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Plasma Micronutrients (Magnesium, Zinc, Selenium) Status and Lipid profile among adults with Type II Diabetes mellitus in Sagamu, South-west Nigeria

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Abstract

Background: Diabetes mellitus (DM) is a group of metabolic disorders characterised by hyperglycemia with secondary derangements in micronutrient status. Various studies had given conflicting reports of increased or decreased levels of micronutrients in Type II DM.
Objective: To measure the plasma micronutrient levels and lipid profile in adults with Type II DM.
Method: Plasma magnesium, zinc and selenium levels were measured among 100 subjects comprising 50 people with DM (age range 36-70 years) and 50 control subjects without DM (age range 29-70 years). The anthropometric parameters were measured; fasting blood glucose, plasma cholesterol, triglycerides, and high-density lipoprotein cholesterol, micronutrients (magnesium, zinc and selenium) levels were also measured using standard methods.
Result: There were statistically significant ($p < 0.05$) higher plasma glucose, blood pressure (systolic and diastolic), LDLC, and lower levels of plasma magnesium, zinc, selenium, HDLC levels among the patients with DM (cases) compared with the normal control subjects. No significant difference was observed in the plasma total cholesterol and triglyceride between the two groups. A significant negative correlation was found between the plasma levels of the trace metals (magnesium, zinc and selenium) and triglycerides ($r = -0.36$, $r = -0.43$, $r = -0.51$ respectively).
Conclusion: Plasma levels of magnesium, zinc and selenium are reduced in Type II DM with associated hyperglycaemia-driven dyslipidaemia.

Keywords: Blood pressure, Diabetes mellitus, Micronutrients, Plasma Glucose, Plasma Lipids.

Introduction

The micronutrients make significant contributions to general metabolism and good health. This vital role of trace element in health makes their deficiency states prominent either as a contributory factor to a disease condition or as a consequence of disease conditions. Zinc, selenium, copper, vanadium and cadmium were reported to have insulinomimetic effects through the activation of protein kinase B and other kinases of the insulin signalling cascade. [1] Metabolic disorders (such as diabetes mellitus, atherosclerosis and obesity) are usually associated with increase or decrease in micronutrient status.

The global increase in the incidence and prevalence of diabetes mellitus (DM) had led to various

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studies and clinical trials in the course of finding a permanent cure to the disease. These studies involved the identification of the various aetiologic, metabolic, hormonal, neurological, and nutritional factors responsible for DM and the associated complications which are pathognomonic of the disease condition. Various discoveries were made, and these have immensely contributed to the management options that are presently available globally. Among the discoveries are the characteristic prominent disturbances in mineral metabolism and the attendant differences in the plasma micronutrients when compared with those of healthy individuals. [2,3]

The relationship of micronutrients with glycaemic controls in DM had been described as controversial. [4] However, it is not clear whether the derangements in micronutrients status in DM is a consequence of the characteristic hyperglycaemia, or the deficiencies of micronutrients contribute to the expression of the disease and its associated complications. [5]

Glucose metabolism and insulin signalling involve series of enzyme activities that require micronutrients (cofactors and vitamins). Deficiencies in any of these micronutrients may impair glucose metabolism and cause insulin resistance [6] and glucose intolerance. The central role played by insulin in metabolism is not limited to carbohydrate but also affects lipid and protein metabolism. Insulin and the counter-regulatory hormones are the major glucoregulatory hormones that assist with carbohydrate metabolism and maintenance of glucose homeostasis. The antihyperglycaemic effect of insulin was reported to be potentiated by micronutrients such as magnesium, zinc, selenium, chromium, vanadium, manganese, and molybdenum. [7]Magnesium and zinc were selected among the previously highlighted micronutrients because of their roles as cofactors in enzyme-catalyzed reactions. Besides, zinc and selenium possess antioxidant properties.

Globally, several reports have been made about the plasma levels of micronutrients (magnesium, zinc and selenium) in Type II DM and the health benefits of their supplementation in the management of the disease condition based on supposedly reported antioxidant properties exhibited by these elements. While some researchers reported low concentrations of these ions in Type II DM, others reported little or no change in their levels. Salem *et al*. [8] and Oyedeji *et al*. [9] reported reductions in the serum magnesium, zinc and selenium levels in Type II DM while D'Ocon [10] reported high levels of zinc in the disease condition. On the other hand, a non-significant difference in the serum levels of magnesium was reported by Naila *et al.* [5] Therefore, this study was designed to determine the plasma levels of micronutrients such as magnesium, zinc and selenium among Nigerian adults with Type II DM and compare these with the levels among healthy controls in the same environment.

