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STATUS OF SOME TRACE ELEMENTS IN TYPE-2 DIABETIC PATIENTS AND ITS RELATIONSHIP WITH LIPID PROFILE

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ABSTRACT

Investigation of the serum level of copper, zinc, magnesium and manganese in type-2 diabetes mellitus and their possible association with lipid profile was carried out. The comparative study included 100 type-2 diabetic patients in Gr-II and 100 non-diabetic as control in (Gr-I). Results indicated that there is a significant lower level ($p < .001$) of serum Zn, Cu, Mg and Mn in diabetic patients compared with the control group, showing p value < .001. In type-2 DM patients (Gr-II) there were significant correlations between serum Zn and TAG ($r = 0.209$) and between Zn and HDL-C level ($r = .199$) showing p value <.05. Non significant relationships were found in between Zn and lipid profile (TAG, Cholesterol, HDL-C and LDL-C) of control (Gr-I) group. Significant correlation was found between serum magnesium and TAG of control (Gr-I) where $p < .01$ and non significant correlations were found in serum Mg and total cholesterol, HDL-C, LDL-C of both type-2 diabetic (Gr-II) and control (Gr-I). Significant correlations were also found in between serum of Cu and Mn and TAG of control (Gr-I) where $p < .05$ and non significant correlations were found in other component of lipid profile of both cases (Gr-II) and control (Gr-I).

Key words: Trace elements, Diabetes mellitus, Lipid profile

INTRODUCTION

Type-2 diabetes mellitus (DM) is on track to become one of the major global public health challenges of the 21st century. It accounts for approximately 90 to 95% of all diagnosed cases of diabetes. Patients with type-2 diabetes may have complications like cardiovascular disease, nephropathy, retinopathy, and polyneuropathy. According to WHO report, the prevalence of diabetes in adults worldwide has risen (Bowen 1967, Mertz 1981). Dietary composition has a big role in control of diabetes mellitus, nowadays composition of our diet has changed considerably which helps increasing the incidence to a great extent of many different diseases such as diabetes mellitus. Trace elements from part of daily diets, which are well known to play vitally important roles in the

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maintenance of health. Although there have been numerous reports yielded inconsistent results (Pidduck *et al*. 1970, Schlienger *et al*. 1988, McNair *et al.* 1981, Klinlaw *et al*. 1983 and Matew *et al.* 1975). Reports show that some trace elements such as Cr, Mg, Va, Zn, Mn, Mo and Se play important role in insulin action (Candilish 2000) including activation of insulin receptor, serving as cofactor or components for enzyme systems involved in glucose metabolism (Murray *et al*. 2000), increasing insulin sensitivity and acting as antioxidant preventing tissue per oxidation (Kruse-Jarres 2000, Bceys 2007, Mueller 2006, Akinloye *et al*. 2010). According to the above information, it is important to determine the essential element concentrations in biological samples of diabetes mellitus patients and to investigate its relationship with lipid profile. Present study was undertaken to estimate the serum levels of Zn, Cu, mg and Mn in diabetic patients and their association with lipid profile.

MATERIALS AND METHODS

The study of population was divided into two groups (Gr-I and Gr-II). Group II consisted of diabetic patients attending BIRDEM and non-diabetic individuals as control in Gr-I. The non-diabetic individuals were selected from the outdoor and indoor workers of BIRDEM.

After an overnight fasting (from 8 p.m. to 8 a.m.) 10 ml blood was drawn from the capital vein of each participant using sterile disposable plastic syringe. The sample left to clot and the serum was separated by centrifugation.

Level of the selected metals was estimated by atomic absorption spectrophotometer. The principle was based on dissociation of the element from its chemical bond, then placed in unexcited state (neutral atom), which can absorb radiation corresponding to its own line spectrum. The amount of radiant energy absorbed is proportional to its concentration.

Individuals who were 30 to 70 years old of both sexes were selected and divided into two groups. The controls formed Group-1 and patients who had diabetes for more than 5 years were considered as Group-II, who are not taking any kind of trace element supplements. A sample with hemolysis and jaundice was excluded. Exclusion criteria: (i) patients who are currently taking nutritional supplementations, mg containing laxatives, alcohol and diuretics, (ii) pregnant women and lactating mother, (iii) type-1 DM, (iv) subjects who have acute complication such as severe infections, major trauma, (v) patients with diabetic ketoacidosis and (vi) age below 30 and over 70 years.

The principle of determination of total serum cholesterol (TC), triglyceride (TG) and high density lipoprotein (HDL) was based on the enzymatic hydrolysis using a readymade laboratory kits; whereas serum low density lipoprotein (LDL) was calculated mathematically from the TG and HDL-cholesterol concentration (Fiancis *et al*. 2001).

Data were analyzed by using SPSS program and results were expressed in means and standard error and means were compared by two-tailed unpaired t test. Pearson's correlation coefficient (r) was calculated to determine associations between parameters. $p < 0.05$ was considered significant.

