunctive biomarkers for monitoring metabolic status in children with

T1DM. Further large-scale prospective studies are required to determine whether correction of trace element imbalance through nutritional intervention or supplementation can improve glycemic control and reduce the risk of long-term diabetic complications.

LIMITATIONS OF THE STUDY

The present study has several limitations that should be considered while interpreting the findings. First, it was conducted at a single tertiary care center, which may limit the generalizability of the results to the broader pediatric population. Second, the relatively small sample size (78 participants) may have reduced the statistical power of the study and limited subgroup analyses. Third, the cross-sectional study design precludes the establishment of a causal relationship between alterations in serum zinc and copper levels and glycemic control in children with Type 1 Diabetes Mellitus (T1DM).

Furthermore, the duration of diabetes and its influence on trace element status and biochemical parameters were not evaluated in detail. Dietary intake of zinc and copper was not assessed, although nutritional factors may significantly affect serum trace element concentrations. Similarly, socioeconomic and environmental factors that could influence nutritional status and metabolic control were not comprehensively evaluated. Treatment adherence was assessed based on patient or caregiver history rather than objective measures, introducing the possibility of recall and reporting bias. In addition, long-term follow-up was not performed; therefore, the progression of disease and the development of diabetes-related complications could not be assessed. Finally, other trace elements, antioxidant enzymes, and oxidative stress biomarkers were not evaluated, limiting a comprehensive assessment of micronutrient status and oxidative stress in children with T1DM.

CONCLUSION

The present study demonstrated that children with Type 1 Diabetes Mellitus commonly presented with classical osmotic symptoms, including polyuria, polydipsia, and vomiting, suggesting delayed diagnosis or inadequate glycemic control in a substantial proportion of patients. A positive family history of diabetes was significantly more frequent among children with T1DM, emphasizing the important contribution of genetic susceptibility to disease development.

Children with T1DM also exhibited significant biochemical abnormalities, including lower hemoglobin levels, markedly elevated blood glucose and HbA1c levels, and alterations in liver and renal function parameters, reflecting the systemic metabolic effects of chronic hyperglycemia. Most importantly, the study demonstrated a significant imbalance in trace element homeostasis, characterized by elevated serum copper levels and reduced serum zinc concentrations in children with T1DM compared with healthy controls.

Furthermore, serum copper showed a significant positive correlation with HbA1c, whereas serum zinc demonstrated a strong negative correlation with HbA1c, indicating that alterations in these trace elements are closely associated with poor glycemic control. These findings suggest that disturbances in zinc and copper metabolism may contribute to the pathophysiology and progression of T1DM through mechanisms involving oxidative stress and impaired insulin metabolism.

Overall, the findings highlight the importance of early diagnosis, optimal glycemic control, regular clinical follow-up, and periodic assessment of micronutrient status in children with T1DM. Monitoring serum zinc and copper concentrations may provide additional information regarding metabolic control and could help identify children at increased risk of diabetes-related complications. Further multicenter prospective studies with larger sample sizes are warranted to validate these findings and to determine whether correction of trace element imbalance can improve long-term clinical outcomes in pediatric T1DM.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

ETHICAL APPROVAL

The study protocol was approved by the Institutional Ethics Committee before the commencement of the study. Written informed consent was obtained from the parents or legal guardians of all participants, and assent was obtained from children whenever applicable.

AI DISCLOSURE

No artificial intelligence (AI) or tools were used in the study design, data collection, data analysis, interpretation of results, preparation of figures, or writing of the original manuscript.

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ABBREVIATIONS

CBC: Complete Blood Count
DM: Diabetes Mellitus
HbA1c: Glycated Hemoglobin
HLA: Human Leukocyte Antigen
LFT: Liver Function Test
RFT: Renal Function Test
T1DM: Type 1 Diabetes Mellitus
TTG-IgA: Tissue Transglutaminase Immunoglobulin A

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