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Ghada ZA Soliman*

Professor of Biochemistry, National Nutrition Institute, Cairo, Egypt

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***Corresponding author:** Ghada ZA Soliman Phd, Professor of Biochemistry, National Nutrition Institute, Cairo, Egypt,
E-mail: amr_soliman2005@yahoo.com

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Research Article

Serum/Urine Zn Level of Egyptian Type II Diabetic Patients and Its relation with Glycemic Control (HbA1c)

Abstract

Introduction: Diabetes Mellitus is a metabolic disorder disease characterized by hyperglycemia due to impaired insulin secretion or action. Percent of Type 2 diabetic patients are getting to increase annually allover the world especially in developing countries. It is estimated to increase to 300 million in 2025. In Egypt around 8.1 million are estimated according to IDF 2015. Zinc is a trace element that acts as co-factor for synthesis, storage, stability and secretion of insulin by pancreas. There is a controversy studies regarding Levels of trace elements as Zinc in diabetic patients.

Aim: To assess the level of zinc in Egyptian type 2 diabetic patients and its relation to glycemic control.

Material and methods: One hundred and twenty type 2 diabetic patients, with duration of diabetes > 2 years, age 30-45 year; and 60 age and sex matched; healthy normal controls receiving oral antidiabetic drugs were included in this study. Serum Zn, Fasting blood sugar (FBS) and HbA1c levels were estimated. Diabetic patients were divided into 2 groups, 60 diabetics /group: controlled diabetics (HbA1c < 7); and uncontrolled diabetics (HbA1c > 7).

Results: Serum Zn levels of uncontrolled diabetics were significantly lower (56.18 ± 0.66 µg/dl) than controlled diabetic (76.61 ± 2.44) and normal controls (84.30 ± 0.98 µg/dl, $p < 0.001$). An inverse significant correlation with found between serum concentration of zinc and FBS; and HbA1c in uncontrolled diabetics.

Conclusion: Altered levels of trace elements as Zn are found to be important predisposing factors for diabetic patients.

Introduction

Diabetes mellitus is the most prevalent disease worldwide that affects millions of individuals every year across the world. It represents a major public health problem. Type 2 diabetes mellitus has a rising attitude globally. The worldwide spread of diabetes among general population is estimated to increase to 300 million in 2025 [1,2]. In Egypt around 8.1 million are estimated according to IDF 2015.

Zinc (Zn) is a trace element that acts as co-factor for synthesis, storage, stability and secretion of insulin by pancreas and it accounts for the conformation integrity of insulin in its hexameric crystalline form [3,4]. Zinc may be involved in the regulation of insulin receptor-initiated signal transudation mechanism and insulin receptor synthesis. Also Zn acts as a cofactor for the function of intracellular enzymes that may be involved in protein, lipid and glucose metabolism or participate as an integral component of several antioxidant enzymes. Zinc has an important role in the glucose utilization by muscle and fat cells [5,6].

Pancreatic β cells contain very high concentrations of zinc compared with various other cells. In particular, Insulin secretory granules have the highest zinc content within β cells [7]. Metallothioneins (MTs), zinc importers (ZIP, SLC39A), and zinc exporters (ZnT, SLC30A) are proteins that regulate cellular zinc homeostasis [4,8]. ZnT8 plays a key role in the accumulation of zinc within insulin secretory granules [9]. Furthermore, zinc is essential for the appropriate synthesis of insulin, as well as its storage and structural stability [4].

Insulin comprises a hexamer of six insulin and two zinc molecules [3], in β-cells of the pancreas. Insulin crystallization occurs under specific conditions in insulin secretory granules, in which both insulin and zinc exist in high concentrations and acidic pH is maintained [10]. Insulin is released into the portal venous system at the time of β-cells de-granulation where it dissociates rapidly into monomers.

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Anderson *et al.*, [5] reported that 30% patients with DM found to be zinc deficient. There are different data regarding Zn level in diabetic patients where some authors (large number) stated that Zn is deficient in diabetics [5,11], others found no change [12,13], others found an increase in Zn concentration [14,15].

Materials and Methods

An informed consent was collected from all the participants. Study was approved by the ethical committee of GOTHI (Egypt).

One hundred and twenty type 2 diabetic patients; and 60 age and sex matched healthy controls were included in this study. Under strict aseptic conditions blood sample was collected from all the participants. Serum Zn, Fasting blood sugar (FBS) and glycated hemoglobin (HbA1c) levels were estimated. Glucose was determined using Randox kit [16]. HbA1c was determined using Stanbio kits procedure No. 0350 (Stanbio laboratory, Boerne, Texas; DN: RBR.0350CE.00) according to Trivelli *et al.*, [17]. Zn in serum/urine was determined using QCA Kits (Spain) according to Makino *et al.*, [18], and Homster and Zak [19]. Diabetic patients were divided into 2 groups, 60 diabetics/ group: controlled diabetics (HbA1c < 7); and uncontrolled diabetics (HbA1c > 7) according to Rohlfing *et al.*, [20], and Gopinath *et al.*, [21]. Urine samples were collected for Zn determination.

