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Serum Chromium, Copper and Manganese Levels of Diabetic Subjects in Katsina, Nigeria

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Abstract: In this study serum copper, chromium and manganese were estimated in 90 diabetic patients attending the outpatient clinic of the Federal Medical Centre, Katsina, an ancient city in North-western Nigeria and the results compared to those of apparently healthy, non-diabetic volunteers of comparable age and social status. Serum glucose level of the diabetic subjects (13.91±2.87 mmol L^{-1}) was significantly ($p<0.05$) higher that the value obtained for the non-diabetic subjects (4.34±0.11 mmol L^{-1}). The serum levels of Cr (0.19±0.05 μg L^{-1}), Cu (0.42±0.18 μg L^{-1}) and Mn ((1.12±0.24 μg L^{-1}) were significantly ($p<0.05$) lowered in diabetic subjects. About 75% of the diabetic subjects in the study area had deficient serum levels of these metals. These results suggest that the diabetic patients in the study area have low serum levels of some antioxidant mineral elements. These observations may be an indication that the diabetic subjects are predisposed to increased oxidative onslaught.

Key words: Diabetes mellitus, serum, chromium, copper, manganese, Nigerians

INTRODUCTION

Diabetes Mellitus is a chronic metabolic disorder affecting carbohydrate, lipid and protein metabolism. It is a heterogeneous group of disorder characterized by hyperglycaemia due to impaired glucose utilization, resulting from defects in insulin secretion, insulin action, or both (Reaven, 1988). It is a multi system disease that is widespread throughout the world, affecting carbohydrate, protein and lipid metabolisms. Along with hyperglycaemia and abnormalities in serum lipids, diabetes is associated with micro vascular and macro vascular complications, which are the major causes of morbidity and death in diabetic subjects (WHO, 1994; Edemeka *et al*., 1999).

The prevalence varies greatly between communities. The global estimate of people living with diabetes mellitus as at 2000 is 2.8% this is expected to reach 4.4% by 2030 (Sarah *et al*., 2004). In African communities, the prevalence is increasing with ageing of the population and life style changes associated with urbanization (Sobngwi *et al*., 2001). It is known to affect 3%, on the average, of adult Nigerians (Akinkugbe *et al*., 1992). The prevalence of diabetes in suburban population of Northern Nigeria is 1.6% (Bakari *et al*., 1999).The prevalence of diabetes in Nigeria is increasing with increasing ageing of the population and life style changes associate with rapid urbanization. Mineral deficiencies and imbalances play major role in the quality of person's health.

Diabetes is a free radical associated disease. Investigations carried out in diabetic patients revealed oxidative stress load (Packer *et al*., 2000). Oxidative destruction of sub cellular membrane lipids has been implicated along with other types of intracellular oxidative damage in the normal aging process and in pathophysiology of a number of chronic illnesses. Complex antioxidant mechanism, including antioxidant vitamins and minerals exists to limit the effects of these reactions (Packer, 2002).

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Diabetes mellitus being a degenerative disease, therefore, may be initiated as a result of peroxidation caused by free radicals. Some trace metals such as manganese, chromium, copper and vanadium possess antioxidant properties. Deficiency of these metal may thus increase susceptibility to the disease. The development of diabetic late complications (cataract, retinopathy, nephropathy and neuropathy) is associated with an increased presence of free radicals and therefore elevated oxidative stress of the human body (Packer *et al*., 2000). Thus diabetics elicit a higher rate of blindness, kidney disease, gangrene and coronary heart disease several times more than non-diabetics.

In this study serum Cr, Cu and Mn were estimated in diabetic subjects and the results compared with those of apparently health non-diabetic subjects of comparable socio-economic status.

MATERIALS AND METHODS

Subjects

The subjects employed for this study were 90 diabetic patients of both sexes who were attending the medical Outpatient clinic of the Federal Medical Center, Katsina, Northwestern Nigeria between the months of February 2004 to June 2005. Thirty one percent of the subjects were male. Information on the age, weight, height and nature of occupation of the subjects was obtained. Ninety apparently healthy non-diabetic subjects of similar socioeconomic status, who were on routine medical checkups in the hospital were recruited to serve as control. The consents of all the subjects were sort and obtained. Ethical Committee approval was also obtained for the research.

