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Research Article

Serum Chromium, Molybdenum, Zinc and Magnesium Levels in Diabetes Mellitus Patients in Sagamu, South West Nigeria

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Abstract: Emerging evidence suggests that the metabolism of several trace elements is altered in diabetes mellitus and that these metals might have specific roles in the pathogenesis and progress of this disease because of their diverse metabolic characteristics and functions. The aim of the present study was to investigate the relationship between diabetes mellitus and the plasma level of essential trace elements, Chromium (Cr), Magnesium (Mg), molybdenum (Mo) and zinc (Zn) in type 2 diabetes mellitus patients. A total of 148 subjects consisting of 98 type 2 diabetes mellitus patients and 50 non-diabetic control subjects were recruited. The element concentrations were measured by means of an atomic absorption spectrophotometer after wet-acid digestion. Results reveal that diabetic status is associated with alterations of levels of analyzed trace metals. Significant ($p<0.001$) elevation of plasma glucose was associated with marked decreases in chromium ($p<0.01$) and zinc ($p<0.05$) with significant ($p<0.001$) increases in magnesium and molybdenum ($p<0.001$) levels when compared with the control. Prevalence of reduced levels of Zn was 65.34, Mg 18.22, Mo 12.87 and Cr 79.2% in diabetes patients compared with Zn 22.36, Mg 16.78, Mo 11.83 and Cr 22.00% respectively in the control subjects. The plasma level of glucose was negatively correlated with the levels of Zn, Cr, Mo and Mg of diabetic subjects. A positive correlation between zinc ($r = 0.65$, $p<0.01$), molybdenum ($r = 0.57$, $p<0.01$) and magnesium as well as between zinc and chromium ($r = 0.53$, $p<0.01$) was observed in diabetic patients. Overall, deficiency of both chromium and zinc co-exist in the diabetes mellitus patients studied and was associated with marked raised molybdenum with slightly raised magnesium.

Keywords: Deficiency, diabetes mellitus, prevalence, trace elements

INTRODUCTION

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both (Odewabi *et al*., 2013). Type 2 diabetes mellitus (T2DM) begins with insulin resistance followed by reduced insulin production as the disease progresses and makes up 90-95% of all diagnosed cases. Type 2 diabetes is associated with older age and obesity. A small percentage of diabetes (1-5%) occurs during pregnancy (gestational diabetes), following corticosteroid and other drug use, or following surgery or illness, (Leigh and Philip, 2006). The chronic hyperglycemia of diabetes if poorly controlled is associated with long-term damage, dysfunction and failure of various organs, especially the eyes, kidney, nerves, heart and blood vessels (American Diabetes Association, 2008).

Diabetes mellitus is a free radical associated disease with an increased flux of reactive oxygen species in the extracellular space and an alteration in the cellular redox system that results in a loss of reducing capacity, with repercussions on antioxidant defence system which includes antioxidant enzymes, vitamins and minerals (Zargar *et al*., 2002). Emerging evidence suggests that the homeostasis of trace elements may be disrupted by diabetes mellitus (Zargar *et al*., 2002). Deficiency of trace metals may thus contribute to the susceptibility to the disease and to the development of severe mineral deficiencies in established diabetes (Adewumi *et al*., 2007).

Mineral deficiencies have been reported to play a major role in the quality of person's health. Trace metals are essential micronutrients that are very important in the metabolic activities. Some trace metals are used as metalloenzymes (e.g., Zn, Fe, Cu and Mn) for the synthesis of hormones (e.g., iodine) and as modulators in enzyme activities (e.g., Cr in insulin actions) (Aspin and Sass-Kortsak, 1981). Cu, Zn and Mn are important co-factors in the antioxidative activities of superoxide dismutase (Preedy *et al*., 1998).

Over the past few decades, the potential alteration of trace metals in diabetes mellitus have been the subject of a vast body of research in both the developed and developing countries of the world. However, results in these study have been inconsistent and contradictory

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(Mumayun *et al*., 2011; Tripathy *et al*., 2004; Adewumi *et al*., 2007; Chinyere *et al*., 2005; Akhuemokhan *et al*., 2010). The differences in these reports have been attributed to study sample size, gender and analytical procedures employed. In this study, we monitored some important serum trace metals in diabetes mellitus and compared the results with apparently healthy age-and sex-matched controls that had similar socioeconomic status in Sagamu, South- West of Nigeria.