Inclusion criteria

Diabetic patients, with duration of diabetes > 2 years, age 30-45 year; oral anti-diabetic drugs (glibenclamide).

Exclusion criteria

Patients who are taking zinc supplementation or drugs that interfere with zinc absorption, patients with chronic disease and pregnancy/ lactation, smokers, patients with history of acute infections and thyroid dysfunction were excluded from this study.

Statistical analysis

Data was expressed as Mean ± SEM. Statistical analysis was performed using SPSS version 11. Statistical tests as t-test, ANOVA/ Duncan post hoc and correlation coefficient were applied. $P < 0.05$ was considered statistically significant.

Results

Results of FBS, HbA1c, Serum / Urine Zn are presented in figures 1-4. A significant increase in mean FBS of uncontrolled diabetic patients when compared with normal control / or control diabetic (252.88 ± 3.13 vs 94.01 ±1.18 &118.49 ± 2.44 mg/dl, $P < 0.001$) was found. A significant increase in mean hbA1c of uncontrolled diabetic patients when compared with normal control / or control diabetic (9.98 ± 0.20 vs 6.19 ± 0.31 &6.98 ± 0.22 g%, $P < 0.001$). Mean serum zinc was significantly lower in uncontrolled diabetic patients (56.18 ± 0.66 µg/dl) compared to healthy subjects (84.30 ± 0.98 mcg/dl, $p < 0.001$), or controlled diabetic (76.61 ± 2.44). Mean urinary zinc was significantly higher in uncontrolled diabetic patients (46.64 ±

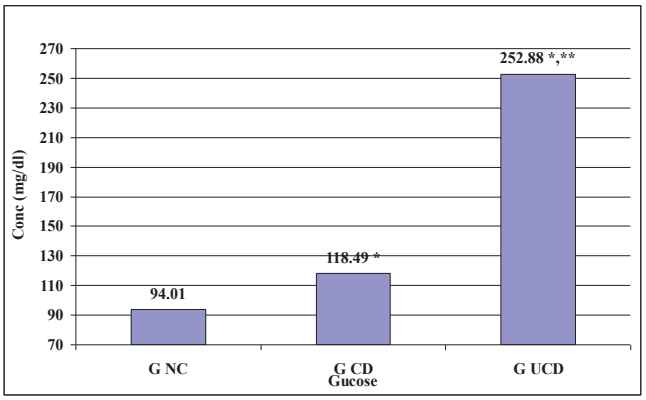

Figure 1: Level of glucose in sera of diabetic and control persons.

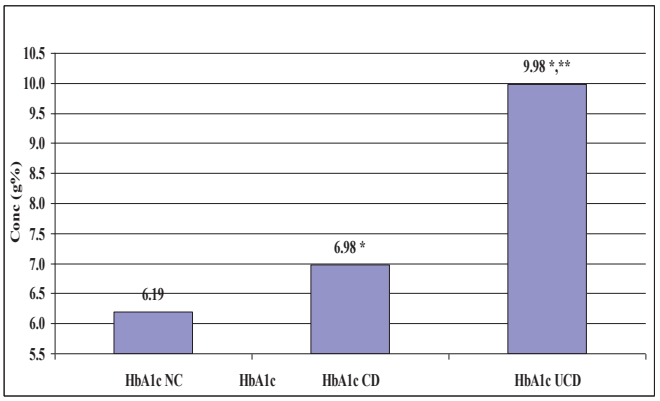

Figure 2: Conc of HbA1c of Diabetic and Control persons.

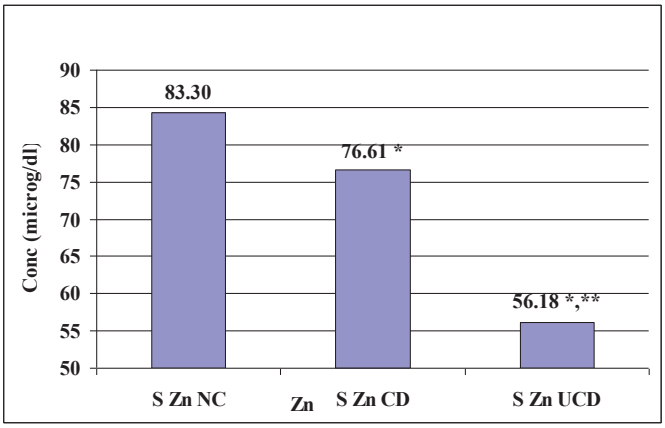

Figure 3: Level of serum Zn in diabetic and normal persons.

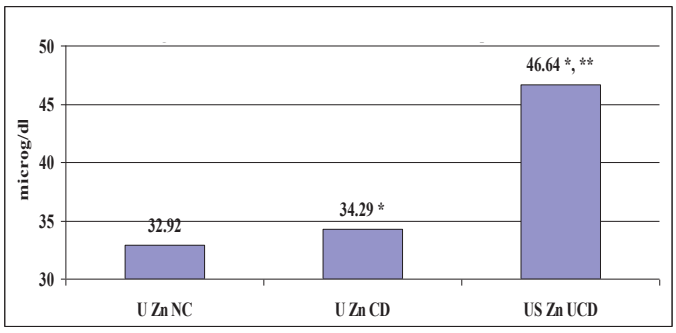

Figure 4: Level of Zn in urine of diabetics and normal persons.

