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Full Length Research Paper

A study of the interactive roles of lead and other selected mineral elements in type-2 diabetes mellitus

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The study investigated the status of lead and selected mineral elements (copper, zinc and chromium) in type-2 diabetes mellitus patients, so as to establish the possible interactive connections of these metals with the disease and with each other in diabetic patients. Thirty-one patients (15 male and 16 female), clinically diagnosed for type-2 Diabetes mellitus at Sacred Heart Hospital, Abeokuta, Nigeria, participated in the study. Twenty-six apparently healthy individuals (14 male and 12 female) served as control group. Blood samples of all the subjects were collected after an overnight fasting for the determination of blood glucose, lead, zinc, copper and chromium. Fasting blood sugar (FBS) was determined by glucose oxidase-peroxidase assay to confirm the status of the patients and the controls while metals' concentrations were measured with Atomic Absorption Spectrometer (AAS). The mean FBS concentrations of the diabetic group were significantly higher ($p<0.05$, $p<0.05$ respectively) than those of the control group. Similarly, the mean blood lead levels of the diabetic male and female patients were 49.40 ± 14.36 and 46.30 ± 15.22 µg/dL respectively and significantly higher ($p<0.05$, $p<0.05$respectivelly) than those of control males and females (38.07 ± 14.00 and 35.51 ± 13.00 µg/dL respectively). Additionally, a positive relationship was observed between the concentrations of FBS and lead ($r = 0.393$; $p<0.01$). These findings in this study revealed that lead has an interactive connection with type 2 diabetes mellitus while zinc, copper and chromium have no such significant relationships with the disease.

Key words: Diabetes mellitus, lead, fasting blood sugar, trace elements.

INTRODUCTION

Type-2 diabetes mellitus results from a defect in insulin secretion and an impairment of insulin action in hepatic and peripheral tissues, especially muscle tissue and adipocytes. A post-receptor defect also is present, causing resistance to the stimulatory effect of insulin on glucose use to occur, and relative insulin deficiency develops. The specific etiologic factors are not known, but genetic input is much stronger in type-2 than in type-1 (Olatunbosun, 2004). However, type-2 diabetes mellitus is also reported to be caused by obesity and sedentary life-style (Parott, 1999)

Diabetes can lead to heart disease, nerve damage, and kidney disease and vision loss. Neuropathy affects about 60 - 70% of diabetics after 10 - 15 years while retinopathy affects 80 - 97% of diabetic patients after 15 years. It is estimated that 15% of diabetes will develop a foot ulcer at some time resulting in approximately 60,000 amputations a year (Parrott, 1999). Diabetes mellitus is also an important factor in accelerating the hardening and narrowing of the arteries atherosclerosis, leading to strokes, coronary heart diseases, and other blood vessel diseases (Rocha et al., 1997; Weber, 2004). Diabetes is indeed a killer disease and there is increased incidence of this disease in this environment.

Chromium has been shown to improve glucose and related variables in people with glucose intolerance and type-1, type-2, gestational, and steroid-induced diabetes (Anderson, 2000). Research has also indicated that chromium-rich brewer's yeast (9 g per day) can be useful in treating diabetes mellitus. (Offenbacher and Pi-Sunyer, 1980). Improved glucose tolerance with lower or similar levels of insulin has been reported in more than ten trials of chromium supplementation in people with varying degrees of glucose intolerance (Anderson, 1998).

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Chromium supplements improve glucose tolerance in people with type-2 (Evans, 1989).

Rao et al. (1987) observed that zinc has an insulin-like effect on the manifestation of diabetes. Zinc supplements have lowered blood sugar levels in people with type-1 diabetes (Rao et al., 1987) though some evidence indicates that zinc supplementation in people with type-2 diabetes does not improve their ability to process sugar (Niewoehner et al., 1986).

It was also reported that *co*pper depletion doubled glucose in blood of diabetic rats that were fed with glucose, and 50% higher for sucrose (Evans, 1989). They also reported that rat fed with copper -deficient diets have high blood sugar due to glycation of hemoglobin. Rocha et al. (1997) consequent concluded that both the early and advanced stages of protein glycation increased significantly in rats fed a copper -deficient diet.

Lead is a heavy metal that is dangerous to most of the human body's organs and systems and interferes with body metabolism and cellular functions. It produces damaging effects in the hematopoetical, hematic, renal, reproductive and gastro-intestinal systems (Fuentes-Aguilar and Soto-pural, 1993). Lead has been investigated in many pathological conditions and the level of this metal in this environment is of great concern.

The present study is aimed at determining the interactive roles of lead and other selected mineral elements (copper, zinc and chromium) in type-2 diabetes mellitus in this environment.

MATERIALS AND METHODS

Study site

The study was carried out in Abeokuta, Ogun State, Southwest Nigeria. The samples of diabetes patients were collected at Sacred Heart Hospital, Lantoro, Abeokuta. The control subjects were sourced outside the hospital environment.

