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Original article

Association of Serum Zinc Levels with Glycemic Control among Patients with Type 2 Diabetes Mellitus

J. Pratheeba[1*], B. Natarajan[2], Muninathan Natarajan[3]

[1]Associate Professor, Department of Biochemistry, Meenakshi Medical College Hospital and Research Institute, Meenakshi Academy of Higher Education and Research, Enathur, Kanchipuram- 631552, Tamil Nadu, India.

[2]Professor, Department of Urology, Meenakshi Medical College Hospital and Research Institute, Meenakshi Academy of Higher Education and Research, Enathur, Kanchipuram-631552, Tamil Nadu, India.

[3]Associate Professor and Scientist, Central Research Laboratory, Meenakshi Medical College Hospital and Research Institute, Meenakshi Academy of Higher Education and Research (Deemed to be University), Kanchipuram-631552, Tamil Nadu

****Corresponding Author-** Dr. Pratheeba. J*

Abstract

Type 2 diabetes mellitus (T2DM) is a significant metabolic disease with a characteristic of chronic hyperglycemia due to insulin resistance and inadequate insulin production. Zinc is a trace element that is involved in glucose metabolism, insulin synthesis, insulin storage, insulin secretion and antioxidant defense mechanisms. A dysregulated zinc metabolism has been linked to the development and course of diabetes mellitus. The present study was done to compare serum zinc levels in patients with T2DM with non-diabetic healthy controls and to evaluate the correlation between serum zinc level and glycemic control reflected in glycated hemoglobin (HbA1c) levels. A case control study was carried out in 150 subjects who came to department of general medicine of Meenakshi Medical College Hospital and research institute, Kanchipuram comprising 75 patients diagnosed with T2DM and 75 control subjects. The standard laboratory procedures were used to estimate fasting blood sugar (FBS), postprandial blood sugar (PPBS), HbA1c and serum zinc levels. The data were analyzed statistically with SPSS version 21. The serum zinc level in the diabetic group (59.31 ± 18.23 mcg/dL) was significantly lower than that of the control group (87.65 ± 19.05 mcg/dL) ($p<0.001$). Among diabetic patients, there was a significant negative correlation between level of S-Zn and HbA1c, FBS and PPBS levels. The risk of low serum zinc level was 19.3 times higher for participants with diabetes mellitus than for those without. There was no statistically significant difference in serum zinc levels with age, gender, BMI, BP, triglycerides or total cholesterol. The results of this study indicate that glycemic control is significantly associated with zinc deficiency in T2DM. Zinc levels in the serum could be useful prognostic and diagnostic marker for early detection of metabolic imbalance and for optimizing diabetic management.

***Key Words:** Type 2 diabetes mellitus, Blood Glucose, Zinc*

Introduction

Diabetes mellitus (DM) is one of the most prevalent chronic metabolic diseases that afflict millions of people worldwide. It is defined as having hyper glycemia that cannot be corrected by insulin. Type 2 diabetes mellitus (T2DM) is responsible for almost 90–95% of all diabetes cases and is becoming a significant global public health challenge because of its increasing incidence and complications [1]. Diabetes continues to be a growing health burden owing to urbanization, sedentary lifestyle, obesity, unhealthy diet habits and genetic susceptibility. The

number of adults suffering from diabetes is likely to rise significantly over the next few decades, particularly in developing nations like India, which is known as the “diabetes capital of the world.”

T2DM is linked to a number of metabolic defects of carbohydrate, protein and lipid metabolism. Long-term damage such as to the kidneys, retina, nervous system, cardiovascular system and others, occurs due to chronic hyperglycemia. In recent years, the importance of the role of trace elements in the development and progression of DM has been much highlighted. Of these trace elements, zinc is the one with extensive research interest due to its importance in insulin metabolism and antioxidant defense mechanisms [2]. Zinc is a micronutrient that plays a role in many biological processes in the body such as enzyme action, immune function, protein synthesis, cell division and wound healing. It is also vital to the function of pancreatic beta-cells and to glucose homeostasis.

Zinc is also highly enriched in pancreatic beta cells, where it plays an important role in insulin biosynthesis, storage, crystallization and secretion. Insulin molecules are stored in secretory granules as zinc-insulin crystals and the zinc renders insulin molecules in a structural stable form. The intracellular transport of zinc into insulin secretory granules and control of insulin secretion is mediated by zinc transporter proteins, especially Zinc Transporter 8 (ZnT8) [3]. Oxidative stress is a major factor in the pathogenesis of diabetic complications. Hyperglycemia causes excessive production of reactive oxygen species (ROS), which results in cell damage and endothelial dysfunction. Zinc has antioxidant properties and it acts as a cofactor of a crucial antioxidant enzyme, the superoxide dismutase, which protects tissues against oxidative damage [4].

