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Assessment of essential trace metals (iron, copper and selenium) and heavy metal (lead) in obese diabetics (type 2 diabetic) patients

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ABSTRACT

It is evident that the metabolism of some trace metals is altered in diabetes mellitus and these micronutrients may have specific roles in the pathogenesis and progression of the disease. The aim of this study was to determine the status of trace elements; iron, copper, selenium and lead in obese diabetic patients. The study was carried out on two hundred and four (204) subjects, aged 20-68yrs which comprised of fifty nine (59) obese diabetic subjects, forty five (45) obese non-diabetic patients, forty (40) non-obese diabetic patients and sixty (60) non-obese non-diabetics (apparently healthy volunteers) as control. The trace metals (Fe, Cu, Se and Pb) studied was analyzed using atomic absorption spectrophotometer. The mean levels of Se and Pb were decreased significantly when obese diabetics were compared with control. The Se level was also decreased significantly when obese diabetic was compared with each of obese non diabetic and non obese diabetic. The mean levels of other trace metals studied were decreased when obese diabetics were compared with non obese non diabetics (normal control) although not significant. Values in obese only (OND) subjects were higher than even the controls but this decreased with complication-diabetes mellitus although not statistically significant. In the obese diabetic group, Cu and Se negatively correlated with BMI and this was

significant. All trace metals studied significantly correlated positively with BMI in both obese only (OND) and control groups. This study showed that essential trace elements (Fe, Cu and Se) and the toxic trace metal Pb studied were depleted in obese diabetics. It is therefore recommended that Fe, Cu and Se supplementation and therapeutic strategies that will enhance Fe, Cu and Se availability in the body been instituted in obese diabetics.

1. Introduction

Obesity is a condition in which excess body fat accumulates to such an extent, that it affects the health adversely. Obesity occurs primarily due to the lack of physical exercise and to a lesser extent, due to decrease in the basal metabolic rate. Body mass index (BMI) is used as an index to measure body fatness and thus, the obesity status. Obesity has been implicated in the pathogenesis of several diseases like diabetes mellitus (DM), myocardial infarction, hypertension etc (WHO, 2006).

Type 2 diabetes mellitus is a major global health problem that affects over 200 million individuals worldwide. It is characterized by insulin resistance in peripheral tissue and an insulin secretory defect of the beta cells of the pancreas. Insulin resistance is a major contributor to the pathogenesis of type 2 diabetes mellitus and plays a key role in associated metabolic abnormalities such as dyslipidemia and hypertension.

Although both diabetes and obesity risk factors are often associated with race, age, and family history, it's becoming more and more clear that the conveniences of modern life also contribute to the development of both conditions. For example, sedentary lifestyles (reduced physical activity) and the popularity of high fat, high energy diets and convenient foods are known to lead to obesity – but do they also cause diabetes? In recent years, there has been increasing interest in exploring the exact role of trace element in human health and various diseases. There is accumulating evidence that the metabolism of several trace element is altered in diabetes mellitus and that these nutrients might have specific role in the pathogenesis of this disease (WHO, 2006).

On the other hand, the homeostasis of trace metals can be disrupted by diabetes mellitus. Conversely, early imbalances of specific element may play an important role in upsetting normal glucose and insulin metabolism. Diabetes mellitus may alter the copper, iron, selenium, and other trace metal status (Idonije et al, 2011a). Alteration in mineral metabolism is more pronounced in population with DM with specific complications. It is not known whether differences in trace metal status are consequence of type 2 diabetes mellitus or whether they contribute to the expression of the disease. According to Bloniarz and Zareba, 2007, metabolism of carbohydrate and fats in human organism is connected with some trace metals (microelements) and the occurrence of obesity may indirectly be connected with the disturbances of homeostatic mechanisms. Changes in the enzymatic activities of several metabolic pathways are seen in obesity induced type 2 DM may as a result of relative magnesium and copper deficiency (Zargar et al, 2002). It is therefore obvious that microelements disturbances, irrespective of the cause or the gene involved are associated with hypertension, diabetes and even in other disease conditions such as schizophrenia (Arinola and Idonije, 2009; Arinola et al, 2010) and sickle cell disease (Idonije et al, 2011b). By implication, a link exists between dietary microelement intake and development of metabolic diseases such as obesity, diabetes and cardiovascular disease such as hypertension. Hence, the balance of the intake of microelements is helpful for the prevention and management of hypertension, diabetes and obesity and in cases where they co-exist.

Copper ions serve as important catalytic co factors in redox chemistry for biological functions that are required for growth and development. Copper requiring proteins are involved in variety of biological processes and deficiency of specific enzymes or alterations of their activities often cause disease states or pathophysiological conditions.

