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Trace Elements in Type2 Diabetes Mellitus

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ABSTRACT

Diabetes Mellitus (DM) is related with variations in metabolism of zinc(Zn), copper(Cu), manganese (Mn) and iron (Fe). The objective of the current study was to evaluate serum level of some trace elements in patient with type 2diabetes mellitus in a relation to their gender, age, duration of diabetes and glycemic status. Fifty type 2 diabetics and 30 clearly healthy age and sex matched control subjects were chosen for this study. Serum Zn and Mn levels were significantly decreased($p<0.05$); while Fe and Cu were significantly increase($p<0.05$) in type 2 diabetes patient as compare to control group. Gender, age and duration of diabetes had no a statistical significant association with trace elements concentration except Cu shows a statistically significant increase with age. Zn, Cu and Fe significantly influenced by glycemic status except Mn. Conclusion: The alteration of trace elements in type 2DM probably responsible for various metabolic disturbances, oxidative stress and other complications related with type2 DM.

Key Words: Type 2diabetes mellitus, Trace elements, Zinc, Copper, Manganese, Iron

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INTRODUCTION

Diabetes mellitus type2 name (Non-Insulin-Dependent Diabetes Mellitus NIDDM or name adult-onset diabetes)[1]is the metabolic disorder which is recognized by hyperglycemia; insulin resistance and the relative impairment in the insulin secretion[2].

Long-term complications of diabetes develop gradually like coronary artery disease; nerve damage (neuropathy); kidney damage (nephron pathy); eye damage(diabetic retinopathy) and Alzheimer's disease, they can be life-threatening[3].

Trace elements are elements, generally metals; required in a little quantity to keep a healthy body. They are necessary mostly as a components of hormones and enzymes or are implicated in the activation of enzymes[4].

An association was detected between DM and trace elements in several research studies[5-8]. Researches have revealed that metabolism of many essential trace element is changed in DM as well as these elements have a special roles in pathogenesis, complication and disease progress [9].

Zinc is one of essential trace element, it is part of many enzymes, also it has an-important role in the conservation of many functions of tissues[10], including synthesis, storage and release of insulin[11], so it is required for the storage and for insulin synthesis as well as it is secreted as zinc crystals. Zinc play main role in conserving the structural integrity of insulin[12], it has also main role in the modulating of immune system and its disorders in DM can be regarding in portion to the status of zinc[13].

Copperis most numerous essential trace element human body; it has vital role in human body, it excites the immune system to struggle the infections; it repairs the infected tissues and it also stimulates the healing. Copper has role in

neutralization the free radicals which can cause intense damage to cells, also it part of two of the most important antioxidant enzymes; super oxide dismutase (Cu-Zn SOD) and ceruloplasm[14]. Both the increased and decreased Cu level were occurred in patients with diabetes mellitus[15-16]. Most studies reveal that diabetic patients have abnormal copper circulation [17].

Manganese is trace element which is existing in human body in very small quantities; predominantly in the bones, liver, kidneys and pancreas[18]. Manganese has a main role in many of physiological process as the component of some enzymes and activator of many enzymes, these Mn-activated enzymes have main role in metabolism of carbohydrate, amino acid and cholesterol[19].

Some studies demonstrate that patients with diabetes mellitus have decrease levels of Mn in their body, however researchers don't recognize if diabetes may be cause level to fall, or whether if decrease level of Mn participate to evolving diabetes so further studies are required. One medical study revealed that diabetic patients who have high blood level of Mn were more safe from LDL(bad-cholesterol) than those patients who have low levels of manganese[20].

Iron is the transitional metal as well as it considers as a strong catalyst in several cellular-reactions which create reactive oxygen species (ROS), these reactions participate in damaging of the tissue and surge oxidative-stress, thus possibly changing type 2 DM risk [21-22].

Proof that systemic iron excess might be participate to irregular of metabolism of glucose was firstly resulting from a monitoring that the occurrence of DM is elevated in classic hereditary hemochromatosis(H-H)[23], but together with an invention of modern genetic disorders of metabolism of iron, regardless of the reason or gene concerned, it is evident that excess iron effects in elevation of occurrence of type2 DM[24].

The aim of this current study is to a compare the level of some essential trace elements including zinc, copper, manganese and iron in sera of type 2 diabetic patients with healthy controls and their correlation with age, gender, duration of diabetes and glycemic status.

MATERIALS AND METHODS

Subjects:
Fifty patients with type 2diabetes mellitus, age ranged between 30-68 years(mean ± SD: 47.16±9.9) years were enrolled in this study (25 female and 25 male). Also 30 normal healthy subjects age ranged between 32-67 years (mean ± SD: 48.8±11)were included as a control. The followings patients were exclude from the study; diabetic patient who had cured with insulin, hypertensive patient, patients who had taken diuretics, patients with acute complications like severe infection, trauma and patients with severe ketoacidosis.