MATERIALS AND METHODS

Subjects: A total of 148 subjects comprising of 98 diabetes patients (64 females and 34 males) and 50 control subjects. Patients were recruited from the Diabetic Clinic while controls were apparently healthy non-diabetic subjects of similar socio-economic status on routine medical check-ups in the out-patients department of the Olabisi Onabanjo University Teaching Hospital, Sagamu. To ensure that individuals with underlying conditions which may influence results of the present study were not recruited, exclusion criteria were set, amongst others, to include presence of conditions (such as asthma, hypertension, malaria) with underlying oxidative stress and the use of trace metal supplement which interfere with may influence trace metals levels. The medical ethics committee of Olabisi Onabanjo University Teaching Hospital (OOUTH)/ Obafemi Awolowo College of Health Sciences (OACHS) of the Olabisi Onabanjo University approved the study (ethical approval number OOUTH/ DA.326/T/1) and participants gave informed written consent in accordance with Helsinki Declaration of 1964 as amended in 1983 (World Medical Organization, 1996). Ten (10) mL of blood sample were collected from the ante-cubital vein of subjects into 5 mL plain specimen bottles and 5 mL fluoride-oxalate bottles after 12-14 h overnight fast for analysis.

Biochemical parameters' measurements:
Determination of plasma glucose: Fasting Plasma Glucose (FPG) was determined according to the spectrophoto metric method described by Barham and Trinder (1972) using commercial kits obtained from Randox Laboratories Ltd (Crumlin, UK).

Determination of plasma levels of trace metals: Plasma levels of these elements were determined with flame Atomic Absorption Spectrophotometer (AAS) using a direct method as described by Kaneko (1999). The method is based on the principle that atoms of the element when aspirated into AAS vaporized and absorbed light of the same wavelength as that emitted by the element when in the excited state.

Statistical analysis: Results are presented as mean±standard deviation (SD). Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 16.0. Comparison between diabetes patients and control was performed using Student's t-test for unpaired data and Pearson's correlation coefficient. The statistical significance was set at $p<0.05$.

RESULTS

Biophysical characteristics: The biophysical data of diabetics and controls are presented in Table 1. Diababetic patients were older in age ($p>0.001$) with marked raised body mass index ($p<0.05$) than the control.

Trace metals and glucose in diabetic patients and controls: Table 2 shows the level of trace metals and glucose in diabetic patients and control subjects. Significant ($p<0.001$) elevation of glucose and molybdenum was associated with marked decreases in zinc ($p<0.01$) and chromium ($p<0.001$). No significant difference was observed in magnesium levels between diabetic patients and controls.

Prevalence of trace metals deficiencies in subjects: Table 3 depicts prevalence of deficiencies of trace metals in diabetics and control. Deficiencies of zinc

Table 1: Biophysical data of diabetic patients and control subjects

Variables	DM patients (n = 98)	Control (n = 50)	t- value	p-value
Age (years)	55.92±12.82*	42.06±7.31	7.039	0.000
Height (m)	1.61±0.07*	1.66±0.08	-3.416	0.001
Weight (kg)	70.94±13.35	70.34±14.94	0.240	0.811
BMI (kg/m^2)	27.36±3.63*	25.53±4.41	-2.401	0.002

Values are expressed as mean±standard deviation (SD); n = number of subjects; BMI = Body Mass Index; DM: Diabetes Mellitus; *: Significantly different from the control

Table 2: Levels of trace metals and glucose in diabetic patients and controls

Variables	DM patients (n = 98)	Control (n = 50)	t-value	p-value
Zn (mg/dL)	104.94±24.79*	115.76±12.66	-2.898	0.004
Mg (mg/dL)	13.51±1.34	13.56±1.62	-0.038	0.969
Mo (nmol/L)	54.35±7.93*	49.16±4.54	4.267	0.000
Cr (µg/dL)	59.24±5.74*	64.98±5.17	-2.959	0.000
Glu.(mmol/L)	7.79±4.23*	4.79±0.70	4.917	0.000

