Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/9am8kb33

EVALUATION OF SERUM TRACE ELEMENTS (ZINC, COPPER, AND SELENIUM) IN TYPE-2 DIABETES MELLITUS

Amit Kumar Yadav[1], Shreya Nigoskar[2*], Satish Kumar Yadav[3]

[1]PhD Scholar, Department of Biochemistry, IMCH&RC, Malwanchal University, Indore (M.P.),
Email id: amiteducation1993@gmail.com
[2*]Professor & Head Department of Biochemistry, IMCH&RC Malwanchal University, Indore (M.P.),
Email id: shreyanigoskar@gmail.com
[3]Assistant Professor, Department of Biochemistry, GMC Azamgarh,
Email Id: satishkumaryadav405@gmail.com

***Corresponding Author:** Dr Shreya Nigoskar
*Professor & Head, Department of Biochemistry, IMCH&RC Malwanchal University, Indore (M.P.)
Email id: shreyanigoskar@gmail.com

ABSTRACT

Background: Diabetes Mellitus is a metabolic disorder in which the balance of various trace elements in the body is affected. This study was done to find out the relationship between diabetes and changes in the levels of these trace elements.

Aim: To compare the levels of trace elements in patients with Type 2 Diabetes Mellitus and healthy individuals.

Materials and Methods: This cross-sectional study included 200 patients with Type 2 Diabetes Mellitus and 200 controls. It was conducted in the Clinical Biochemistry section of the Central Laboratory, Department of Biochemistry, IMCH and RC, Indore.

Results: The study showed that serum copper levels were higher and serum zinc levels were lower in patients with Type 2 Diabetes Mellitus compared to healthy controls.M,.

Conclusion: Changes in copper and zinc levels are important factors that may increase the risk of complications in people with diabetes. Based on the present study, it can be concluded that alterations in trace elements such as copper and zinc may play a role in the development and progression of Diabetes Mellitus.

Keywords Diabetes Mellitus, Trace Elements, Zinc, selenium, Copper, Manganese, Iron, Type-2 Diabetes

Introduction.

Diabetes is a group of metabolic diseases characterized by hyperglycaemia caused by insulin secretion, insulin action, or both. Diabetes-related chronic hyperglycaemia has been linked to long-term organ damage, dysfunction, and failure, including the eyes, kidneys, nerves, heart, and blood vessels.[1] Diabetes is a widespread disease in developed countries and is the fourth leading cause of mortality. [2] According to the "International Diabetes Federation," Atlas 10th Edition (2021), a total of 537 million adults (20-79 years old) have diabetes mellitus. By 2030, this figure is expected to reach 643 million, and by 2045, it will reach 783 million. In addition, it is anticipated that 541 million individuals would have impaired glucose tolerance by 2021. In 2021, nearly 6.7 million persons aged 20–79 is expected to die from diabetes-related causes.[3] Diabetes is rapidly approaching epidemic levels in India, with over 62 million diabetics presently diagnosed. In the year 2000, India (31.7 million people) had the highest number of people with diabetes mellitus worldwide, followed by China (20.8 million) and the United States (17.7 million). According to Wild et al, the global prevalence of diabetes is expected to double from 171million people in 2000 to 366 million people in 2030, with India experiencing the greatest growth. Diabetes mellitus is expected to impact up to 79.4 million people in India by 2030, with considerable rises in the number of people afflicted in China (42.3 million) and the United States (30.3 million) as well.[4] Significant changes in the metabolism of minerals, including trace elements (zinc, selenium, copper, iron, chromium, manganese & magnesium) and inflammatory markers (C-reactive protein & interleukin 4) have been described in patients with diabetes mellitus, and several mineral deficiencies have been associated with some of the complications of diabetes. [5] Zinc deficiency disrupts insulin homeostasis, leading to reduced insulin secretion by β-cells.[6] This may be due to the fact that magnesium ions are an essential cofactor in several processes. increases the affinity of insulin receptors for ATP and is thus essential for their autophosphorylation and tyrosine kinase activity, which results in magnesium sensitising cells to insulin. The role of copper in glucose homeostasis is not well defined. Experimental data suggest that impairment of glucose tolerance can be secondary to a Cu-deficiency.[7] Studies comparing the amounts of iron, copper, manganese, and zinc in individuals with T2D to healthy individuals have produced contradictory results. For instance, some research has shown that individuals with type 2 diabetes had higher amounts of certain trace elements than controls, while other studies have shown lower levels.[8] Thus, meta-analysis aimed to gather the literature on the differences in iron, copper, manganese, and zinc levels between people with type 2 diabetes & people without the condition. Additionally, iron and copper statuses were indicated by ferritin and ceruloplasmin levels, respectively. Compared to nondiabetic controls, diabetics should have greater copper and iron statuses and lower zinc and manganese concentrations. This study's secondary objective is to investigate, using a moderator analysis, how age, gender, & body mass index (BMI) affect the main outcomes of interest. It is often known that being over 45, being a woman, and being overweight or obese.[9] Many metabolic processes, those involving the metabolism of insulin and glucose, are facilitated by trace elements. For insulin to be produced and packaged into vesicles effectively, zinc must be transported into the pancreatic beta-cells.[10]