The patients were divided into two age groups (30-49 and 50-68 years) and their relations with disease complications were studied. Also we have graded patients glycemic control into two groups based on fasting blood glucose values taking the following ranges (the optimum < 145 gm/dl and > 145 gm/dl) and studied their relation with disease complications. Also we have divided patients into two groups, based on the duration of diabetic(< 10 years and > 10 years). The gender of patients was also studied.

Sample: Blood samples were drained fasting from all the subjects, after coagulation the blood was centrifuged at 3000 RPM for 10 minutes then sera were separated and stored at-20 ºC.

Methods:
Fasting blood glucose was measured by enzymatic colorimetric method using commercial Randox, UK kit[25].

The serum contents of Zn; Cu; Mn and Fe were measured by using atomic absorption spectrophotometer. (AA-6300, Shimadzu, Japan)[26].

Biostatistical analysis:
Analysis of data was done by using (SPSS) statistically package for social science version 15.0. Results were expressed as mean; standard deviation (SD); range (minimum-maximum) and student- test was used to illustrate the different between groups variation which considered significant when P- values are ≤ 0.05.

RESULTS

Fifty patient with NIDDM (25 male , 25 female) and 30 healthy subject comprised the study group.

Table 1 showed the mean fasting blood glucose(FBG); Zn; Cu; Mn and Fe concentration in all subjects. The results of Zn and Mn concentrations were significantly lowered in sera of patients with NIDDM as a compare to control group($p<0.05$).

In contrast, the results of Cu and Fe concentrations were significantly higher in sera of patients with NIDDM as compared to control group($p<0.05$) while there was no difference was found between male and female with respect to Zn, Cu, Mn and Fe levels as shown in table 2.

Table 3 showed that the age had no statistically significant association with serum Zn, Mn and Fe while Cu shows a statistically significant increase with age.

Table 4 it was found that FBG, Zn, Cu and Fe significantly influenced by glycemic status except Mn.

The results in table 5 revealed that there was no significant association between duration of diabetes and FBG; Zn; Cu; Mn and Fe respectively.

Table(1): Biostatical calculation of age, FBG, Zn,Cu, Mn and Fe Concentration for type 2DM patients and normal healthy control

Parameters	Type 2 DM Patients N= 50 Mean ± SD	Normal Healthy Control N= 30 Mean ± SD	P - Value
Age (years)	47.16 ± 9.9	48.8 ±11	N.S
FBG (mg/dl)	136.44±21.5	87.86±9.4	P<0.05
Zn (µg/dl)	64.15±5.8	91.27±4.9	P <0.05
Cu (µg/dl)	143.05 ±18.5	102.62±3.2	P <0.05
Mn (µg/dl)	0.302± 0.04	0.363±0.04	P<0.05
Fe (µg/dl)	95.45±4.2	65.79±3.3	P<0.05

N.S= Not significant
FBG= Fasting blood glucose

Table (2): Concentration of Zn, Cu, Mn, Fe and FBG in sera of type 2 DM patients according to their gender

Parameters	Male N=25 Mean ±SD	Female N=25 Mean ±SD	P-Value
FBG (mg/dl)	134.2±21.7	138.6±21.5	N.S
Zn (µg/dl)	60.8±4.4	63.8±3.2	N.S
Cu (µg/dl)	140.1±3.1	138.7±2.5	N.S
Mn (µg/dl)	0.303±0.04	0.302±0.04	N.S
Fe (µg/dl)	93.7±4	90.1±4.3	N.S

N.S= Not significant
FBG= Fasting blood glucose

Table (3): The effect of age in concentration of Zn, Cu, Mn, Fe and FBG in sera of type 2 DM diabetic

Parameters	Age 30-49 N=33 Mean ±SD	Age 50-68 N=17 Mean ±SD	P-Value
FBG (mg/dl)	132±15.5	129.4±28	N.S
Zn (µg/dl)	62.5±4	59.8±3.6	N.S
Cu (µg/dl)	120.7±2.9	163.5±2.7	P<0.05
Mn (µg/dl)	0.3±0.04	0.307±0.04	N.S
Fe (µg/dl)	88.4±4.6	92.8±3.1	N.S

N.S= Not significant
FBG= Fasting blood glucose

Table (4): Concentration of Zn, Cu, Mn, Fe and FBG in sera of type 2DM diabetic patients according to their glycemic status

Parameters	<145 mg/dl N= 30 Mean ±SD	>145 mg/dl N=20 Mean ±SD	P-Value
FBG (mg/dl)	123.9±13.9	155.2±16.7	P<0.05
Zn (µg/dl)	59.9±3.3	74.1±6.3	P<0.05
Cu (µg/dl)	160.1±2.8	127.7±2.5	P<0.05
Mn (µg/dl)	0.299±0.04	0.308±0.04	N.S
Fe (µg/dl)	118.3±4.1	77.7±4.3	P<0.05