Values are expressed as mean±standard deviation (SD); n = number of subjects; DM: Diabetes Mellitus; Zn: zinc; Mg: Magnesium; Mo: molybdenum; Cr: chromium; Glu: glucose; *: Significantly different from the control

Table 3: Prevalence of trace metals deficiencies in subjects

		Percentage of subjects with deficiencies	
Parameters	Lower limit of reference interval**	Diabetic (%)	Control (%)
Zn (mg/dL)	103.10	65.34*	22.36
Mg (mg/dL)	11.94	18.22	16.78
Mo (nmol/L)	44.62	12.87	11.83
Cr (µg/dL)	59.81	79.20*	22.00

**: Serum levels of trace metals of apparently healthy non-diabetic subjects were used as reference range for the analyzed metals in the study area. Zn: zinc; Mg: magnesium; Mo: molybdenum; Cr: chromium; *: Significantly different from the control

Table 4: Coefficient of correlation between analyzed trace metals and glucose in diabetic patients (n = 98)

	Correlation coefficient (r)				
Parameter/Glucose	Glucose	Zn	Mg	Cr	Mo
Glucose	1.00	-0.136	-0.080	-0.15	-0.09
Zn	-0.136	1	0.651[a]	0.538[a]	0.042
Mg	-0.080	0.651[a]	1	-0.129	0.576[a]
Cr	-0.150	0.538[a]	-0.129	1	-0.122
Mo	-0.090	0.042	0.576[a]	-0.122	1

Coefficient of correlation (r): [b]p<0.05; [a]p<0.01; Zn: zinc; Mg: magnesium; Cr: chromium; Mo: molybdenum

and chromium were 65.34 and 79.20% in diabetics as against 22.36 and 22.00% for control respectively (p>0.05). While the prevalence of deficiencies of magnesium and molybdenum between diabetic and control subjects were comparable (p>0.05).

Correlation of glucose and some of the analyzed trace metals: Table 4 shows the degree of association between analyzed trace metals and glucose in diabetic patients. Magnesium (r = 0.651; p<0.01) and chromium (r = 0.538; p<0.01) exhibited significant positive correlation, respectively, with Zinc Glucose showed negative correlation with all trace metals. Furthermore, significant correlation between magnesium (r = 0.576; p<0.01) and molybdenum level was observed in diabetic patients but such correlation was not seen in control group.

DISCUSSION

Trace elements are uniquely required for growth and maintenance of life and health, deficiency of which may result in body functional impairment leading to disease. Trace metals are essential micronutrients that are very important in the metabolic activities, some of which acts as antioxidant and prevent lipid membrane peroxidation. Oxidative stress has been suggested as potential contributor to the development of diabetes mellitus and its subsequent complications which is probably due to low antioxidant status including trace elements.

Low level of chromium or its under-utilization has been linked with the causes of diabetes mellitus and glucose intolerance (Garry, 2001). Present study reports a significant decrease in serum chromium level when compared with control and this is in agreement with earlier studies (Adewumi *et al*., 2007; Esfahani *et al*., 2011). Chromium is an important cofactor that modulates the action of insulin (Akhuemokhan *et al*., 2010) and regulates blood glucose fluctuations; this may explain reason for an inverse relationship between chromium and blood glucose levels observed in this study.

In diabetic subjects, chromium metabolism is altered by inadequate intake, decreased absorption and increase loss, leading to abnormal blood, tissues and urine chromium levels (Cefalu *et al*., 2002). Current data strongly suggest that low levels of chromium in serum, hair and toe nail tissues are significantly correlated with diabetes. However, people with diabetes show high urine chromium levels which indicates that mobilized chromium was not reabsorbed by the kidneys (Mita *et al*., 2005). For these reasons, chromium supplementation has been recommended to provide significant clinical benefit in type 2 diabetes mellitus (Anderson, 2000), which has been documented to be essential in the maintenance of glucose metabolism (Anderson, 2000).

