



## Original Article

## Zinc Deficiency in Type II Diabetes Mellitus

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## ABSTRACT

Zinc (Zn) is an essential trace element for various biochemical, physiological and immunological functions in the human body. Zn deficiency affects up to 25% of the population in poor countries and up to 15% in industrialized countries. Diabetes Mellitus (DM) refers to impaired glucose metabolism, which leads to a constellation of disorders and is marked by poor immunity in the diseased subject. Zn deficiency has an inverse relationship with glycemic control. **Objective:** To assess the serum Zn level in diabetic patients in comparison with healthy subjects. **Method:** A cross sectional study was conducted at Department of Biochemistry, Niazi Welfare Foundation Teaching Hospital, Sargodha, Pakistan from 1st June, 2023 to 31st December, 2023. Data were collected after institutional review board (IRB) approval (NM&DC-IRB-53; Dated 1st Dec, 2022) and informed consent was taken from all the participants. A total of 150 participants were equally divided into two groups based on glycemic control. Serum Zn levels of all participants were estimated via atomic absorption spectrophotometry. Descriptive statistic was used to calculate mean and standard deviation on SPSS version 23.0. **Results:** The mean value of serum Zn level was significantly lower ( $8.83 \pm 1.64 \mu\text{mol/L}$ ) in diabetic subjects as compared to healthy participants ( $18.63 \pm 6.13 \mu\text{mol/L}$ ). **Conclusions:** Deficiency of serum Zn level has a negative relationship with the body's glycemic control.

## INTRODUCTION

Diabetes mellitus (DM) refers to a spectrum of disorders characterized by hyperglycemia [1]. Multiple factors play a role in its etiogenesis, including defects in insulin secretion, insulin action, or both, and disorderly metabolism of carbohydrates, fat and protein. It has two subtypes, Type 1 DM and Type 2 DM, depending on the absence of insulin secretion in cases of autoimmune destruction of pancreatic beta cells or its reduced secretion with resistant insulin receptors [2]. The diagnostic criteria for confirmation of disease is fasting plasma glucose  $\geq 7.0$  mmol/L or 2-hour post-load plasma glucose  $\geq 11.1$  mmol/L or HbA1c  $\geq 48$  mmol/mol [1]. The international diabetes federation (IDF) estimated the

presence of 463 million cases of DM in 2019, which is expected to reach 700 million in 2045 [3]. It is a disease of urbanization, predominant among residents of urban (10.8%) regions than rural (7.2%) inhabitants, and in developed (10.4%) than underdeveloped countries (4.0%) [4]. Due to diverse pathogenic pathways, DM affects the human body in various harmful ways. One such phenomenon is the defective homeostasis of trace elements in the body. Trace elements include chromium (Cr), copper (Cu), iron (Fe), manganese (Mn), mercury (Hg), nickel (Ni), lead (Pb), selenium (Se), and zinc (Zn) etc. They are an integral part of a healthy life. These trace elements are crucial for many physiological and biochemical

processes in the body, including several enzymatic reactions [5]. Zn is the 2nd most abundant element in the human body, responsible for several biochemical reactions including bone metabolism, numerous hormone regulations, as well as cellular immune functions [6]. One of its major functions is the metabolism of carbohydrates in the human body. Zinc is stored with the insulin, in the beta cells of the pancreas and stimulates the phosphorylation of insulin receptor beta subunit [7]. Moreover, it facilitates the entry of glucose into the cells with the help of an enzyme insulin-responsive aminopeptidase (IRAP), being abundant in muscles and adipose tissues [8]. There is another enzyme glycogen synthase kinase  $\beta$  which produces insulin resistance at the level of the cell membrane and it is directly affected by the protective effect of Zn [9]. The approximate quantity of Zn in an adult's body is 1.4 - 2.3 gm, whereas 85% is concentrated in bone and muscles [10]. It is richly available in the earth's crust and resultantly gains access to the human body via drinking water and various plant-based diets [11]. Zn deficiency in human beings was identified in 1963 and the United States National Academy of Sciences established a recommended dietary allowance (RDA) for Zn (11mg) in 1964 [12]. The World Health Organization (WHO) estimation for Zn deficient population is nearly 2 billion subjects, living in the developing world. The phytates present in the cereal-protein diet of the people living in poor countries impede the absorption of Zn. The clinical manifestation depends on the severity of its deficiency, thus they vary from impaired taste and smell, reduced immunity exhibited as recurrent respiratory infections, gastrointestinal upset, skin changes, impaired glucose tolerance, progression of DM [13]. The lack of data on predictors and indicators of Zn deficiency has hindered accurate estimation of its prevalence. DM is widely spreading in our impoverished country.

