Serum Copper, Zinc and Cu/Zn Ratio in Diabetics

Tawfeeq F. R. AL-Auqbi * FICMS/CM

Abbas M. R. Al-Mussawi* CABM, FRCP

Abdul Kareem Y. J. ◌◌Al-Sammraie* MSc, PhD

Abstract:

Background: The altered status of some essential trace elements and antioxidant minerals which observed in diabetic patients could have deleterious influences on the health of diabetics.

Objectives: To estimate serum levels of Copper, Zinc and Cu/Zn ratio in type 1, type 2 diabetics and healthy subjects.

Patients & Method: A case control designed study was carried out at the National Diabetes Center (NDC) / Al-Mustansirya University; on a total of 94 participants formed of 32 type 1 diabetics, 32 type 2 diabetics and 30 healthy control participants. Data collected about age and BMI; and blood samples examined for FPG, HbA1C and participants' samples of serum were examined for S.Cu, S.Zn by using atomic absorption technique and Cu/Zn ratio was calculated.

Results: The mean FPG of type 1 and type 2 diabetics and BMI of type 2 diabetics show statistically significant difference from control group. Mean serum Copper of type 1 and type 2 diabetic's show statistically significant difference from control group. Simple linear correlation and regression analysis of the FPG level shows strong positive correlation to the Cu and Cu/Zn values in all study groups; and negative correlation to the Zn values in all study groups. Also, HbA1c shows strong positive correlation to the Cu and Cu/Zn values among type 1 diabetics and control groups; and negative correlation to the Zn values among type 1 diabetics and control groups. BMI and duration of diabetes shows no correlation with the Cu, Zn and Cu/Zn values among all the study groups.

Conclusions: Serum Copper, Cu/Zn ratio increase significantly more than healthy control subjects; while serum Zinc shows insignificantly reduced less than healthy control participants, both in type 1and 2 diabetes. Simple linear correlation and regression model analysis shows strong positive correlation of serum Copper and Cu/Zn ratio as well as strong negative correlation of Zinc toward the FPG values in all studied groups; furthermore, toward HbA1c in type 1 diabetes and control group.

Key Words: Copper, Zinc, Cu/Zn ratio, diabetes mellitus.

Introduction:

Background:

Diabetes mellitus is a growing important health problem which triggers major mass pathologies and micro-vascular complications.[1,2] Diabetes mellitus, cardiovascular disease (CVD) and dyslipidemia continue to be the main health scourge of most developed countries and are becoming dominant in many populous areas of the developing countries.[2]) In the United States, between 2000 and 2001, the prevalence of diabetes rose from 7.3% to 7.9%.[3] Type 1 diabetes mellitus is the first common endocrine and metabolic disease during childhood; also, it is considered as the third common chronic disease in childhood.[4] At present time, the most prevalent form of DM is type 2 (approximately 90 % of diabetic patients)[5] which has reached epidemic proportions.[3] Diabetes, in general, is considered as the fourth most common cause of death in USA.[6] Moreover, The overall prevalence of diabetes approaches 8 % of adult population of the USA and most of Europe.[7]

The altered status of some essential trace elements and altered antioxidant minerals ratio observed in type 1 diabetic patients could have deleterious influences on the health of the diabetics.[8] Diabetes is characterized by hyperglycemia which considered a primary cause of diabetic vascular complications and it is associated with oxidative stress, impaired trace element and lipid metabolism.[9] Trace element concentrations were believed not to be dependent on the degree of glucose control as determined by correlation analysis between HBA1c versus mineral levels in the blood.[10]

Copper deficiency has long been associated with disturbed carbohydrate metabolism and with oxidative stress.[11]

Zinc is an essential micronutrient and its deficiency is related to many diseases like diabetes mellitus.[12] Zinc has numerous targets to modulate insulin activity, including its antioxidant capacity. Zinc status is decreased in most type 2 diabetic patients.[13]

Zinc deficiency may provoke polymorphonuclear leukocyte activation, and contributes to the

development of vascular complications in type 2 diabetic patients.[14] Furthermore, Copper/Zinc ratio may be used as important markers to evaluate the presence of vascular complications. [14]

Objectives

To estimate serum levels of Copper, Zinc and calculate Cu/Zn ratio in type 1, type 2 diabetics and healthy subjects.