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1.84 µg/dl) compared to healthy subjects (32.92 ± 1.00 µg/dl, p < 0.001), or controlled diabetic (34.29 ± 0.86). Urine Zn level of uncontrolled diabetic is significantly higher than healthy control persons, diabetic.

Discusion

Diabetes has been shown to be major causes of death all over the world. The prevalence of diabetes in developed countries represents a major public health problem. Insulin is stored inside secretory vesicles or granules, where two Zn^{2+} ions coordinate six insulin monomers to form the hexameric-structure on which maturated insulin crystals are formed [22].

Our study revealed that diabetic subjects had significantly low mean zinc levels than control subjects (p < 0.001) either uncontrolled diabetic or normal persons. Our results agree with Al-Maroof *et al.*, [23], Kazi *et al.*, [24], Sahria and Goswami [25], Saha-roy *et al.*, [26], where they found a significant decrease in serum Zn level in uncontrolled diabetic patients when compared with normal persons or versus diabetic patients.

The low zinc level in the diabetic patients may be due to the decreased gastrointestinal absorption and increased urinary excretion [27], or due to some effects of alteration of other minerals, especially copper [28], or due to the interfering of hyperglycemia with the active transport of zinc back into the renal tubular cells leading to more urinary excretion of zinc as stated by Tripathy *et al.*, [11]. Also Kinlaw *et al.*, [29], explained that zinc absorption has been defect or reduced, by uncontrolled blood sugar (hyperglycemia) and it would lead to an elevation of HbA1c.

Our results disagree with Zargar *et al.*, [12], and Unjiati *et al.*, [13], where they found no significant change when compared with normal persons. Also our results disagree with Osman *et al.*, [14], and Mumza *et al.*, [15], where they found significant change (increase) when compared with normal persons.

Zn deficiency in diabetic patients diminish its role as antioxidant against free radical oxidation (characteristic of diabetes mellitus, hyperglycemia) since Zn is a component / cofactor of the important antioxidant enzyme superoxide dismutase (Cu-Zn SOD) that regulates the expression of metallothioneins and glutamate-cysteine ligase, thus affecting glutathione levels [30,5,6). Also it might affect the release of vitamin A from the storage site in the liver and metabolism [31], and it also affect synthesis, storage and structural stability of insulin [3]. Zn deficiency may cause impaired glucose tolerance, insulin degradation, insulin resistance and reduced pancreatic insulin content [32,33].

In our study the FBS was negatively inverse correlated with serum concentration of zinc (r=-0.672, p <0.001) in uncontrolled diabetics which disagree with Mumza *et al.*, [15], where they found no significant relation of zinc concentration with FBS.

In the present study, it was observed that the mean HbA1c concentration in uncontrolled type 2 diabetic patients had an inverse relation with serum zinc concentration (r=-0.615, p <0.001) which agrees with Al-Maroof *et al.*, [23], i.e. with the increase in HbA1c levels there is decrease in zinc levels. Lower Zn level might lead to higher blood glucose as a result of low insulin synthesis or action and consequently, higher HbA1c. It also agrees with Viktorinova *et al.*, [34], and Somayeh *et al.*, [35]. In contrast, Dorre *et al.*, [36], showed no significant correlation between serum Zn level and HbA1c. The disagreement may be due to dependence of HbA1c on treatment of diabetes not on Zn level (Table 1, Figure 5).

Table 1: Correlation of Zn with FBS and HbA1cfor the studied groups.

	Normal Control		Uncontrolled Diabetics		Controlled Diabetics	
	G NC	HbA1c NC	GUCD	HbA1c UCD	G CD	HbA1c CD
r	0.119	0.156	-0.672	-0.615	-0.263	-0.279
P <	NS	NS	0.001	0.001	NS	NS

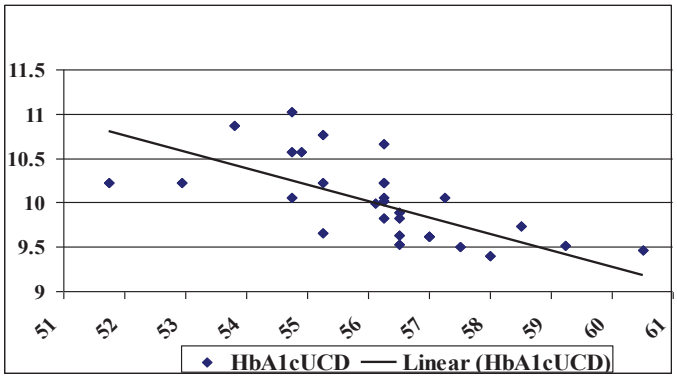

Figure 5: Person correlation betweens Zn vs HbA1c of uncontrolled diabetics.

Conclusion

Egyptian diabetic patients had significantly low level of Zn. There was a negative relationship among serum zinc and FBS; and HbA1c.Further studies are required.

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