The aim of this study was to find out the evidence of Zn deficiency in controls vs. diabetic subjects. It is an easily modifiable risk factor of DM, participates as a causative agent and speeds up the disease progression as well. Zn-supplemented diets may reverse the fatal outcomes of DM to fair control status.

## METHODS

This cross sectional study was conducted from 1st June, 2023 to 31st December, 2023 in the Department of Biochemistry at Niazi Welfare Foundation Teaching Hospital, Sargodha, Pakistan. A sample size of 150 was calculated on the basis of prevalence of type II diabetes at 95% confidence interval and 5% margin of error. The prevalence was determined to be 11.77 % in a prior study conducted in Pakistan [14]. Inclusion criteria of the study were a) Age group of 25- 65 year (type II diabetes is dominant in this age group) [15] b) willing to participate in

the study c) absence of any medical illness that can affect glycemic control such as hepatitis, cirrhosis, kidney or heart disease. Patients with a debilitating illness or any endocrine disability were excluded from the study. Data were collected after approval (NM&DC-IRB-53; Dated 1st Dec, 2022) from institutional review board and an informed consent was taken from all the participants. The study utilized non-probability convenient sampling technique. All participants were divided into two groups: "Group A" consisted of controls with a glycemic level below 7 mg/dl, and "Group B" consisted of cases with glycemic levels of 7 mg/dl or higher. Each group had 75 individuals. The age and sex of the participants were documented, and blood samples were collected using aseptic techniques in vacuum containers to measure HbA1C and serum zinc levels. HbA1c was measured by using Immunospectrometric method (Hitachi 917). Serum Zn levels were estimated via atomic absorption spectrophotometry (Hitachi Z-2000) [16]. Descriptive statistics were used to calculate the frequency and percentages. The mean and standard deviation was calculated for age and serum Zn level. Statistical analysis was done using SPSS version 23.0.

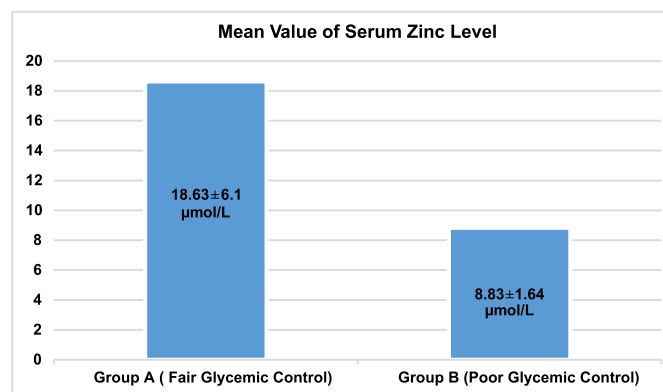
## RESULTS

Group A with fair glycemic control showed 49 (65.3%) males and 26 (34.6%) females with mean age (Years) of  $51.42 \pm 8.62$ . Group B with poor glycemic control, included 34 (45%) male and 41 (55%) females having mean age (Years) of  $53.22 \pm 6.88$  as depicted (Table 1).

**Table 1:** Frequency of Sex distribution in Group A vs. Group B (n=150)

Gender Distribution	Group A (n=75)	Group B (n=75)
Male	49 (65.3%)	34 (45%)
Female	26 (34.6%)	41 (55%)
Mean Age	$51.42 \pm 8.62$	$53.22 \pm 6.88$

The estimated mean value of serum Zn was higher in Group A ( $18.63 \pm 6.13 \mu\text{mol/L}$ ) as compared to Group B ( $8.83 \pm 1.64 \mu\text{mol/L}$ ) illustrated (Figure 1).