The association between serum zinc levels and DM has been studied previously. Some studies have reported significantly low zinc levels in serum of diabetic patients as compared to healthy controls. Likewise, few other studies found that there was an inverse correlation between serum zinc level and glycated haemoglobin (HbA1C) indicating poor glycemic control with zinc deficiency. However, some studies like [5] and [6] did not find that zinc was statistically significantly associated with glycemic indices. The conflicting results suggest that further studies are needed to understand the role zinc plays in the diabetes mellitus.

The level of glycated hemoglobin (HbA1c) is regarded as a reliable indicator of long-term glycemic control and is a reflection of the average level of blood glucose for the past 2–3 months. High HbA1c levels are correlated with a greater risk of diabetic complications. The correlation between serum Zinc levels and HbA1C may be useful in gaining insight into metabolic aberrations in T2DM patients. The identification of zinc deficiency in diabetes patients can also contribute to the development of nutritional and therapeutic strategies for better glycemic control and prevention of diabetes complications.

Diabetes has increased considerably in India in recent decades. Although diabetes is an increasing disease burden, there is limited information available about the correlation between glycemic statuses with serum zinc levels in Indian patients of T2DM. Hence the present study focused on estimating the serum zinc level in T2DM patients and normal healthy controls and also determined the correlation of serum zinc level with HbA1c level. The study also wanted to evaluate the association of serum zinc level with other biochemical parameters like Fasting Blood Sugar and Postprandial Blood Sugar. The results of this study could help the understanding of the imbalance of trace elements in diabetes mellitus and their clinical relevance.

Methodology

Study Design

The present study was conducted as hospital-based case control study; to compare the level of zinc in the blood of patients with type 2 diabetes mellitus (T2DM) with the non-diabetic healthy controls in the blood and to evaluate the association between serum zinc concentration and glycemic control (glycated haemoglobin (HbA1c)). This study used the quantitative analytical approach to assess the correlation of biochemical parameters with diabetic and non-diabetic status. Case control studies can be used to look for links between exposure factors and disease outcomes, particularly in chronic metabolic diseases like diabetes mellitus.

Study Setting

The study was conducted at Meenakshi Medical College Hospital and Research Institute, a tertiary care teaching hospital at Enathur, Kanchipuram, Tamilnadu and India in Biochemistry and General Medicine Department. The hospital serves the needs of a large population from both rural and urban areas and specialized health care facilities are provided such as diabetic clinics, laboratory investigations and inpatient management. The institution has well equipped diagnostic laboratories which can carry out biochemical estimations and advance clinical investigations required for the present study.

Study Population

The subjects for the study were the patients who visited the outpatient and in-patient departments of the General Medicine from January 2025, to January 2026. The participants were split into two groups: cases and controls. Patients included were those with T2DM, and controls were healthy non-diabetic patients matched by age and sex.

Study Period

The research was carried out in the time frame from January 2025, to January 2026. Eligible subjects were identified, screened, enrolled and assessed during this period according to the study protocol.

Sample Size

A total of 150 study participants were included in the study. Of this group 75 cases of T2DM and 75 healthy controls were diagnosed. Appropriate statistical comparisons between the groups were made by distributing the cases and controls evenly. The sample size was deemed sufficient from a previous study and institutional feasibility to identify significant differences in the zinc level of serum of diabetic patients and non-diabetic participants.

Data Collection Procedure

Those participating in the visit to the Department of Biochemistry and General Medicine were eligible. With informed consent, participants were classified as diabetic cases or as non-diabetic controls using laboratory tests and clinical history. The demographic data, treatment history, duration of diabetes, dietary habits and associated co-morbidities were taken on a proforma. A thorough clinical examination was performed for all participants. Standardised procedures were used to measure anthropometric variables, such as height and weight. After sufficient rest blood pressure was checked using a standard sphygmomanometer. Systolic (SBP) and diastolic (DBP) blood pressure were measured.

Biochemical Investigations

All participants had venous blood samples taken under aseptic precautions with fasting blood sugar, postprandial blood sugar, HbA1c, lipid profile and serum zinc level estimations.