Materials & Methods

Materials and Methods The study was conducted in IMCH and RC, Department of Biochemistry. Ethical clearances were obtained from the Institutional Ethical Committee, and written informed consent was taken before carrying out the study.

Parameters:

- Fasting Blood Sugar (FBS) was measured using the GOD-POD method
- HbA1c estimation by the Resin Binding Method.
- Atomic absorption spectrometry by flame is a direct method of determining zinc.
- Estimation of Copper by the Titrimetric method
- Estimation of Selenium by electrothermal atomic absorption spectrometry

Sample size: A total of 400 subjects were recruited, 200 severe diabetes mellitus patients of the case group in the Department of Biochemistry, Index Medical College & Research Center, and 200 healthy controls. Sample Collection: Overnight fasting, 5 ml of blood was drawn from the antecubital vein of all the study participants.

Statistics Analysis: Categorical data are given as frequencies and percentages, and continuous variables as mean ± SD. Categorical variables were compared using the Chi-squared/Fisher's exact test. Continuous variables were compared using the independent samples t-test. All variables were checked to ensure that the data followed a normal distribution. The Pearson / Spearman correlation coefficients were used to investigate the possible associations between case-control and other biochemical parameters, employing both parametric and nonparametric variables. P-value <0.05 was considered a significance level.

Results:

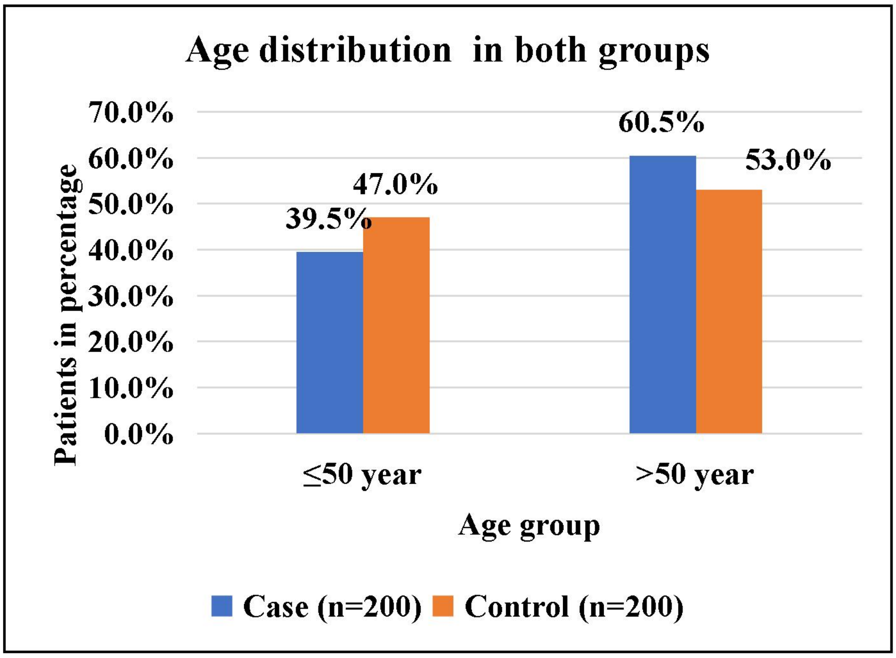

Figure 1: Distribution of the studied patients based on age in both groups

In Figure 1 and Table 1, the Distribution of studied patients based on age in both groups shows that in the case group (n = 200), 79 patients (39.5%) were aged 50 years or less, while 121 patients (60.5%) were aged more than 50 years.
In contrast, the control group (n=200) had 94 patients (47.0%) aged 50 years or less, and 106 patients (53.0%) aged more than 50 years.
The mean age of the case group was 53.57±8.0 years, which was slightly higher than the control group's mean age of 52.10±8.4 years. However, the difference in age distribution between the 2 groups was not statistically significant, with a p-value of 0.130 for the age groups and 0.062 for the mean age, indicating that the age distribution was similar between the case and control groups.