Selenium, an essential trace metal, is involved in the complex system of defence against oxidative stress through selenium-dependent glutathione peroxidases and other selenoproteins (Burt, 2007). Because of its antioxidant properties, selenium might thus prevent the development of complications in diabetic patients. In

addition, selenate, an inorganic form of selenium, mimics insulin activity in experimental models (Mueller, 2006; Pallauf et al., 2008; Mueller et al, 2008). The role of selenium in the regulation of free radical production has been documented; its role in preventing glucose intolerance and the complications of diabetes mellitus has also been postulated. For instance, insulin reserves are decreased with selenium deficiency causing glucose intolerance. Selenium has been shown to mediate a number of insulin like action in vivo and in vitro, including stimulating glucose uptake and regulating metabolic processes such as glycolysis, glucogenesis, and fatty acid synthesis and pentose phosphate pathway. Selenium and copper concentration in erythrocytes can improve the antioxidative status by decreasing the malondialdehyde level in type 2 diabetes mellitus (Thomson, 2004).

Lead is a heavy metal that is dangerous to most of the human body organs, systems and interferes with body metabolism and cellular functions. It produces damaging effect in the hematopoietic, renal, reproductive, gastro intestinal systems (Babalola et al., 2007). The effects of lead poisoning in diabetes subjects have been recognized (Tsaih et al., 2004; Lin et al., 2003; Wedeen et al., 1975). Epidemiologic studies, mortality studies and experimental studies in animals have reported lead toxic effects at high levels of exposure and it is possible that high blood concentration of lead may contribute to the progression of diabetic complications in diabetic patients (Lin et al., 2003). Lead has been investigated in many pathological conditions and the level of this metal in the environment is of great concern.

Evidence that systemic iron overload could contribute to abnormal glucose metabolism was first derived from the observation that the frequency of diabetes is increased in classic hereditary haemochromatosis. It is obvious that iron overload, irrespective of the cause or the gene involved, result in an increased incidence of type 2 diabetes mellitus (Bothwell, 1999). Recently, a link has been established between increased dietary iron intake, particularly eating red meat and increased body iron stores, and the development of diabetes (Beard et al., 1996). Although the exact mechanism of iron induced diabetes is uncertain, it is likely to be mediated by three mechanism; insulin deficiency, insulin resistance, and hepatic dysfunction (Kuhn, 1998). This study therefore investigated the levels of iron, copper, selenium and leads in order to ascertain the status of these trace metals in obese diabetic patients.

2. Materials and methods

2.1. Study area

This study was conducted in Ekpoma, Benin City, Kwale and Asaba, all in the south-south zone of Nigeria.

Study Design: This study is a cross-sectional study involving simple random sampling and cohort sampling for subjects recruitment.

2.2. Ethical consideration

Ethical approval was sought and given by the research and Ethic Committee of AAU, Ekpoma. The intervention and control community gave their permission after the aims and objectives of the study were explained to them. Also, informed consent was sought and obtained from the respondents before enrollment into the study. At the end of the study the control group was also given the same intervention, for ethical reasons. Written informed consent/ questionnaire were administered to all subjects.

2.3. Subjects and grouping

Subjects were classified into the following four (4) groups to meet the set goals of this research. Group 1: Obese Diabetic (OD); Group 2: Obese non diabetic (OND); Group 3: Non Obese Diabetic (NOD) and Group 4: Non Obese Non Diabetic (NOND) [normal control(C)]

They were classified as obese using BMI ≥ 30 kg/m2, non-obese using BMI ≤ 24.5 kg/m2, diabetic using fasting plasma glucose (FBG) ≥ 7mmol/l (126mg/dl) and A total of about two hundred and four subjects were recruited and was distributed as follow; OD=59; OND=45; NOD=40 and NONDH=60

Inclusion Criteria: All Subjects with BMI ≤ 24.5kg/m2 (control group) and ≥30kg/m2 (obese groups) and not on any form of medication were recruited.

2.4. Exclusion criteria

All Subjects who are overweight (BMI ≥ 24.5 to ≤ 29.5kg/m2) and non obese and obese who are hypertensive or with any co morbid conditions were excluded from this study.

2.5. BMI measurement

Heights were measured in standing position, with shoulder and buttocks against the wall, the subject looking straight ahead with joined feet, and arms hanging on both sides with a graduated tape. In addition, body weights were measured with a calibrated beam scale. These were used to calculate the BMI which is weight (kg)/height (m2).

2.6. Fasting blood glucose (FBG) measurement

Preliminary measurement of FBG in all the subjects was done using Glucometer at least two different times with the mean value recorded. Subjects were asked to fast overnight (no food, drink, alcohol or smoking).

2.7. Sample collection and analysis

About 10.5mls of fasting blood was collected from each subject with 0.5ml immediately used for preliminary FBG estimation and 2.0mls immediately placed in fluoride oxalate container for FBG estimation spectrophotometrically as these served as basis for comparing FBG levels. Two (2.0) mls was placed in lithium heparin container for trace metals analysis using atomic absorption spectrophotometer.

2.8. Duration of study

The study was conducted within a thirty months period (from July, 2009 to June, 2012). The first 0-6mths was selection of subjects and baseline measurements of BP and FBG, 7-12mths was repeat measurements of BP and FBG, 13-18mths was repeat measurements of BP and FBG, 19-24mths was final measurements of BP and FBG and collection of sample for analysis and 25-30mths was analysis, collation and processing of data

2.9. Statistical analysis

Data were presented as mean±S.D (standard deviation) and then analyzed using Statistical Package for Social Sciences (SPSS) at a P value of 0.05 and 95% level of confidence and results presented in suitable tables.