Fasting blood sugar (FBS)

Venous blood samples were obtained following a 24-hour fast (overnight, 8 hours minimum). The FBS levels were measured by the normal enzymatic method in the biochemistry laboratory of the institution.

Postprandial Blood Sugar (PPBS)

Blood samples were obtained 2 h after breakfast for estimation of PPBS levels. Standard biochemical methods were used for blood glucose estimation**.**

Glycated Hemoglobin (HbA1c)

Diabetic participants had their long-term glycemic control estimated by calculating their HbA1c. HbA1C measures the average levels of glucose in the plasma for the last 2-3 months and is a good predictor of the control of the diabetes.

Serum Zinc Estimation

Serum zinc was analyzed in usual laboratory techniques. Blood levels of zinc less than 70mcg/dl were defined as low and those between 70–120mcg/dl as normal. Since trace elements estimation requires strict precautions in the laboratory, care was taken to avoid contamination during the collection and processing of sample.

Lipid Profile

Cholesterol and triglyceride were determined by conventional enzymatic colorimetric assay. The parameters were added to evaluate the metabolic abnormalities of diabetes mellitus.

Ethical Considerations

Ethical clearance has been taken from the Institutional Human Ethics Committee of Meenakshi Medical College Hospital and Research Institute.

Statistical Analysis

The data collected were analyzed by entering all the data into MS-EXCEL and further analyzed by using statistical package for social sciences (SPSS) software version 21. Demographic and biochemical variables were summarized using descriptive statistics, including mean, standard deviation, frequency and percentage. The association between the study groups was analyzed by the Chi-square test for categorical variables. Independent sample t-test or analysis of variance (ANOVA) was used to compare continuous variables as appropriate. A p-value less than 0.05 were considered statistically significant. There was also an odds ratio analysis to evaluate the risk level of the low level of serum zinc in diabetic patients relative to controls. The statistical analysis allowed assessing the association between serum zinc level and glycemic parameters (HbA1c, FBS and PPBS).

Results

A total of 150 study participants were included in the present study, comprising 75 patients with type 2 diabetes mellitus (T2DM) and 75 non-diabetic healthy controls. Various demographic, anthropometric, clinical, and

biochemical parameters were assessed and compared between the two groups. The results demonstrated significant differences in serum zinc levels and glycemic parameters between diabetic patients and controls.

Demographic Characteristics of Study Participants

Among the total participants, 58% belonged to the age group of 41–50 years, whereas 42% were between 51–60 years of age. The mean age of the study population was 49.7 ± 8.5 years. On assessing the association between age distribution and study groups, there was no statistically significant difference observed between diabetic cases and controls (p=0.619). This finding indicates that the study groups were comparable with respect to age distribution. Gender-wise distribution showed that 51.3% of participants were females and 48.6% were males. Among diabetic cases, males constituted 26.6% and females constituted 23.3% of the total study population, whereas among controls, males and females constituted 22% and 28%, respectively. The association between gender and study groups was statistically insignificant (p=0.252), suggesting adequate matching between cases and controls.

Body Mass Index and Blood Pressure Distribution

Body mass index (BMI) analysis revealed that 36.7% of participants had normal BMI values, 47.3% were overweight, and 16% were obese. Among diabetic cases, 17.3% had normal BMI, 22.7% were overweight, and 10% were obese. In the control group, 19.3% had normal BMI, 24.7% were overweight, and 6% were obese. The association between BMI categories and study groups was statistically insignificant (p=0.408). Mean BMI among diabetic patients was 28.48 ± 4.37 kg/m², whereas controls had a mean BMI of 29.35 ± 5.36 kg/m², which also did not show statistical significance (p=0.277). Evaluation of systolic blood pressure (SBP) showed that 21.3% of participants had SBP ≤120 mmHg, 50% had SBP between 121–140 mmHg, and 28.7% had SBP >140 mmHg. Among diabetic cases, 10% had SBP ≤120 mmHg, 26.7% had SBP between 121–140 mmHg, and 13.3% had SBP >140 mmHg. The association between SBP and study groups was not statistically significant (p=0.716). Mean SBP among diabetic patients was 137.60 ± 12.97 mmHg compared to 135.68 ± 20.54 mmHg among controls (p=0.520). Similarly, diastolic blood pressure (DBP) analysis demonstrated that 48% of participants had DBP ≤80 mmHg, 35.3% had DBP between 81–90 mmHg, and 16.7% had DBP >90 mmHg. No statistically significant association was observed between DBP and diabetic status (p=0.805). Mean DBP among diabetic patients was 87.52 ± 8.89 mmHg, whereas controls had a mean DBP of 85.88 ± 7.76 mmHg (p=0.211).

