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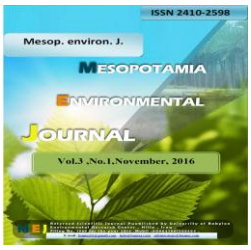

Serum Trace Elements in Patients with Type 2 Diabetes Mellitus

Iqbal Fadhel Alwan[1] **Amar M.Hamood[1]**

Ministry of Science and Technology , Research Department material , Bag. Iraq .

Corresponding author : ekbalfadhel @ gmail.com

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Abstract

To assess serum zinc , copper, and magnesium level in type 2 - diabetic patients and the effect of age , gender, glycemic control on these trace elements in comparison with those of control subjects. There were 45diabetic patients and 45 age matched non- diabetic (control) subjects included in this study .Serum zinc , serum magnesium and serum copper and fasting blood sugar measured among the diabetic and control groups and association of both trace elements were assessed with glycemic status , age, gender of diabetes , using SPSS for analysis. The result show the significantly decreased levels of Zn and Mg , whereas increased levels of Cu($p<0.001$) in type 2 DM patients when compared to control groups. There was no association of age , gender glycemic status. We suggest that evaluate the above trace elements in early stage of diabetes , otherwise it may contribute in the development of further vascular complications in diabetes mellitus.

Keyword : Type 2 DM , Trace element , glycemic status.

Introduction

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces [1]. The aehtiological types of disorders of glycemia includes Type 1 diabetes (TID), TID indicates the process of ß-cell destruction that may ultimately lead to diabetes mellitus in which " insulin is required for survival" to prevent the development of keto acidosis , coma, and death. Type 2 diabetes (T2D) , T2D is the most common form of diabetes and individuals are characterized by disorders of insulin action and secretion , either of which may be the predominant feature , Gestational diabetes mellitus (GDM) , Gestational diabetes is carbohydrate intolerance resulting in hyperglycemia of variable severity with onset or first recognition during pregnancy [2]. The number of patients suffering from diabetes mellitus was reported to be over 200 million people worldwide , a big part of it being Non –insulin – dependent diabetes mellitus(NIDDM),patients [3] . Divalent cations of trace element play important roles in human body .Insulin action on reducing blood glucose was reported to be potentate by some trace elements as

magnesium . zinc, and copper . The proposed mechanism of trace elements enhancing insulin action includes activation of insulin receptor sites, serving as cofactors or components for enzyme systems involving in glucose metabolism , increasing insulin sensitivity and acting as antioxidants preventing tissue per oxidation. Trace elements are accepted as essential for optimum health, because of their diverse metabolic characteristic and function. Trace element deficiencies are frequently associated to chronic diseases or to problems with its absorption. Zinc (Zn) is one of the essential trace elements which are involved in the synthesis , storage, secretion and conformational integrity of insulin. Zn deficiency is associated with many chronic illnesses. Zinc plays an important role in glucose metabolism. It helps in the utilization of glucose by muscle and fat cells. It is required as a cofactor for the function of intracellular enzyme that may be involved in protein , lipid and glucose metabolism. Zinc may be involved in the regulation of insulin receptor-initiated signal transudation mechanism and insulin receptor synthesis[4]. Zinc is a structural part of key antioxidant enzymes such as superoxide dismutase , and zinc deficiency impairs their synthesis , leading to increased oxidative stress. Zinc has a biphasic effect in that it is required for insulin storage and cellular binding , although high concentrations can lead to a reduction in insulin release[5] . Oxidative stress contributes to the pathogenesis of many disease including DM. So many studies shown that copper (Cu) causes oxidative stress and acts as a pro oxidant and may participate in metal catalyzed formation of free radicals. The increased production of free radicals is likely to the associated with development of type 2 DM. Copper is considered as both a powerful enzyme catalyst and a dangerous reactant that generates hydroxyl radical [6]. A deficiency of copper results in glucose intolerance , decreased insulin response, and increased glucose response . It is associated with hypercholesterolemia and atherosclerosis . Copper possesses an insulin-like activity and promotes lip genesis. Magnesium (Mg) is an important divalent cation mostly localized intracellular. It is an essential ion involved in multiple levels in insulin's secretion and its binding and its activity ; and it is a cofactor in the glucose transporting mechanisms of the cell membrane various enzymes in carbohydrate oxidation[7] . It is also involved at multiple levels in insulin secretion , binding and enhancing the ability of insulin to activate tyrosine kinase. Magnesium deficiencies have been implicated in insulin resistance , carbohydrate intolerance , dislipidemia and complications of diabetes. Lower serum levels of these elements have been reported in the diabetic state [8]. It is unknown whether difference in trace elements status is a consequence of diabetes and hyperglycemia or alternatively whether their deficiencies contribute to the expression of the disease. The aim of the present study was to evaluate the serum levels of Zinc, Copper and Magnesium, in patients with type 2 DM and compared with normal healthy controls and their possible association with age , gender, glycemic status.