Blood Samples

Fasting blood samples were collected into labeled centrifuge tubes, after an 8-12 h overnight fast, from the subjects by veno-puncture. The blood samples were centrifuged at 2000 rpm for 10 min using a desktop centrifuge and the serum separated and kept in labeled sample bottles at 20°C until required.

Reagents

Glucose oxidase assay kits were obtained from Randox Laboratories Switzerland. All other chemicals and reagents were of analytical grade and purchased from Sigma Chemical Company USA.

Analytical Methods

Serum glucose was estimated using the glucose oxidase method of Trinder (1964) within few hours of sample collection. Serum levels of Cr, Cu and Mn were estimated within 72 h using UNICAM 969 Atomic Absorption Spectrophotometer.

Statistical Analysis

Results are presented as mean±standard deviation and separated on the basis of gender. Significance differences in mean, at 5% level were determined using student t-test. Serum levels of the trace antioxidant elements were correlated with the serum glucose levels of both the diabetic and control subjects and correlation coefficients determined.

RESULTS

The diabetic patients were generally heavier than the control subjects (Table 1). The result of the Body Mass Index (BMI) indicated that the diabetic subjects were over weight. There was a significant difference ($p<0.05$) between serum glucose level of the diabetics and non-diabetics. When separated on the basis of gender, the results showed no significant difference ($p>0.05$). Serum levels of Cr, Cu and Mn were significantly higher ($p<0.05$) in normal than in the diabetic subjects.

Table 1: Serum levels of Cr, Cu and Mn of the diabetic and apparently healthy non-diabetic control subjects of the subjects

	Control			Diabetics		
Parameters	Male	Female	Total	Male	Female	Total
N	50	40	90	28	62	90
Age of subjects (years)	47.54±11.3	43.29±10.7	45.37±9.7	45.12±13.3	44.65±11.4	44.63±8.9
Duration of the disease (years)	-	-	-	5.23±3.21	4.22±2.76	4.76±2.83
BMI (kg m^{-2})*	23.54±1.13	25.34±0.93	24.24±1.43	29.79±1.58[a]	28.77±1.72[a]	29.24±2.34[a]
Fasting blood glucose (mmol L^{-1})*	4.40±0.09	4.26±0.07	4.34±0.11	13.39±2.88[a]	14.15±2.85[a]	13.91±2.87[a]
Chromium (μg L^{-1})*	0.36±0.13	0.44±0.10	0.40±0.12	0.13±0.03[a]	0.21±0.04[a]	0.19±0.05[a]
Copper (μg L^{-1})*	1.10±0.14	0.99±0.10	1.05±0.13	0.40±0.23[a]	0.43±0.15[a]	0.42±0.18[a]
Manganese (μg L^{-1})*	1.33±0.20	1.38±0.26	1.35±0.23	1.14±0.20[a]	1.14±0.21[a]	1.12±0.24[a]

* Values bearing asterisk differ significantly ($p<0.05$) using ANOVA, [a]Values differ significantly from the respective contol

Table 2: Prevalence of trace mineral element deficiencies in diabetic subjects

		Percentage of subjects with deficiencies		
Parameters	Normal range* (μg L^{-1})	Male	Female	Total**
Chromium	0.22-0.75	100.00	30.64	52.22
Copper	0.85-1.33	100.00	100.00	100.00
Manganese	0.91-1.75	25.00	6.45	12.22

* Serum levels of trace mineral elements for apparently healthy non-diabetic subjects were used to for deciding the normal range for these metals in the study area, ** Total is the pooled values for both the male and female subjects

Table 3: Correlation coefficients (r) of serum glucose with serum Cr, Cu and Mn of diabetic subjects

	Diabetics*		
Independent variable	Male	Female	Total
Cr	-0.98	-0.96	-0.61
Cu	-0.97	-0.83	-0.92
Mn	-0.91	-0.82	-0.88

*All the serum mineral elements assayed showed significant ($P<0.05$) negative correlation with serum glucose level of the diabetic subject of the study area

Values obtained for the control subjects, who were apparently healthy subjects of comparable social background, economic status and age were used as the reference range (Table 2). The reference range was obtained by taking the values between the lowest and highest of the control subjects.

Table 3 indicated significant ($p<0.05$) negative correlation coefficients between serum glucose and the mineral elements.