Lipid Profile Analysis

Assessment of total cholesterol levels showed that 32.7% of participants had cholesterol values ≤200 mg/dL, 32% had levels between 201–250 mg/dL, and 35.3% had levels >250 mg/dL. Among diabetic cases, 18.7% had cholesterol ≤200 mg/dL, 14.7% had cholesterol between 201–250 mg/dL, and 16.7% had cholesterol >250 mg/dL. No statistically significant association was found between total cholesterol levels and diabetes status (p=0.471). Mean total cholesterol level among diabetic patients was 230.76 ± 52.90 mg/dL compared to 217.96 ± 51.11 mg/dL among controls (p=0.133). Triglyceride analysis revealed that 28% of participants had triglyceride levels ≤150 mg/dL, 48.7% had levels between 151–250 mg/dL, and 23.3% had levels >250 mg/dL. Among diabetic cases, 15.3% had triglyceride levels ≤150 mg/dL, 24% had levels between 151–250 mg/dL, and 10.7% had levels >250 mg/dL. No significant association was observed between triglyceride levels and diabetic status (p=0.721). Mean

triglyceride levels among diabetic patients and controls were 201.58 ± 54.30 mg/dL and 211.04 ± 58.27 mg/dL, respectively (p=0.301).

Table 1. Comparison of Biochemical Parameters Between Diabetic Patients and Controls

Parameters	Diabetic Group (n=75) Mean ± SD	Control Group (n=75) Mean ± SD	P value
Fasting Blood Sugar (mg/dL)	194.40 ± 52.14	97.04 ± 24.55	<0.001*
Postprandial Blood Sugar (mg/dL)	273.3 ± 46.61	143.6 ± 21.5	<0.001*
HbA1c (%)	9.1 ± 2.51	5.41 ± 0.82	<0.001*
Serum Zinc (mcg/dL)	59.31 ± 18.23	87.65 ± 19.05	<0.001*
Body Mass Index (kg/m²)	28.48 ± 4.37	29.35 ± 5.36	0.277
Systolic Blood Pressure (mmHg)	137.60 ± 12.97	135.68 ± 20.54	0.520
Diastolic Blood Pressure (mmHg)	87.52 ± 8.89	85.88 ± 7.76	0.211
Triglycerides (mg/dL)	201.58 ± 54.30	211.04 ± 58.27	0.301
Total Cholesterol (mg/dL)	230.76 ± 52.90	217.96 ± 51.11	0.133

Glycemic Parameters Among Diabetic Cases

Among the diabetic patients, HbA1c levels demonstrated varying degrees of glycemic control. About 40% of diabetic patients had HbA1c values ≤8%, another 40% had HbA1c levels between 8.1–10%, and 20% had HbA1c levels >10%. Mean HbA1c among diabetic cases was significantly higher (9.1 ± 2.51%) compared to controls (5.41 ± 0.82%), and the difference was statistically significant (p<0.001).

Fasting blood sugar (FBS) analysis among diabetic patients showed that 60% had FBS values <200 mg/dL, 32% had FBS between 201–250 mg/dL, and 8% had FBS >250 mg/dL. Mean FBS among diabetic patients was 194.40 ± 52.14 mg/dL, whereas controls had a mean FBS of 97.04 ± 24.55 mg/dL. The difference between the two groups was highly significant statistically (p<0.001).

Postprandial blood sugar (PPBS) levels showed that 46.7% of diabetic patients had PPBS values <200 mg/dL, 37.3% had PPBS between 201–300 mg/dL, and 16% had PPBS >300 mg/dL. Mean PPBS among diabetic cases was 273.3 ± 46.61 mg/dL compared to 143.6 ± 21.5 mg/dL among controls. This difference was also statistically significant (p<0.001).

Serum Zinc Levels Among Study Participants

The present study demonstrated a marked reduction in serum zinc levels among diabetic patients compared to non-diabetic controls. Overall, 52.7% of participants had low serum zinc levels (<70 mcg/dL), while 47.3% had normal serum zinc values. Among diabetic patients, 42% had low serum zinc levels and only 8% had normal zinc levels. In

contrast, among controls, 10.7% had low zinc levels while 39.3% had normal serum zinc concentrations. The association between serum zinc levels and diabetic status was statistically highly significant (p<0.001).