Table 1: Distribution of the studied patients based on age in both groups

Age group	Case (n=200)	Control (n=200)	p-value
≤50 year	79 (39.5%)	94 (47.0%)	0.130
>50 year	121 (60.5%)	106 (53.0%)	
Mean±SD	53.57±8.0	52.10±8.4	0.062

Table 2: Details of the studied patients based on blood glucose in both groups.
The mean Fasting Blood Sugar (FBS) level was 185.7±50 mg/dl in the Case group, which was significantly higher than the 92.0±9.8 mg/dl in the Control group, with a p-value of <0.001. Similarly, the mean Post-Prandial Blood Sugar (PPBS) level was 267.8±81.4 mg/dl in the Case group, which was significantly higher than the 170.1±24.9 mg/dl in the Control group, with a p-value of <0.001.
The mean HbA1c level, which is a measure of long-term blood glucose control, was also significantly higher in the Case group at 9.17±2.2%, compared to 5.66±0.33% in the Control group, with a p-value of <0.001.

Table 2: Details of the studied patients based on blood glucose in both groups

Blood glucose	Case (Mean±SD)	Control (Mean±SD)	p-value
FBS (Mg/dl)	185.7±50	92.0±9.8	<0.001
PPBS (Mg/dl)	267.8±81.4	170.1±24.9	<0.001
HbA1c (%)	9.17±2.2	5.66±0.33	<0.001

Table 3: Details of the studied patients based on trace elements in both groups.

The mean zinc level was significantly lower in the Case group at 60.6±6.6 µg/dl, compared to 96.5±6.0 µg/dl in the Control group, with a p-value of <0.001.

In contrast, the mean copper level was significantly higher in the Case group at 161.0±10.0 µg/dl, compared to 133.6±10.6 µg/dl in the Control group, with a p-value of <0.001.

The mean selenium level was also slightly higher in the Case group at 133.0±8.0 µg/dl, compared to 127.0±10.6 µg/dl in the Control group, with a p-value of <0.001.

Table 3: Details of the studied patients based on trace elements in both groups.

Trace elements	Case (Mean±SD)	Control (Mean±SD)	p-value
Zink (µg/dl)	60.6±6.6	96.5±6.0	<0.001
Copper (µg/dl)	161.0±10.0	133.6±10.6	<0.001
Selenium (µg/dl)	133.0±8.0	127.0±10.6	<0.001

Table 4: Association of diabetic profile with trace elements

		DM duration	FBS	PPBS	Hba1c
Zink	r-value	0.044	-0.739**	-0.598**	-0.682**
	p-value	0.541	**<0.001**	**<0.001**	**<0.001**
Copper	r-value	-0.071	0.638**	0.503**	0.551**
	p-value	0.317	**<0.001**	**<0.001**	**<0.001**
Selenium	r-value	0.092	0.226**	0.138**	0.267**
	p-value	0.193	**<0.001**	0.006	**<0.001**
**. Correlation is significant at the 0.01 level (2-tailed).					
*. Correlation is significant at the 0.05 level (2-tailed).					
r-value = Pearson's Correlation coefficient					

Duration of diabetes (DM duration) does not show a significant correlation with any of the trace elements. However, Fasting Blood Sugar (FBS), Post-Prandial Blood Sugar (PPBS), and HbA1c levels show significant correlations with copper and Selenium.

Notably, FBS, PPBS, and HbA1c levels are negatively correlated with Zinc levels, indicating that poor glycemic control is associated with decreased levels of these essential nutrients.

In contrast, FBS, PPBS, and HbA1c levels are positively correlated with copper levels, suggesting that poor glycemic control is associated with increased Copper levels.

The correlations with Selenium are weaker, but still significant.

Discussion

Trace elements have been considered essential for optimum health. [11] The clinical importance of trace elements is still controversial. Among the trace elements, copper and zinc are of particular importance. [12] In the modern era, chronic disorders such as diabetes mellitus and hypertension are major causes of death worldwide. [13] Sufficient evidence is present that shows alteration in the metabolism of several trace elements in diabetes mellitus. [14-15] Zinc is a dietary metal required for the healthy functioning of the body. Zinc is one of the most important trace elements in the body, and it is essential as a catalytic, structural, and regulatory ion. It is involved in homeostasis, in immune responses, in oxidative stress, in apoptosis, and in ageing. Zinc deficiency is linked to decreased immunity, leading to increased infection susceptibility. But the role of Zn in the prevention, treatment, and complications of DM is not clear. [16] In our study, we evaluated the status of serum selenium levels in Type 2 diabetes mellitus patients. Our study showed an increase in serum level of Se (133.0±8.0) in cases as compared with the control group, which was (127.0±10.6). This finding shows that the level of serum Se was significantly different between cases as compared to controls. Impaired Se homeostasis was frequently associated with either hyper-or hypoinsulinaemia in the animal models discussed above. A likely explanation for these observations stems from the fragile redox homeostasis in pancreatic β-cells and the role of selenoenzymes therein [17-18]

Most of the studies we reviewed found that older people with diabetes tend to have higher copper levels. In our study, we measured the amount of copper in the blood of people with Type 2 diabetes. We found that the average copper level was higher in patients with diabetes (161.0 ± 10.0) compared to those without diabetes (133.6 ± 10.6). This means that the difference in copper levels between the two groups was significant.