Patients & Method:

A case control designed study was carried out at the National Diabetes Center (NDC) / Al-Mustansirya University; on a total of 94 participants formed of 32 type 1 diabetics, 32 type 2 diabetics and 30 healthy control subjects, after obtaining their agreements according to the medical research and ethical regulations, thus an oral consent was taken from all enrolled people.

Data were collected from all participants regarding their age sex, BMI, duration of diabetes and other comorbid conditions. Blood samples were taken for laboratory investigations which included; Fasting Plasma Glucose (FPG), glycosylated hemoglobin (HbA1c) and the atomic absorption technique were used to measure serum Copper and Zinc levels.

All the statistical work and reporting of obtained data were carried out by using Microsoft Excel - Windows XP professional program. Differences considered of significance according to the t-test at level of $P \leq 0.05$ and ≤ 0.01.

Results

A total of 94 participants had been completed the study successfully without any health problems.

The mean age, BMI, FPG and HbA1c (table-1) were examined statistically (t-test, $P < 0.05$) and shows statistically significant difference from healthy control group for the FPG of type 1 and type 2 diabetics and BMI of type 2 diabetics.

Table-1: The mean of age, BMI, FPG and HbA1c of type 1, type 2 diabetics and control groups.

	Type 1 diabetes (n=32)	**Type 2 diabetes** (n=32)	**Control** (n=30)
Age (years)	26.18±6.89	51.28±14.13	28.8±9.49
BMI (kg/m^2)	21.68±4.42	27.40±5.05 *	21.81±4.11
FPG (mmol/L)	11.84±5.0 *	8.44±2.01 *	4.91±0.71
HbA1c (%)	8.19±1.80	7.08±1.59	4.1±0.82

* T-test ($P \leq 0.05$)

The mean serum Copper, Zinc and Cu/Zn ratio (table-2) were examined statistically (t-test, $P < 0.05$) and shows statistically significant difference only for the serum Copper of type 1 and type 2 diabetics as compared to the control group.

Simple linear correlation and regression analysis (table-3) of the FPG level shows strong positive correlation to the S. Cu and Cu/Zn values in all study groups; and negative (reverse) correlation to the Zn values in all study groups.

Glycosylated hemoglobin (HbA1c) shows strong positive correlation to the S. Cu and Cu/Zn values among type 1 diabetics and the control group; while the Zn values among type 1 diabetics and the control group shows a negative (reverse) correlation with HbA1c.

Table-2: The mean of Serum Copper, Zinc and Cu/Zn ratio of type 1, type 2 diabetics and control groups.

	Type 1 diabetes	Type 2 diabetes	Control
S. Copper (µmol/L)	28.06±11.83 *	26.10±6.17 *	17.64±3.48
S. Zinc (µmol/L)	6.70±3.78	8.2±3.20	10.99±4.11
Cu/Zn ratio	6.18±5.94	3.97±2.55	1.90±0.92

* T-test ($P \leq 0.01$)

Table-3: Simple linear correlation and regression analysis of Serum Copper, Zinc and Cu/Zn ratio versus FPG and HbA1c of studied groups.