DISCUSSION

The significance of trace elements in normal growth, development and overall body metabolism cannot be overemphasized. There is, however an accumulating evidence that the metabolism of several trace elements is altered in diabetes mellitus (Tuvemo and Gebre-Medhin, 1983; Prasad, 1998). Some of these trace elements act as antioxidants and prevent membrane peroxidation. The beta cells of the pancreas, the cells that produce insulin, are sensitive to oxidative stress. This is due largely to the fact that their intracellular antioxidant defence mechanisms are weak compared to those of such tissues as the liver (Rasilainens *et al*., 2002). Oxidative stress is thus, suggested to be a potential contributor to the development of diabetes mellitus and the associated complications (Mohamad *et al*., 2004). This may not be unconnected to the fact that the antioxidant status including antioxidant mineral elements may be inadequate in diabetic subjects. The metabolic significance of the evaluation of antioxidants in diabetics is therefore of paramount importance. In addition to the antioxidant roles of some of these mineral elements, they may act directly on glucose metabolism.

The results of the current work indicated that serum Cr of the diabetic patients in the study area were significantly ($p<0.05$) lower than the values obtained for the normal subjects. The results further

revealed that male diabetic subjects had lower serum Cr compared to their female counterparts. Almost all the diabetic subjects showed Cr deficiency. The implication of this finding cannot be overemphasized. Chromium has been reported to increase insulin binding to cells, number of insulin receptors and activates insulin receptor kinase leading to increase in insulin sensitivity (Anderson, 2000). Trivalent Cr acts as a cofactor for insulin and is an integral part of the cellular response to this hormone (Finney and Gonzalez-Compoy, 1997). Accordingly severe chromium deficiency was implicated to cause impaired glucose tolerance and subsequent hyperglycaemia and glucosuria (Anderson, 2000). Baker and Campbell (1992) also reported an association between chromium deficiency on hand and hyperinsulinaemia, diabetic neuropathies or vascular pathologies on the other. Cr, which is a component of glucose tolerance factor (Murray, 1996), is also known to inhibit tyrosine phosphatase, an enzyme responsible for the termination of insulin receptor response (Anderson, 1998). Cr was reported to raise plasma HDL cholesterol and HDL:LDL ratio (Tuvemo and Gebre-Medhin, 1983).

Diabetic subjects of the study area also showed significant serum copper deficiency. The serum level of Cu in the diabetic subjects, in the current work, was significantly ($p<0.05$) lower than that of non-diabetic subjects. The results are not affected by sex difference. Cu is an essential trace element involved in the metabolism of several key enzymes including cytochrome oxidase of the mitochondrial electron transport and cytosolic superoxide dismutase (Murray, 1996). Reactive Oxygen Species (ROS) such as H_2O_2, superoxide and hydroxyl radicals are the most important source of oxidative stress and mutagenic alterations in DNA. Cells are endowed with an elaborate defence system to destroy these species, including enzymes such as catalase and superoxide dismutase (Nelson and Cox, 2000). El-Yazigi *et al.* (1991) reported significantly higher urinary excretion of Cu by diabetics with neuropathy or infection than by those without.

Serum manganese (Mn) level of diabetic subjects in the current work was significantly ($p<0.05$) different from the value obtained for the control subjects. The percentage of the diabetic subjects with Mn deficiency was however lower compare to the subjects with Cr or Cu deficiencies. Mn has been shown to be important in insulin synthesis and secretion (Korc, 1983). It has been shown that type 2 diabetic subjects responded well to oral doses of Mn (Rubeenstein *et al*., 1962). Mn is a cofactor of many enzymes including mitochondrial superoxide dismutase (Murray *et al*., 1996). Manganese-activated enzymes play important roles in the metabolism of carbohydrates, amino acids and cholesterol (Nicollof *et al*., 2004). There are conflicting reports of Mn deficiency in diabetes mellitus (El-Yazigi *et al*., 1991). Diabetics with 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 (Leonhardt *et al*., 1996). Diabetics with liver diseases have been reported to excrete more Mn than those without liver problems (El-Yazigi *et al*., 1991).

Generally these mineral elements have reported to be excreted at higher than normal rates in patients with diabetes mellitus (El-Yazigi *et al*., 1991). This may not be unconnected to the hyperglycaemia-mediated polyuria in the patients. Consequently there is a decrease in the plasma levels of the elements in these subjects. This may predispose the subjects to further oxidative onslaught and decrease glucose tolerance leading ultimately to the development of late complications of diabetes mellitus. It may therefore be pertinent to suggest the evaluation of inclusion of dietary supplementation of these mineral elements in the management of diabetes mellitus.

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