Material and methods

Collection of data was carried out at the university hospital. The diabetic group included (80 NIDDM patients) , aged 35-70years, who chosen from patients with diabetes , attended the medical examinations during the period of the study. An agent matched control group included (50) apparently healthy subjects who were selected the workers from of the same center.

Sample collection : About 10 ml of venous blood was obtained after an over night fast using disposable needle and syringe. Samples were collected in sterile dry acid washed vials .Each sample was centrifuged at 3500 rpm and the serum was separated and stored at – 20 ^{o}C until analysis .

Determination of fasting blood sugar (FBS): Fasting blood glucose was estimated by enzymatic colorimetric method using commercial kit , GOD/POD method[9] .

Determination of copper , zinc and magnesium: Serum zinc and magnesium were estimated by colorimetric kit method . serum copper was also estimated by colorimetric kit method.

Statistical analysis: The statistical analysis of data was performed by using SPSS version 17.0 software. All values are expressed as mean ±SD. For the comparison of values between the groups,

student t- test was used, represented by 'p' value. Statistical significance was considered at a 'p' value of < 0.05 [10] .

Results

80 patient with NIDDM (46 male , 34 female) and 50 healthy subject (25 male , 25 female) comprised the study group . The mean fasting blood sugar (FBS) , blood Zn, Mg and Cu concentration in all subject . The mean levels of Zn and Mg were significantly lowered ($p < 0.05$) in NIDDM as a compare to control group .On the other hand , the mean levels of Cu was significantly higher ($p<0.001$) in NIDDM as compared to control group as shown in table 1 and Fig.1. Table 2 and Fig.2: showed that the age had a weak and statistically on significant effect on serum Zn, Mg, while Cu shows a statistically significant increase with age. Table 3 and Fig.3: showed that no difference was found between gender (male and female) with respect to Cu, Zn and Mg levels ($p<0.05$). But in table 4 and Fig.4 ; it was found that trace elements significantly influenced by glycemia status ($p<0.011$).

Table I . concentration of fasting blood sugar and trace elements in healthy control and diabetic patients.

Parameter	Diabetic patients ±SD	Normal healthy control ±SD	T-test (p value)
Glucose (mg/dl)	262.2± 84.01	87.1± 17.1	P<0.01
Cu (µg/dl)	172.1±23.1	93.4±6.82	P<0.01
Mg (mg/dl)	1.85 ± 0.19	2.01±0.23	P<0.01
Zn (µg/dl)	84.9 ±14.3	98.1±9.62	P<0.01

P< 0.001 highly significantly compound to controls

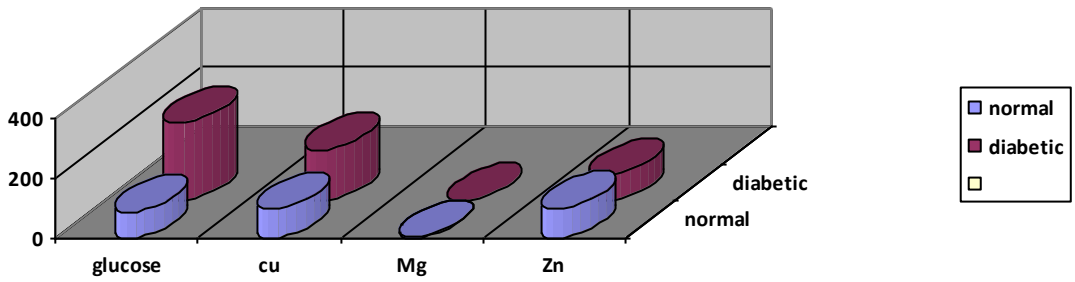

Fig.1 concentration of fasting blood sugar and trace elements in healthy control and diabetic patients.

Table 2 The effect of age in glucose and trace elements level at Diabetic patients.