Magnesium is known to be related to the carbohydrate and fat metabolism. Serum magnesium levels have been shown to be inversely related to the severity of diabetes. Magnesium depletion has an atherogenic potential. Hypomagnesaemia has been postulated as a possible risk factor in the development and progression of diabetic retinopathy (Paolisso and Revussin, 1995). Magnesium is an essential ion involved in glucose homeostasis at multiple levels. A complex interplay exists between magnesium and glucose metabolism. Hypomagnesaemia has been reported in both type 1 and type 2 patients. Furthermore, magnesium plays an important role in the activities of various enzymes involved in glucose oxidation and may play a role in the release of insulin (Paolisso and Barbagallo, 1997). In the present study, no difference between mean value of magnesium in diabetes and control was observed. This is in contrast to the studies of Sjogren *et al*. (1988), Fujii *et al*. (1982), De-Valk (1992), Resnick *et al*. (1993), Schnack *et al*. (1992) and McNair (1978) who reported reduced serum magnesium levels in their diabetic patients. Serum Mg levels may not accurately reflect the level of total body Mg stores, persistent glycosuria with osmotic diuresis leads to Mg wasting and contributes to high frequency of hypomagnesemia in poorly controlled diabetes (Mumayun *et al*., 2011). The present study demonstrated negative correlation of serum glucose

with Mg levels in diabetic patients. Similar associations between serum glucose and serum Mg have been reported by different authors (Tripathy *et al.*, 2014).

Studies on trace metals are complicated due to their multi-functional role. Zinc is required in several enzymes and so its deficiency is likely to affect a number of different systems (Dardenne, 2002). Significantly low serum level of zinc was obtained in the present study. Alteration of zinc homeostasis in diabetes is supported by a large body of experimental and clinical evidence (Akhuemokhan *et al*., 2010; Esfahani *et al*., 2011). Tripathy *et al.* (2004) demonstrated the decrease level of zinc in type 2 diabetes subjects; which was consistent with our findings in this study whereas Zargar *et al.* (1998) reported no difference in level of zinc between their diabetic patients and the control subjects. It has been postulated that low level of zinc in diabetic patients may be due to excessive urinary output especially in patients with diabetic nephropathy and gastro intestinal malabsorption (Esfahani *et al.*, 2011). High urinary excretion of Zn in diabetic patients may be a result of hyperglycemia rather than any specific effect of endogenous or exogenous insulin on the renal tubules. Hyperglycemia has been postulated to interfere with the active transport of Zn back into the tubular cells (Esfahani *et al*., 2011). Zn and insulin concentrations in the pancreas change concomitantly in a variety of physiological and pathological changes in humans (Akhuemokhan *et al*., 2010). Zn is required for the synthesis, storage and secretion of insulin (Ekmekcioglu *et al*., 2001).

Akhuemokhan *et al.* (2010) reported that zinc may improve glycemia and a restored zinc status in diabetics may counteract the deleterious effects of oxidative stress, thus preventing complications associated with diabetes (Esfahani *et al*., 2011). In the present study a negative correlation was observed between zinc and glucose level. This is in consonance with the report of Esfahani *et al.* (2011) who found a significant negative correlation between zinc and glycemic control in their study.

Molybdenum (Mo), plays an important role in insulin action, including activation of insulin receptor sites (Esfahani *et al*., 2011), serving as cofactors or components for enzyme systems involved in glucose metabolism (Murry *et al*., 2000), increasing insulin sensitivity and acting as antioxidants preventing tissue peroxidation (Ankush *et al*., 2009). Present study reports a significant increase in serum molybdenum level when compared with control. Much human studies have been conducted on molybdenum concentration in diabetes mellitus, molybdenum has been reported to lower hyperglycemia, glycosuria and corrected the elevation of plasma non esterified fatty acids in Streptozotocin diabetic rats (Ozcelikay *et al*., 1996). The increase in molybdenum level observed may be related to these functions in diabetes patients.

In spite of the observed biochemical changes described above, BMI, which is the most commonly used indicator to determine general nutritional status and known to positively correlate with certain health and longevity indicators, (Calle *et al*., 1999; Keller and Ostbye, 2005) was within the normal range for both diabetes patients and control.

CONCLUSION

In conclusion, the results of the present study suggest that deficiencies in chromium and zinc co-exist in diabetic patients studied with slightly raised magnesium level while there is a marked increased in concentration of molybdenum.

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