The odds ratio analysis revealed that diabetic patients were 19.3 times more likely to have low serum zinc levels compared to non-diabetic controls. This finding strongly suggests a significant relationship between zinc deficiency and T2DM.

Mean serum zinc levels among diabetic patients were 59.31 ± 18.23 mcg/dL, whereas controls had significantly higher mean zinc levels of 87.65 ± 19.05 mcg/dL. The mean difference between the groups was statistically highly significant (p<0.001).

Association between Serum Zinc and Glycemic Control

The present study demonstrated a strong inverse relationship between serum zinc levels and glycemic parameters among diabetic patients. When serum zinc levels were analyzed according to HbA1c categories, diabetic patients with HbA1c ≤8% had mean serum zinc levels of 75.2 ± 17.4 mcg/dL, whereas patients with HbA1c levels between 8.1–10% had mean zinc levels of 58.8 ± 15.9 mcg/dL. Participants with HbA1c >10% demonstrated the lowest serum zinc levels (44.3 ± 14.8 mcg/dL). The difference in zinc levels among various HbA1c categories was statistically highly significant (p<0.001).

Table 2. Association between Serum Zinc Levels and HbA1c Among Diabetic Patients

HbA1c Category	Number of Patients (N)	Mean Serum Zinc Level (mcg/dL)	P value
≤ 8%	30	75.2 ± 17.4	<0.001*
8.1–10%	30	58.8 ± 15.9	
>10%	15	44.3 ± 14.8	

Similarly, diabetic patients with fasting blood sugar ≤200 mg/dL had mean serum zinc levels of 77.5 ± 21.5 mcg/dL, whereas those with FBS between 201–250 mg/dL had zinc levels of 59.3 ± 16.8 mcg/dL. Patients with FBS >250 mg/dL demonstrated the lowest zinc levels (51.7 ± 18.1 mcg/dL). The association between serum zinc levels and fasting blood sugar was statistically significant (p=0.026).

Table 3. Association Between Serum Zinc Levels and Fasting Blood Sugar Among Diabetic Patients

Fasting Blood Sugar (mg/dL)	Number of Patients (N)	Mean Serum Zinc Level (mcg/dL)	P value
≤200	45	77.5 ± 21.5	
201–250	24	59.3 ± 16.8	
>250	06	51.7 ± 18.1	0.026*

Analysis of postprandial blood sugar and serum zinc levels also demonstrated a significant inverse association. Patients with PPBS <200 mg/dL had mean serum zinc levels of 76.6 ± 19.6 mcg/dL, whereas patients with PPBS between 201–300 mg/dL and >300 mg/dL had mean zinc levels of 55.1 ± 18.9 mcg/dL and 45.3 ± 13.6 mcg/dL, respectively. This association was statistically highly significant (p<0.001).

Table 4. Association between Serum Zinc Levels and Postprandial Blood Sugar among Diabetic Patients

Postprandial Blood Sugar (mg/dL)	Number of Patients (N)	Mean Serum Zinc Level (mcg/dL)	P value
<200	35	76.6 ± 19.6	<0.001*
201–300	28	55.1 ± 18.9	
>300	12	45.3 ± 13.6	

Overall, the findings of the present study indicate that serum zinc deficiency is significantly associated with poor glycemic control among patients with type 2 diabetes mellitus. Lower serum zinc concentrations were consistently observed in individuals with elevated HbA1c, fasting blood sugar, and postprandial blood sugar levels, emphasizing the potential role of zinc in glucose metabolism and diabetic management.