**Figure 1:** Mean Serum Zinc Value; Group A vs. Group B

## DISCUSSION

Zinc is crucial for  $\beta$ -cell function, insulin action, and glucose homeostasis, thus influencing the pathogenesis of diabetes mellitus. Moreover, zinc deficiency may contribute to the development of diabetic complications [7, 8]. Zinc deficiency in type 2 diabetes can lead to complications such as impaired glucose metabolism, increased oxidative stress, and immune dysfunction, resulting in poor glycemic control, higher infection risk, and delayed wound healing. It also exacerbates inflammation and contributes to cardiovascular issues and diabetic neuropathy [10]. Glycemic control has an inverse relationship with serum zinc level. Zn is responsible for controlling cytokine-induced immune destruction processes, thus autoimmune destruction of insulin-secreting islet cells is seen in cases of Zn-deficient type 1 DM [17]. Genetic polymorphism is seen in the zinc transporter 8 genes and in metallothionein (MT)-encoding genes related to type 2 DM. Moreover, higher urinary excretion of Zn is seen in cases of DM, which consequently contributes to its deficiency [8, 9]. The study found higher proportion of female patients with poor glycemic control. This suggests that women with diabetes may face additional challenges in managing their blood sugar levels effectively. This finding is supported by a previous study reporting poorer glycemic control among females as compared to males, owing to late presentation, different lifestyles and hormonal changes [18]. The messenger RNA ratio of the Zn transporter i.e. ZnT1(zinc export) to Zip1(zinc import) was lower in diabetic females as compared to healthy controls; it indicating the suboptimal zinc homeostasis in them [17]. Our results revealed that diabetic patients have significantly lower serum zinc level than control group. There was a statistically significant negative correlation between zinc serum level and HbA1C in diabetics. Consistent with our findings, another study demonstrated that serum zinc concentration was lower in diabetics compared to controls and identified a negative correlation between serum zinc and glycated protein [19]. Similarly, another study documented that serum zinc was significantly lower in diabetics than healthy controls [20]. In our study, the mean value of serum Zn level in healthy control subjects was  $18.63 \pm 6.13 \mu\text{mol/L}$ . Similarly, a study determined serum Zn level  $17.91 \pm 2.86 \mu\text{mol/L}$  in control group [11]. In present study, serum Zn level were deficient in diabetic group i.e.  $8.83 \pm 1.64 \mu\text{mol/L}$ . Compared to a study conducted by Farooq et al., found the mean Zn level as  $9.3 \pm 1.6 \mu\text{mol/L}$  in the diabetic group, the deficient group's result almost matches our findings [21]. A systematic review and meta-analysis encompassing 25 studies explored the effects of zinc supplementation on clinical and biochemical parameters in patients with diabetes,

demonstrated significant benefits. The analysis revealed that zinc supplementation positively impacts glycemic control, helping to regulate blood sugar levels more effectively. This finding underscores the potential role of zinc in diabetes management, highlighting its importance in improving clinical outcomes and biochemical markers associated with the disease. The comprehensive nature of this review, including a diverse range of studies, strengthens the evidence, supporting the use of zinc as a beneficial supplement for individuals with diabetes [22]. Serum zinc (Zn) deficiency is recognized as a modifiable risk factor for diabetes mellitus (DM). Given its modifiable nature, addressing zinc deficiency represents a practical and effective strategy in the broader effort to combat diabetes and its associated complications. This study provided the data of a limited population, more studies are needed to be carried out to conclude the role of Zn and other trace elements in diabetic patients and find out their part in the disease progression and its complications.

## CONCLUSIONS

Diabetic patients significantly suffer from the deficiency of serum Zn level. There is a need for preventive measures which should be promptly implemented for early supplementation of Zn in identifiable risky groups.

## Authors Contribution

Conceptualization: MFJ

Methodology: MFJ, ERC

Formal analysis: SR, BH, AAR

Writing-review and editing: RAS, AAR

All authors have read and agreed to the published version of the manuscript.

## Conflicts of Interest

The authors declare no conflict of interest.

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