N.S= Not significant
FBG= Fasting blood glucose

Table (5): The effect of duration of diabetes in concentration of Zn, Cu, Mn, Fe and FBG in sera of type 2 DM diabetic

Parameters	< 10 years N= 30 Mean ±SD	> 10 years N=20 Mean ±SD	P-Value
FBG (mg/dl)	133.6±16.1	127.8±25.6	N.S
Zn (µg/dl)	59.7±4.2	62.7±3.1	N.S
Cu (µg/dl)	140.9±2.8	139.2±2.6	N.S
Mn (µg/dl)	0.306±0.04	0.298±0.04	N.S
Fe (µg/dl)	92.7±4.5	93.3±4.8	N.S

N.S= Not significant
FBG= Fasting blood glucose

DISCUSSION

Many studies have stated a link between DM and variation in the metabolism of some trace elements [27].

In this current study, there was a significant decrease in Zn concentration in sera of patients with type 2DM as a compare to healthy control($p<0.05$), which is in correlation with findings of Chausmer AB *et al*.[12], A C Nsonwu *et al*.[28]and Alena Viktorinovaa *et al*.[29].

DM can influence the balance of zinc in various ways though it is the most probable that hyperglycemia instead of any primary disorder associated to diabetes causes elevated in urinary lack and consequent decreases in all body zinc[30], also some researches have proposed defect in zinc absorption related with hyperglycemia or DM.Kinlaw *et al*., confirmed abnormal zinc tolerance tests in patients with DM revealing of lowering in absorption[31].

Also the present study revealed that Cu concentration in sera of patients with type 2DM significantly increase than those in the healthy control ($p<0.05$). Increased levels of Cu in sera of diabetic patients correspond with other studies[32-34]. High levels of cupper in diabetic patients are due to a hyperglycemia which maycatalyzeglycation and liberate Cu ions which can accelerate oxidative stress[35].

In addition to that the present study showed significant decrease in Mn concentration in sera of type 2 DM patient as compare to healthy control ($p<0.05$), which is in correlation with Kazi*et al.*, who demonstrated significantly decrease level of manganese in patients with type 2DM when compared with healthy controls[36]. Decrease level of Mn in patients with type2 DM could be as a consequence of the elevation of urinary excretion of Mn. This result corresponds with some researchers works, which described that urinary excretion of Mn was elevated in patients with type2 DM as compared to healthy controls[37].

On other hand, the results of Fe concentration was significantly higher in sera of patient with type 2DM as a compare to healthy control ($p<0.05$). There are revealing proofs that Fe has apathogenic functions in DM and its complication like microangiopathy and arteriosclerosis (Swaminathan*et., al.* 2007) [38].

The present study demonstrated that there was no significant differences between female and malewith regards to Zn,Cu,Mn and Fe levels,this was with agreement with the studies done before for Zn and other trace metals [39-40]. In contrast to these results, gender related difference was also described by Ruiz *et al.*, (1998) who noticed significant differences in cupper levels between females with DM and healthy females[41].The gender related reference in the levels of trace element in patients with DM could be due to the irregular of hormones with the state of diabetes [40].

Also the present study showed that the age had no statistically significant association with serum Zn, Mn and Fe while Cu shows a statistically significant increase with age, These finding consistent with finding of Aquilar *et al.*, 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 content of Cu was elevated level in diabetic liver and lower in adipose tissue[42].

The physiological changes which related to age like adjusted dietary requirements, drug therapy and chronic diseases due to or related to increased consuming or secretion of trace elements could lead to low levels of trace elements in old people [43].

Also the present study found that Zn, Cu and Fe significantly influenced by glycemic status except Mn but the duration; of diabetes had no statistical significant association with a serum Zn, Cu, Mn and Fe.Mertz, (1998) confirmed that there was no correlation observed between plasma and urinary Zn level with the duration of diabetes[44].

CONCLUSION

This study conclude that, the increases in Cu and Fe concentrations besides with decreases of Zn and Mn concentration in sera of patients with type2 DM may be implicated in disorders of insulin excretion or implicated in its action. Due to lack of the concentration of Zn and Mn, therefore this study suggests the supplementation of patients with Zn and Mn rich food.

Also this study showed there was no association of gender, age and the duration of diabetes on serum level of FBG, Zn, Cu, Mn and Fe except Cu show increase level in elderly type 2 DM patients, also this study conclude that Zn, Cu and Fe significantly influenced by glycemic status except Mn. These changes may be responsible for oxidative stress, altered metabolic disturbances and other complications related with DM.

This study support further clinical study so as to realize the role of trace elements in type2 DM patients.

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