Conclusion

Changes in copper and zinc levels are important factors that may increase the risk of complications in people with diabetes. From our study, it can be concluded that changes in these trace elements — low zinc and high copper levels — may play a role in the development and progression of diabetes. These findings suggest that checking zinc and copper levels can help in predicting and managing diabetes. Since both elements are important for health, diabetic patients should ensure they get enough of them through their diet.

To understand their effects more clearly, more studies with larger groups of patients and advanced methods are needed.

Reference:

1. American Diabetes Association Professional Practice Committee; Classification and Diagnosis of Diabetes:Standards of Medical Care in Diabetes—2022.Diabetes Care1 January 2022; 45 (Supplement_1): S17–S38.
2. Burtis, C. A., Bruns, D.E, (2016) Tietz Fundamental of Clinical Chemistry & Molecular Diagnostics: Diabetes (7thEdition). Elsevier
3. International Diabetes Federation, Atlas 2021 –10th edition, www.diabetesatlas.org
4. Kaveeshwar, S. A., & Cornwall, J. (2014). The current state of diabetes mellitus in India.The Australasian medical journal,7(1), 45–48.
5. Stanimirovic J, Radovanovic J, Banjac K, Obradovic M, Essick M, Zafirovic S, Gluvic Z, Gojobori T, Isenovic ER. Role of C-Reactive Protein in Diabetic Inflammation. Mediators Inflamm. 2022 May 17;2022:3706508.
6. Sobczak, A. I. S., Stefanowicz, F., Pitt, S. J., Ajjan, R. A., & Stewart, A. J. (2019).Total plasma magnesium, zinc, copper and selenium concentrations in type-I and type-II diabetes. BioMetals.
7. Ruíz C, Alegría A, Barberá R, Farré R, Lagarda J. Selenium, zinc and copper in plasma of patients with type 1 diabetes mellitus in different metabolic control states. J Trace Elem Med Biol. 1998 Jul;12(2):91-5.
8. Al-Maroof RA, Al-Sharbatti SS. Serum zinc levels in diabetic patients and effect of zinc supplementation on glycemic control of type 2 diabetics. Saudi Med J. 2006;27(3):344–50
9. Azab SF, Saleh SH, Elsaeed WF, Elshafie MA, Sherief LM, Esh AM. Serum trace elements in obese Egyptian children: a case-control study. Ital J Pediatr. 2014; 40:20. doi: 10.1186/1824-7288-40-20
10. Chistiakov DA, Voronova NV. Zn (2+)-transporter-8: a dual role in diabetes. Biofactors. 2009;35(4):356–63. doi: 10.1002/biof.49.
11. Dormonday TL. Trace element analysis of hair. BMJ. 1986;293:975–976.World health Organisation document. Diabetes. 2005.

12. Walter RM, Uriu-Hare JY, Olin KL, Oster MH, Anawalt BD, et al. Copper, Zinc, Manganese, and Magnesium Status and Complications of Diabetes Mellitus. Diabetes Care. 1991;14(11):1050–1056.
13. Fujimoto S. Studies on the relationship between blood trace metal concentration and the clinical status of patients with cerebrovascular disease, gastric cancer and diabetes mellitus. Hokoido Igaku Zasshi. 1987;62:913–932.
14. Salwen M. Vitamins and trace elements, McPherson: Henry’s Clinical Diagnosis and Management by Laboratory Methods. vol. 22nd edn. ; 2011,. p. 417–428.
15. Chausmer AB. Zinc, Insulin and Diabetes. J Am Coll Nutr. 1998;17(2):109–115.
16. Mamza YP, Abdullahi ZA, Gali RM, Mshelia DS, Genesis RY, Habu SA. Status of serum zinc and magnesium among type 2 diabetic subjects in Maiduguri.J Dent Med Sci.2016;15:66–70.Benakova S., Holendova B., Plecita-Hlavata L. Redox homeostasis in pancreatic beta-cells: from development to failure.Antioxidants.2021;10(4)
17. Steinbrenner H. Interference of selenium and selenoproteins with the insulin-regulated carbohydrate and lipid metabolism.Free Radic. Biol. Med.2013;65:1538–1547