3. Results

Table 1 showed the mean±SD of Fe, Cu, Se and Pb among the groups. The mean levels of Se and Pb were decreased significantly when obese diabetics were compared with control. The Se level was also decreased significantly when obese diabetic was compared with each of obese non diabetic and non obese diabetic. The mean levels of other trace metals studied were decreased when obese diabetics were compared with non obese non diabetics (normal control) although not significant. Values in obese only (OND) subjects were higher than even the controls but this decreased with complication-diabetes mellitus also not statistically significant.

Table 1
Mean±SD (µg/dl) of Fe, Cu, Se and Pb among the groups.

Parameter (µg/dl)	Obese diabetic (OD) n=60	Obese non diabetic (OND) n=50	Non obese diabetic (NOD) n=50	Non obese non diabetic [NOND (C)] n=60
Fe	56.20±17.65	61.55±11.01	62.85±19.10	60.25±13.79
Cu	55.57±15.27	59.03±12.89	60.58±17.56	58.40±14.61
Se	25.10±6.586[abc]	28.78±5.821[b]	29.05±9.886[c]	28.91±8.382[a]
Pb	7.32±195[a]	7.92±1.46	8.71±3.69	8.76±4.37[a]

P<0.05 is significant. Values with superscripts were significantly different.

Table 2 showed the correlation between the trace metals studied and BMI among the groups. In the obese diabetic group, Cu and Se negatively correlated with BMI and this was significant. All trace metals studied significantly correlated positively with BMI in both obese only (OND) and control groups.

Table 2
Correlation between BMI with Fe, Cu, Se and Pb in all the groups.

		Obese Diabetic (OD)		**Obese non Diabetic (OND)**		**Non Obese Diabetic (NOD)**		**Non Obese None Diabetic [NOND (C)]**	
Dependent Variable	Independent Variable	r	P value /remark	r	P valve/ remark	R	P valve/ remark	r	P value/ remark
BMI	Fe	-0.201	NS	0.478	S	0.077	NS	0.281	S
BMI	Cu	-0.338	S	0.515	S	0.112	NS	0.295	S
BMI	Se	-0.37	S	0.484	S	0.068	NS	0.335	S
BMI	Pb	-0.195	NS	0.46	S	0.033	NS	0.277	S

$p<0.05$ is significant.

4. Discussion

Trace metals have long been known to be essential for optimum health. The role or clinical significance of trace elements in obese diabetics is still somewhat controversial. It is therefore obvious that microelements disturbances, irrespective of the cause or the gene involved are associated with obesity and diabetes. By implication, a link exists between dietary microelement intake and development of metabolic diseases such as obesity and diabetes. Hence, the balance of the intake of microelements is helpful for the prevention and management of diabetes and obesity and in cases where they co-exist. Therefore, among the trace elements, iron, copper, selenium and the toxic trace metal lead were studied.

From this study, it was observed that the mean levels of iron and copper of obese diabetic subjects were similar compared to non obese non diabetic subjects (normal control) and copper significantly correlated negatively with BMI. It is in agreement with the work of Sjogren et al., (1986) who stated that obese diabetic subjects without retinopathy, hypertension, or macrovascular disease had lower plasma copper concentrations when compared with non obese non diabetic subjects (i.e control subjects) and Cu is decreased due to copper depleted diet and copper chelation with tetrathiomolybdate reversed and levels decreases with increase in BMI. But this is not in line with Bothwell, (1999) and Jehn et al (2005) who stated that iron level is significantly increased in obese diabetic patients resulting from the consumption by these individuals of more red and processed meat, less fiber and more calories, than the non obese diabetic individuals. Excess iron appears to contribute to diabetes risk thereby prompting the formation of free radicals which in turn compromises insulin sensitivity (Medvei and Victor, 1993).

It was also observed that the mean level of selenium and lead were decreased in obese diabetics compared to the normal control (non obese non diabetic) and this was significant ($p<0.05$) and Pb also significantly correlated negatively with BMI. This decrease in Se levels has been described in an earlier study by Burt (2007) and Idonije et al (2011a). Selenium is known to act as an antioxidant and peroxynitrite scavenger when incorporated into selenoproteins (Gramm et al., 1995; Beytut and Akasakal, 2003). It is the main element in glutathione peroxidase (an active enzyme against oxidative stress) that reduces formation of free radicals and peroxidation of lipoproteins. The low concentration of selenium in serum could potentially expose the subjects to oxidative stress which is known to be associated with the pathogenesis of diseases such as diabetes mellitus (Schwartz and Reis, 2000). On the other hand, low concentration of this element in blood might be an indication of active production of free radical and increased scavenging activity of selenium. This decrease in selenium levels could contribute to oxidative stress and low selenium level has been shown to reduce insulin secretion and increased insulin resistance in some experimental models, thereby possibly playing a causal role in the development and pathogenesis of type 2 diabetes (Evans et al., 2005).

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