Subjects

Thirty-one (31) diabetic patients (age: 35-70 years, 15 males, 16 females) who had been clinically diagnosed at least 6 months prior to this study participated voluntarily in the study. While twenty six (26) age matched apparently healthy subjects served as the controls

Anthropometric measurements

Height and weight of the subjects were measured with meter -rule and weighing scale respectively. The body–mass index (BMI) was calculated from Mass/ (Height) ^{2} and expressed in kg m^{-2}.

Sample collections

Venous blood samples (about 10 ml each) were collected from the antecubital vein of the subjects using sterile needles and syringes (Normject, Germany). About 8 ml of the collected blood was released into lithium-heparinized bottles and the remaining 2 ml into fluoride oxalate bottles. The samples in the lithium-heparinized bottles were transferred into a deep freezer and stored at –20^{o}C while those in fluoride oxalate bottles were centrifuged at 4000 rpm for 5 min to separate the plasma from the blood cells. The plasma was gently decanted into labeled plain bottles. The plasma was stored in a refrigerator at +2 to +8^{o}C.

Fasting blood sugar (FBS) determination

FBS concentrations were determined spectrophotometrically by a commercial kit (Randox Laboratories, Crumlin, England.) using glucose oxidase-peroxidase enzymatic assay.

Blood digestion

The frozen blood samples in the lithium-heparinized bottles were retrieved and allowed to thaw. One (1) ml blood sample was pipetted into conical flask. 9 ml concentrated trioxonitrate (v) acid (HNO_3) was added to the blood sample in the conical flask and then, it was heated on a hot plate. When the fume became clear and the solution, almost colorless, the solution was removed and allowed to cool. After this, the solution was made up to 25 ml by adding distilled and de-ionized water

Determination of metals' concentrations

The blood levels of lead, copper, chromium and zinc were analyzed by atomic absorption spectrometry (Buck Scientific Model, 200AAS)

Statistical analysis

Data are expressed as mean $\pm$ SD. Statistical difference between each parameter of the diabetic and control groups were evaluated for significance by Analysis of variance (ANOVA) while multiple comparisons test (Least Significant Difference, LSD) was applied to find out significant difference between the parameters based on group's genders comparison. Means were considered significantly different where $p < 0.05$. Correlation analyses were also carried out by Pearson's method to investigate the relationships between the metals and Diabetes mellitus, and amongst the metals.

RESULTS

Table 1 showed the mean age and body mass indices (BMI) of all the subjects. The mean age of the test subjects and the controls are statistically similar. However there is significant difference in the mean BMI of the diabetic male and the diabetic female when compared with the corresponding controls.

Table 2 showed the mean fasting blood sugar (FBS), blood lead, zinc, copper, and chromium concentrations in all subjects. The FBS is statistically higher as expected in the diabetic subject, the controls. The mean blood lead levels in the diabetic male and female patients were significantly higher ($p<0.05$) than those found in control male and female subjects (Table 2) . The mean blood lead levels in both diabetic male and control male were higher compared with those in diabetic female and control female respectively. However, the mean blood zinc, copper and chromium levels in the diabetic male and

Table 1. Anthropometric indices of the subjects

Parameter	Gender	Control	Diabetic
Age(Year)	Male	45.0 ± 11.8	57.0 ± 11.8
	Female	48.0 ± 15.9	52.5 ± 16.0
	Total	46.5 ± 13.9	54.5 ±13.9
BMI(kg m^{-2})	Male	23.40 ± 1.76	27.16 ± 70**
	Female	30.81 ± 4.40	27.10 ± 5.30**
	Total	27.11 ± 3.80	27.13 ± 5.60

** = significantly different from the controls, p<0.05. BMI = Body Mass Index

Table 2. Fasting blood sugar (FBS), blood lead, zinc, copper, and chromium concentrations in all subjects.

Parameter	Gender	Control	Diabetic	Reference value
al(mg/dL)	Male	67.87 ± 4.00	279.11 ± 103.70**	125 Butler et al 2003
	Female	69.00 ± 6.67	256.67 ± 53.47**	
Lead (g/dL)	Male	38.07 ± 14.00	49.40 ± 14.36**	40 Froom et at 1998
	Female	35.51 ± 13.00	46.30 ± 15.22**	
Zinc (mg/dL)	Male	63.58 ± 14.78	61.55 ± 16.05	86 Froom et at 1998
	Female	66.41 ± 17.23	64.26 ± 11.10	
Copper(mg/dL)	Male	43.30 ± 11.50	41.38 ±10.12	75 Milne et al 1990
	Female	43.52 ± 7.00	43.62 ± 6.10	
Chromium(mg/dL)	Male	21.76 ± 9.78	24.43 ± 10.81	26.2 Morris et al 1999
	Female	17.72 ± 8.08	20.96 ±10.54	

** = significantly different from the controls, p<0.05. FBS = Fasting Blood Sugar

female patients were not significantly different from those found in the control male and female subjects.