Parameters	35-50 years ±SD	51- 70 years ±SD	T-test (p value)
Glucose (mg/dl)	248.91± 80.1	274.9±85.3	No significant
Cu (µg/dl)	167.1 ±22.31	176.1± 21.1	P < 0.05
Mg (mg/dl)	1.83 ± 0.17	1.87 ± 0.23	No significant
Zn(µg/dl)	86.1 ± 15.2	83.96 ± 14.1	No significant

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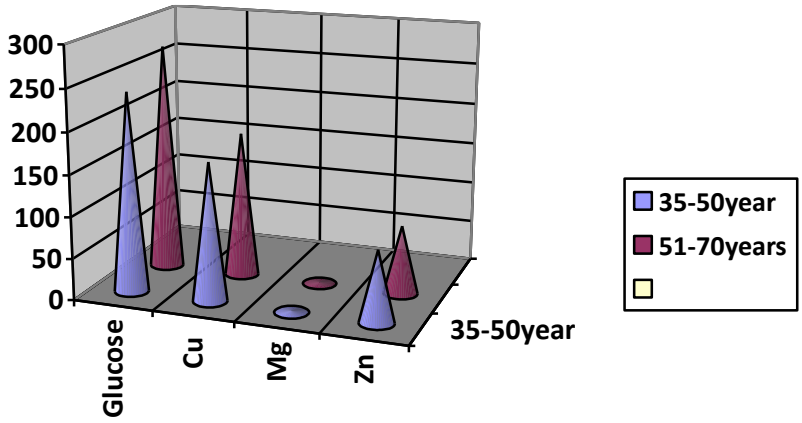

Fig. 2 : The effect of age in glucose and trace elements level at Diabetic patients.

Table 3 . concentration of fasting blood sugar and trace elements in serum of diabetic patients according to their gender.

Parameters	Male ±SD	Female ±SD	T-test (p value)
Glucose (mg/dl)	266.2 ± 87.61	256.1 ± 79.0	No significant
Cu (µg/dl)	172.53 ± 22.31	170.20 ± 23.1	No significant
Mg (mg/dl)	1.82 ± 0.21	1.88 ± 0.12	No significant
Zn(µg/dl)	85.19 ± 14.9	85.10 ± 14.83	No significant

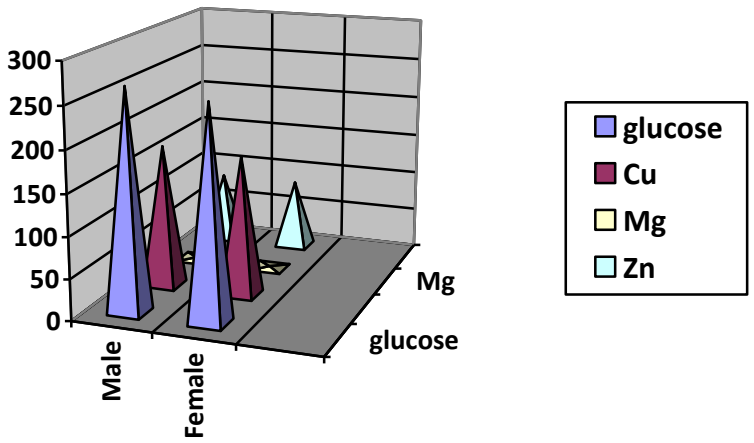

Fig.3: concentration of fasting blood sugar and trace elements in serum of diabetic patients according to their gender.

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Table 4 : The effect of glucose and trace elements level at Diabetic patients.

Parameter	Glucose> 270 ±SD	Glucose < 270±SD	T. test (P value)
Cu (µg/dl)	160.21 ± 18.30	185.60 ± 19.68	P<0.01
Mg (mg/dl)	1.89 ± 0.23	1.77 ± 0.16	P<0.01
Zn(µg/dl)	92.13 ± 0.67	81.61 ± 0.62	P<0.01

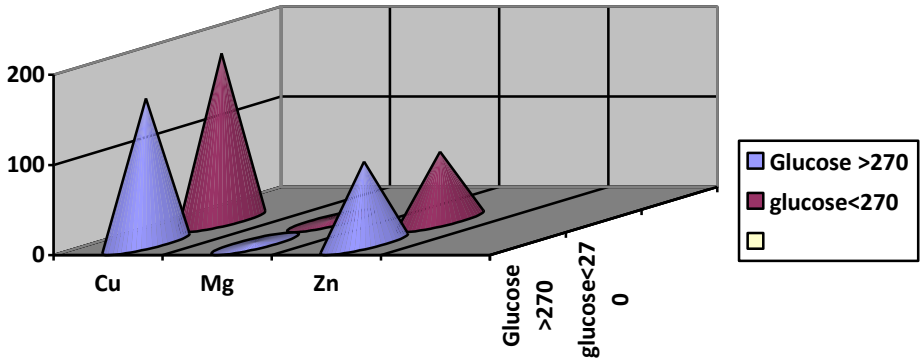

Fig.4 :The effect of glucose and trace elements level at Diabetic patients.