RESULTS AND DISCUSSION

Diabetic patients (Gr-II) had mean age (48 ± 10.44) years, while the mean age of non-diabetic control (Gr-I) was (42 ± 9.37) years. The BMI, Hip circumference, waist circumference and waist hip ratio were significantly higher in type-2 DM (Gr-II) than the control (Gr-I) and were (25.04 ± 3.29, 101 ± 7.94, 94 ± 8.52 .924 ± .033), respectively and p < .05, < .001, <.001 and < .001, respectively. Tables-1 and 2 show that TAG, cholesterol, LDL-C, HBA1C are significantly higher in type 2 DM (Gr-II) than control (Gr-I) and the p < .001 and serum Zn, Cu, Mg and Mn level were significantly lower in type-2 DM (Gr-II) than in control (Gr-I) and p value was <.001, <.001, <.001 and <.01, respectively. Tables 3, 4, 5, 6 show a significant correlations between serum Zn and TAG of type-2 DM(Gr-II) (r = 0.209) and serum Zn and HDL-C of type 2 DM (Gr-11) (r = 0.199) where p < .05 and non-significant relationships in between Zn and lipid profile (TAG, cholesterol, HDL-C and LDL-C) of control (Gr-I) group.

Table 1. Descriptive physical characteristics of diabetic patients (Gr-II) and controls (Gr-I).

Characteristics	Type-2 DM(Gr-II)	Non-diabetic controls (Gr-I)	p value
Age (years)	48 ± 10.44	42 ± 9.37	< .001
Height (cm)	158 ± 11.77	163 ± 7.7	< .001
Weight (kg)	62 ± 9.004	65 ± 7.7	< .01
B.M.I (Ht/m^2)	25.04 ± 3.29	25 ± 2.71	< .05
Hip (cm)	101 ± 7.94	96 ± 8.26	< .001
Waist (cm)	94 ± 8.52	86 ± 8.22	< .001
W : H	0.924 ± .033	0.881 ± .04	< .001

Significant correlation was found between serum magnesium and TAG of control (G-1) where p was < .01 and non-significant correlations were found in serum Mg and TC, HDL-C, LDL-C of both type-2 diabetic (Gr-II) and control (Gr-I). There were significant correlations in between serum Cu and Mn and TAG of control (Gr- I) where p was < .05 and non-significant correlations were found in other components of lipid profile of both cases (Gr-II) and control (Gr-I).

Table 2. Descriptive chemical characteristics of diabetic patients (Gr-II) and controls (Gr-I).

Biochemical characteristics	Type-2 DM (Gr-II) mean ± SE	Non-diabetic controls(Gr-I) mean ± SE	p value
TAG	226 ± 124.16	138 ± 89.23	< .001
Cholesterol	192 ± 42.11	165 ± 33.06	< .001
LDL-C	113 ± 34.52	95 ± 30.05	< .001
HDL-C	37 ± 5.49	41 ± 9.003	< .001
HBA1C	8.41 ± 1.62	5 ± .330	< .001
Zn	0.941 ± .246	1.21 ± .105	< .001
Cu	0.771 ± .483	1.142 ± .239	< .001
Mg	14 ± 3.613	18 ± 1.72	< .001
Mn	0.091 ± .049	0.106 ± .030	< .01

Table 3. Correlation of serum Zn concentration with lipid parameters in type-2 DM (Gr-II) and controls (Gr-I).

Lipid profile	Serum Zn in type-2 DM (Gr-II) (r value)	p value	Serum Zn concentration in controls (Gr-I) (r value)	p value
TAG	r = .209	<.05	r = .026	Ns
Cholesterol	r = .148	Ns	r = .087	Ns
HDL-C	r = .199	<.05	r = .038	Ns
LDL-C	r = .004	Ns	r = .132	Ns

Ns = Non significant.

Table 4. Correlation of serum Mg concentration with lipid profile parameters in type-2 DM (Gr-II) and controls (Gr-I).

Lipid profile	Serum Mg of type-2 DM (Gr-II) (r valu)	p value	Serum Mg of Control (Gr-I)	p value
TAG	r = –.023	Ns	r = .260	<.01
Cholesterol	r = –.130	Ns	r = .182	Ns
HDL-C	r = –.151	Ns	r = –.180	Ns
LDL-C	r = –.076	Ns	r = .117	Ns

Table 5. Correlation of serum Cu concentration with lipid profile parameters in type-2 DM (Gr-II) and controls (Gr-I).

Lipid profile	Serum Cu of type-2 DM (G11) (r value)	p value	Serum Cu of Control (G1)	p value
TAG	r = .049	Ns	r = .232	<.05
Cholesterol	r = .086	Ns	r = .011	Ns
HDL-C	r = –.051	Ns	r = .060	Ns
LDL-C	r = .129	Ns	r = –.129	Ns

Table 6. Correlation of serum Mn concentration with lipid profile parameters in type-2 DM (Gr-II) and controls (Gr-I).