A significant positive relationship was observed only between fasting blood sugar and lead concentrations (r = 0.393; p<0.01). However the levels of zinc, copper and chromium showed no significant relationships with fasting blood sugar. This is indicative of a connection between lead and diabetes mellitus and non-association of zinc, copper and chromium with the diseases. The metals also showed no significant correlations with each other (Table 3).

DISCUSSION

In this study, an association was established between the blood lead and diabetes mellitus. There is positive correlation between fasting blood sugar and blood lead concentration. Barbagello et al. (2000) had reported that as a result of high calcium levels in diabetics, the absorption of lead is expected to be low. But lead from endogenous sources, such as lead in bone and /or from previous environmental exposure will remain in circulation in the blood. This is probably responsible for the observed high blood lead level in diabetic patients.

In view of the observed association between blood lead and diabetes mellitus in this study, one may suggest that increase blood lead in diabetes is probably a contributory factor to the decline in renal function observed among diabetics. Moreover many other works have linked decline in kidney function to either/both bone or blood lead levels (Steassen et al., 1992; Payton et al., 1994; Kim et al., 1996; Tsaih et al., 2004). Furthermore, since one of the signs of lead toxicity is impaired renal function and also one of the most prominent complications of diabetes mellitus is kidney damage, chances are that this observed higher blood lead in diabetics may be associated with the kidney damage complication of diabetes mellitus.

Table 3. Correlation between fasting blood sugar, lead, zinc, copper and chromium in all subjects (N = 57).

	FBS	Lead	Zinc	Copper	Chromium
FBS	1	0.393**	-0.015	-0.170	0.097
Correlation	.	0 .000	0.901	0.145	0.410
N	57	57	57	57	57
LEAD	0.393	1	-0.051	-0.023	0.151
Correlation	0.000	.	0.665	0.842	0.195
N	57	57	57	57	57
ZINC	-0.015	-0.051	1	0.024	-0.057
Correlation	0.901	0.665	.	0.838	0.626
N	57	57	57	57	57
COPPER	-0.170	-0.023	0.024	1	0.140
Correlation	0.145	0.842	0.838	.	0.231
N	57	57	57	57	57
CHROMIUM	0.097	0.151	0.057	0.140	1
Correlation	0.410	0.195	0.626	0.231	.
N	57	57	57	57	57

** Correlation is significant at the 0.01 Level (2-tailed). FBS = Fasting Blood Sugar

However, contrary to some findings in literature zinc, chromium and copper showed no significant relationships with diabetes mellitus. Cooper et al. (2005) showed that copper metabolism in diabetics is abnormal. Many studies have reported higher copper level in diabetics, especially in those with complications (Walter et al., 1991). In contrary to this however, this work revealed no significant difference between blood copper levels in diabetics and the controls, our result is however consistent with the findings of Smith et al. (1988) and Ito et al. (2001).

Zinc has been found to have insulin-like effects, in that it causes or enhances glucose up-take. It has been proposed that zinc enhances glucose up-take by inhibiting glycogen synthetase, (Ilouz et al., 2002). The inhibition of glycogen synthetase blocks the conversion of glucose to glycogen. Some past studies have reported low zinc level in diabetics (Nakamura et al., 1991). Some of the reasons adduced for this observation are, excessive zinc loss in urine in diabetes (Pidduck et al., 1970) and low zinc absorption rate (Selinus, 2002). Nevertheless, Zargar et al. (2002) reported higher zinc level in type-1 diabetic subjects. However our result showed no association between this metal and diabetes, this may be that there is no zinc deficiency in this environment.

Chromium participated in increasing the number of insulin receptors present in a target organ and also increases the binding of insulin to its receptors (Anderson, 1996). Morris et al. (1999) found that plasma chromium was lower by 33% and urine chromium by 100% higher in diabetics and that plasma chromium was inversely correlated with plasma glucose during the onset of non-insulin- dependent diabetes mellitus (NIDDM) but the correlation was lost in patients with more than two years of NIDDM. However, Cooper et al. (2005) found that diabetes did not alter chromium balance (difference between elemental intake and output), and urinary or fecal excretion rates. Our result is consistent with these findings.

Conclusively, this study revealed that lead has an interactive connection with type 2 diabetes mellitus while other mineral elements namely: zinc, copper and chromium have no such significant relationships with the disease. The high blood lead level in the diabetics may also be related to the kidney damage complication associated with the disease

Based on these findings, it is therefore recommended that healthcare providers should consider testing diabetic patients for complications due to lead toxicity as part of the treatment regimen. Also government should ensure a sweeping ban on the use of leaded gasoline particularly in third word country.

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