Discussion

Many trace elements are important for human metabolic function. Numerous studies have demonstrated the essential roles of trace element as chromium, zinc, magnesium, selenium , vanadium , molybdenum and copper in insulin action and carbohydrate metabolism [11]. The actual role of these trace elements in the pathogenesis and progress of diabetes is still unclear[12]. The observed alterations in the status of these elements in diabetics have been attributed to hyperglycemia and increased protein glycosylation seen in this condition[13]. The serum levels of zinc , magnesium and copper in diabetics and control group were determined in this study and related with the age , gender, glycemic status and duration of diabetes.

Cu metabolism in diabetics is abnormal. Many studies have reported higher copper level in diabetics especially in complicated cases. Our study showed that copper concentrations were significantly higher in NIDDM patients than control group which is consistent with finding of [14],[15] .Copper levels have been found to be elevated in IDDM subject , while urinary excretion of copper has been found to be affected by diabetes mellitus. In the present study Cu showed a statistically significant increase with age. These finding consistent with finding of [16] which found that in diabetic patients the age had a statistically significant association with serum copper for each year increase in age which is different , the copper content was higher in the liver of diabetic and lower in adipose tissue. **Magnesium** is an essential ion involved in multiple levels in insulin's secretion, its binding and its activity , and it is also a critical cofactor of many enzymes in carbohydrate metabolism. n this study , serum magnesium level was not significantly different between the groups, which are similar to the study done by [17], which showed no difference in plasma magnesium level between control subjects and diabetic patients. In contrast to these results , [18] reported that serum magnesium levels were significantly low in diabetic patients when compared with control group. Lower serum magnesium level in diabetics than in controls was also reported by [19]. Sharma[20] reported an inverse correlation between serum magnesium level and poor glycemic control, and a strong association.

Zinc plays a clear role in the glucose metabolism . The results in this study indicate a significant decrease in serum zinc levels in NIDDM patients compared to the normal healthy control. Which consistent with finding of [21],[22]. Diabetes can affect the balance of zinc in several ways , although it is most likely that hyperglycemia , rather than any primary lesion related to diabetes , causes the increased urinary loss and subsequent decreases in total body zinc.n addition , a review of the literature has show that in addition to the zincuria , there is evidence that type1 and type2 diabetics can cause zinc malabsorption . Some researchers have indicated that diabetics may lose zinc by excreting more zinc into intestine during the digestive processes. Zinc plays a key role in the synthesis , storage and secretion of insulin , and it accounts for the conformational integrity of insulin in its hexametric crystalline form[23]. The addition of zinc to the insulin structure will increase the insulin's ability to bind to its receptor. A decrease in zinc affects the ability of the islet cells to produce and secrete insulin , which could compound the problems of Type 2 diabetics in particular. In addition to the findings that zinc levels are often low in diabetic, it is also felt that zinc (in concert with other micronutrients) may participate as an integral component of antioxidant enzymes . Many of the complication of diabetes may relate to an increase in intracellular oxidant and free radicals associated with decrease in intracellular zinc and zinc dependent antioxidant enzyme [14]. Although this study shows a decrease in zinc with the age yet this was not significant and this consistent with results obtained by many studies , which showed that the elderly are at particular risk of zinc deficiency due to their low energy intake and poor dietary zinc consumption[25] .

In this study , there were no significant associations of serum trace element with age ,gender , blood sugar or duration of diabetes. The gender references in trace element levels in diabetics might be attributed to hormonal imbalance with the diabetic state.

Conclusions

The present findings demonstrate that impaired trace element metabolism to be an additional risk factor in the development and progress of disease and they contribute to the pathogenesis of type 2 DM [26]**.** Serum zinc level was significantly lower in Type-2 diabetics , whereas no significant difference was found in serum magnesium and serum copper levels was increase and significant high when compared with control subjects. There was no association of age , gender, glycemic status and duration if diabetes on the serum concentration of these trace elements in type -2 diabetic patients. We suggest that evaluate the above trace elements in early stage of diabetes, otherwise it may contribute in the development of further vascular complications in diabetes mellitus.

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