Discussion

The current study aimed to compare the levels of zinc in the serum of type 2 diabetes mellitus (T2DM) patients with healthy non-diabetic controls and to assess the relationship between serum level of zinc and glycemic control. The study results showed significant reduction in the serum zinc level in diabetic patients compared with controls. Moreover, there was a strong negative correlation between serum zinc concentration and glycated hemoglobin (HbA1c) level, fasting blood sugar (FBS) level and postprandial blood sugar (PPBS) level. The results indicate that zinc deficiency could contribute significantly to the etiology of diabetes mellitus and/or poor glycemic control. Zinc is an essential trace element with a wide variety of physiological and metabolic activities such as insulin synthesis, storage, secretion and action. Zinc is stored in pancreatic beta cells and involved in the stabilization of insulin hexamers in insulin secretory granules. Thus, any abnormalities in zinc metabolism may play a role in the diminished insulin secretion and insulin resistance. The previous studies have also revealed that there is a change in the zinc homeostasis in diabetic patients as urinary zinc loss in diabetic patients as reported by [7] due to hyperglycemia and osmotic diuresis. The mean serum zinc of the groups of diabetic patients was significantly decreased (59.31 ± 18.23 mcg/dL) than that of non-diabetic group (87.65 ± 19.05 mcg/dL) with highly significant p-value (<0.001). A similar study showed that the serum level of zinc was significantly lower in diabetic patients than in healthy individuals. The study also showed that a high prevalence of zinc deficiency was found in T2DM patients, and it was found to be significantly associated with high HbA1c. The result of present study also substantiated with other studies [8] which also reported reduction in serum zinc level among diabetic patients and inverse correlation between the level of zinc and glycemic markers. A statistically significant negative correlation was found between serum zinc levels and HbA1c values suggesting that declining zinc levels were associated with worsening glycemic control. Similarly, a study found that sufficient zinc status is beneficial for glycemic control. The inverse relationship of serum zinc levels and HbA1c was one of the major findings of the present study. The serum Zinc concentration was significantly lower in the diabetic patients with HbA1c levels >10% when compared to those with good glycemic control. The reduction in zinc levels indicates that hyperglycemia worsens and zinc level decreases as the hyperglycemia progresses. Higher glucose levels can lead to zinc excretion in urine, decreased absorption of zinc in the intestine and improved oxidative stress, which all lead to lower zinc levels in the blood. The fasting and

postprandial blood glucose levels were also statistically significant in relation to serum zinc level in the present study. Patients with the high level of FBS and PPBS had significantly lower zinc level than patients with relatively controlled blood glucose levels. Comparable findings were reported that serum zinc level was significantly negatively correlated with fasting blood glucose and HbA1C concentrations in diabetic patients. The results support the hypothesis that zinc deficiency could exacerbate glucose intolerance and be a factor in metabolic imbalance. Diabetic complications are believed to be due to oxidative stress as a major pathogenic mechanism. Chronic hyperglycemia causes overproduction of reactive oxygen species (ROS), which causes endothelial dysfunction, lipid peroxidation and tissue damage. The antioxidant effects of zinc are mediated through its ability to stabilize cell membranes and also as a cofactor of antioxidant enzymes, including superoxide dismutase. Therefore, low zinc could lead to increased oxidative stress, and exacerbate diabetic complications, such as nephropathy, retinopathy, neuropathy and cardiovascular disease [2].

The present study revealed that diabetic patients were 19.3 times more likely to have low serum zinc level than controls. The high odds ratio reflects a strong association between zinc deficiencies with T2DM. Consistent results were reported whose metanalysis revealed that diabetes is a common condition associated with compromised zinc status in diabetic patients relative to healthy people. They also proposed the possibility of zinc imbalance being a part of metabolic derangements in diabetes mellitus.

Unlike the serum zinc, no statistically significant relationship was seen between the diabetes status and different parameters like age, gender, BMI, blood pressure, triglycerides, and total cholesterol in the present study. This is likely due to similarities in demographic and metabolic features of cases and controls. Similar findings were also reported in some previous studies with zinc levels being reported as an independent risk factor for glycemic control, not the demographic factors.

The study results highlight the clinical relevance of the monitoring of serum zinc levels in T2DM patients. Prompt diagnosis and correction of zinc deficiency could help support glycemic control and mitigate complications of oxidative stress. Thus, dietary counseling and zinc supplementation may be used as supportive therapeutic methods in diabetes treatment; however, more interventional studies are needed to verify the effectiveness and long-term results of these interventions.

Conclusion

The present study showed that there is a significant correlation between zinc deficiency and type 2 diabetes mellitus (T2DM). Serum zinc was found to be significantly low in diabetic patients as compared to non-diabetic healthy controls showing that diabetes mellitus has a significant biochemical abnormality in zinc metabolism. The study also showed a significant negative correlation between the serum zinc levels and the glycemic parameters such as glycated hemoglobin (HbA1c), fasting blood sugar (FBS) and postprandial blood sugar (PPBS). There was a significant reduction in serum zinc levels in patients with poor glycemic control, indicating that a worsening hyperglycemia could be a cause of zinc depletion.

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