Lipid profile	Serum Mn of type-2 DM (Gr-II) (r value)	p value	Serum Mn of control (Gr-I)	p value
TAG	r = .090	Ns	r = .191	<.05
Cholesterol	r = .167	Ns	r = .228	Ns
HDL-C	r = –.148	Ns	r = .120	Ns
LDL-C	r = –.082	Ns	r = .045	Ns

In diabetes mellitus, the disturbed concentrations of Zn, Cr and Mg in the body are often found (Mueller and Pallauf 2006). Some trace elements act as antioxidants and prevent membrane per oxidation while others act directly on glucose metabolism (Akinloye *et al.* 2010). In the present study, diabetic subjects showed an elevated fasting plasma glucose level as compared to healthy controls, which is the hallmark of diabetes and in this study were found to have lower levels of Zn in serum as compared with healthy controls, this finding confirms results are in conformity Fiancis *et al.* (2001). Diabetes has become an international health care crisis that required new approaches to prevention and treatment. Diabetes management should begin with exercise and diet (Chalmers 2005) and dietary modification the simplest and cheapest form of diabetes treatment is the primary therapy in type-2 diabetes (Muula 2000). Diabetes has been shown to be associated with abnormalities in the metabolism of Cu, Zn, Fe, Se and the impairment of these metals had been reported as aggravating factors in the progression of disease. Zinc and insulin concentration in the pancreas change in the same direction in a variety of situations in humans (Diwan *et al.* 2006), it is useful in synthesis, storage, and secretion of insulin (Retnam and Bhandarkar 1981). The present results showed that the level of zinc decrease in the serum of diabetic patients (Table 2). The loss of these minerals might be attributed to impaired absorption or to the excess excretion of these metals in urine in these patients, which may include a deficiency of these metals in serum of diabetic patients and that is consistent with the works of (Kazi and Afridi 2008). Clinical studies of type-2 diabetes have shown alterations in copper metabolism in this disease (Ito *et al.* 2001). The present results showed a decrease in serum copper level in diabetic individuals which is consistent with the findings of Smith *et al.* (1988), Ito (2001) and Babalola *et al.* (2007). It is not yet known, whether that abnormalities in copper metabolism noted in these subjects are a consequence of the disease or they play a role in the progression of the disease. Magnesium (Mg) is the fourth most abundant in the body and second in the intracellular environment. It takes part in more than 300 enzymatic reactions (Bowen 1967, Mertz 1981). Deficiency of Mg has been associated with the variety of clinical conditions; including type-2 DM. Mg depletion has a negative impact on glucose homeostasis and insulin sensitivity in patients with type-2 diabetes (Muula 2000) as well as on the evolution of complications such as retinopathy, thrombosis and hypertension. Moreover, low serum Mg is a strong independent predictor of the development of type-2 diabetes (Retnam and Bhandarker 1981). Recent studies have also indicated that Mg deficiency may be associated with increased oxidative and nitrosamine stress through reduction in antioxidants and increased lipid per oxidation. The mean serum Mg in diabetics was significantly lower than controls and this agreed with the study of Fujii (1994). Present study demonstrated negative correlations of plasma glucose with serum Zn, Cu and Mg levels in diabetics compared to controls (Table 2), moreover the altered Zn, Cr and Mg levels were related to the degree of glycemic control. The inverse correlations between plasma glucose and the trace elements (Zn, Cu and Mg), suggest that Zn, Cu and Mg may deteriorate due to abnormal metabolic process in diabetes (Diwan *et al.* 2006). The serum Mn level of diabetic subjects in the current work was significantly ($p < 0.01$) different from the value obtained for the control subjects. The percentage of diabetic subjects with Mn deficiency was, however lower compared to the subjects with Cr deficiency. Mn has been shown to be important in insulin synthesis and secretion (Kazi and Afridi 2008, Ito *et al.* 2001). It has been shown that type-2 diabetic subjects responded well to oral doses of Mn (Smith *et al.* 1988). Mn is a cofactor of many enzymes including mitochondrial SOD (Babalaq *et al.* 2007). Mn-activated enzymes play important roles in the metabolism of carbohydrates, amino acids, and cholesterol (Thompson 2004). There are conflicting reports of Mn deficiency in DM (Bleys *et al.* 2007). Diabetic patients with the higher blood levels of Mn were reported to be better protected from oxidation of LDL cholesterol. LDL oxidation contributes to the development of intra-arterial plaque, which can lead to heart attack and stroke (Rajpathak *et al.* 2005).

CONCLUSION

The type-2 DM patients should receive long term micronutrients (Zn, Cu, Mg and Mn) supplementation to avoid micronutrient deficiency related complications.

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