Coefficient of correlation (r)	FPG			HbA1c		
	Type 1	Type 2	control	Type 1	Type 2	control
Serum Copper	0.757	0.923	0.969	-0.941	0.578	-0.970
Serum Zinc	-0.727	-0.745	-0.972	-0.809	-0.490	-0.977
Cu/Zn ratio	0.761	0.859	0.928	0.859	0.584	0.933

Discussion

Significantly more information about trace elements status could be obtained by investigating its concentrations in blood cells instead of only evaluating its concentrations in plasma. Ignoring this important biochemical role, trace elements concentrations determined in whole blood or plasma very often lead to conclusions contrary to the actual intracellular concentration.[15] However, the current study using the atomic absorption technique to measure actual serum levels of Copper and Zinc among study population because of its availability and to make clear the real status of serum Copper, Zinc and Cu/Zn ratio in the sera of diabetics.

Hyperglycemia is the major pathgnomonic finding in type1 and 2diabetes as proved by our study when compared to control group, (table 1). Abou-Seif et. al., Proved the same relation [9]; that means hyperglycemia leads to oxidative stress which plays an important role in vascular degenerative lesions observed in diabetics [16]; moreover, hyperglycemia is considered as the primary cause of diabetic vascular complications and it is associated with oxidative stress, impaired trace element and lipid metabolism as well as pancreatic enzyme abnormalities.[9]

The BMI of type 2 diabetics were significantly different from the control group, (table 2), because obesity was a major predisposition for type 2 diabetes.[17] As Mokdad et. al. stated that the prevalence of type 2 diabetes is rising in parallel with the rise in obesity.(18) In addition, obesity and type 2 diabetes became an increasing medical problem with its associated disorders.[17]

Serum Copper was found to be significantly elevated in diabetics as compared to the control group (table 2), which is in agreement with the results published by Kruse-Jarres et. al..[15] The significant increase in serum Copper and diminished serum Zinc levels in type 1 diabetes as compared to healthy control subjects, these findings were in harmony with Abou-Seif et. al. findings.[9] Karahan et. al. has been stated a conclusion that decrement in S.Zn and increment in Cu/Zn ratio is regarded as a marker of vasculopathy in diabetic subjects.[14]

Both Al-Saleh et. al. and Ekin et.al. found that S.Cu was significantly elevated in the sera of diabetic subjects, while the reduction in the level of S.Zn in their sera was found to be not significant when compared to non diabetic healthy subjects.[8,19] These results were consistent with results obtained by the current study (table 2).

Simple linear correlation and regression analysis (table 3), shows strong positive correlation of Copper and Cu/Zn ratio and strong negative correlation of Zinc toward the FPG values in all

studied groups; and toward HbA1c values in type 1 diabetics and control group. Cooper et. al. found that the extra cellular superoxide dismutase, an important antioxidant enzyme containing both Copper and Zinc, was elevated in diabetic subjects; and its activity correlated strongly with the interaction between serum Copper and HbA1c.[18] So they suggest that cardiovascular complications in diabetes might be better controlled by therapeutic strategies that focus on lowering plasma glucose and loosely bound systemic Copper.[18] Also, Karahan et. al., concluded that Zinc deficiency may contributes to the development of vascular complications in diabetic patients. Furthermore, Copper/Zinc ratio may be used as important markers to evaluate the presence of vascular complications.[14] Likewise, Agte et. al., consider diabetes as an oxidative stress-related disorder in which erythrocyte Zinc uptake may vary as compared to healthy individuals.[20] So they suggest that erythrocyte Zinc uptake could be biomarkers of long-term Zinc status and decrease of Zinc uptake may be one of the features of diabetic patients.[20] On the contrary, Lezo et.al., suggested a significant inverse association of dietary intakes and serum levels of Zinc with hyperglycemia.[21]

Conclusions

Serum Copper, Cu/Zn ratio increase significantly in diabetics more than control; while serum Zinc shows insignificantly reduced less than control, both in type 1and 2 diabetes.

Simple linear correlation and regression analysis shows strong positive correlation of serum Copper and Cu/Zn ratio as well as strong negative correlation of Zinc toward the FPG values in all studied groups; furthermore, toward HbA1c in type 1 diabetes and control group.

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* **National Diabetes Center (NDC), AL-Mustansirya University, Baghdad.**