Methods

Subject Selection

The research was a cross-sectional study. A total of 100 participants (comprising of 50 adults with Type II DM [cases] and 50 control subjects without DM) were enrolled into this study. The cases attended the Endocrinology Clinic at the Olabisi Onabanjo University Teaching Hospital Sagamu, Ogun State, Nigeria between November 2015 and April 2016 while the non-diabetic control subjects were randomly selected and recruited for the study. The controls were drawn from the non-diabetic subjects who accompanied the patients with Type II DM to the clinic and some OOUTH Staffs. After explaining details of the study to both the cases and control subjects, informed consent was obtained from each of them before the commencement of the survey. Ethical approval was also obtained from the Health Research Ethics Committee of the hospital (HREC REG. NUMBER: NHRREC/08/10/2012).

A structured questionnaire was administered on both the cases and the control subjects to obtain some data such as age, sex, educational status, duration of diabetic illness, previous health status and social habits (cigarette smoking and alcohol intake). Anthropometric measurements

including height (m) and weight (kg) were carried out, and the body mass index (BMI) was computed using the formula: BMI = Weight/Height^2 (kg/m^2). Blood pressure was measured using Acousson® Sphygmomanometer.

Sample collection, processing and storage

About 10ml of fasting venous blood sample was collected from the antecubital vein of each subject in both groups by venepuncture with minimum stasis using sterile disposable needles and syringes. The blood sample was kept in a heparinized bottle. Blood for glucose estimation was collected into a bottle containing fluoride-oxalate anti-coagulant (to prevent glycolysis), blood sample for lipid profile and assay of micronutrients (magnesium, zinc and selenium) was dispensed into Lithium heparinized bottles. The blood sample in Lithium heparinized bottles was centrifuged at 5000 rpm for five minutes to obtain the plasma which was stored at -2^{0}Ctill assayed.

Biochemical parameters

Biochemical parameters measured included fasting blood glucose (FBG), plasma cholesterol, triglyceride and high-density lipoprotein cholesterol (HDLC). Glucose estimation was done using glucose oxidase method. [11] Fasting plasma lipid profiles (including triglyceride, total cholesterol, HDL-C) were assayed enzymatically with commercial test kits (Randox Laboratories®, Crumlin, England), based on standard methods. [12 - 14] The LDL-C was calculated as recommended [15] and the plasma levels of micronutrients (magnesium, zinc and selenium) were determined using colorimetric and atomic absorption spectrophotometric techniques.

Statistical analysis

The analysis was done using SPSS version 21. Continuous variables were expressed as Mean ± Standard deviation (Mean ±SD). The differences between mean values were compared using Independent Student's t-test. Pearson Correlation of biochemical parameters was also carried out for the cases. Statistically significant difference was set at p values less than 0.05.

Results

The cases were aged 36-70 years and comprised 19 males (38%) and 31 (62%) females while the controls were aged 35-70 years with 21 males (42%) and 29 females (58%).

Analysis of the duration of illness showed that 36% of the cases had been diagnosed with DM for < 2 years, 30% for 3- 5 years, 20% for 6 - 8 years and 14% for 9 – 11 years as shown in Figure 1.

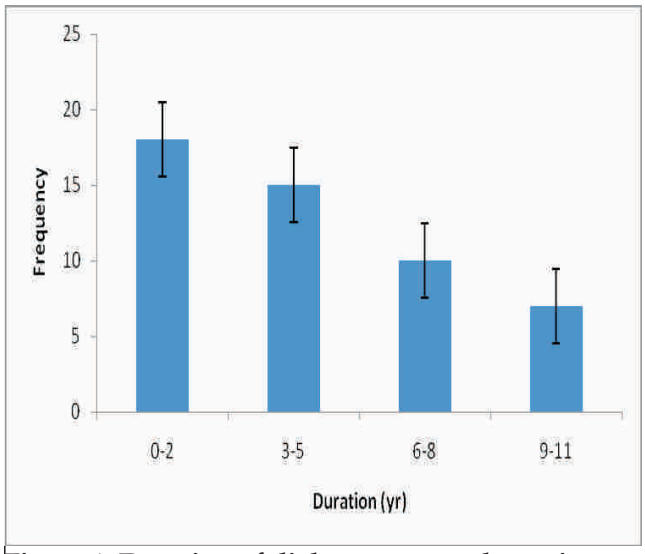

Figure 1: Duration of diabetes among the patients.

The mean age of the cases and the control subjects was 58.8 ± 10.3 years and 57.5 ± 10.0 years respectively. There was no statistically significant difference in the mean weight, mean height, and mean BMI of the cases compared to controls (Table I).

The mean BMI for both groups were less than 30 kg/m^2 (28.9 ± 5.3 kg/m^2 and 27.9 ± 3.8 kg/m^2 for the cases and control subjects respectively). Systolic and diastolic hypertension was observed among 42% (21 out of 50) and 34% (17 out of 50) respectively of the diabetic patients. A statistically significant higher mean blood pressure (systolic and diastolic) was also observed among the cases compared with the control subjects (Table I).

Table I: Comparison of the mean values of the anthropometric parameters and blood pressure of the subjects

Parameters	Cases Mean ± SD	Controls Mean ± SD	t-test	p-value
Age (years)	58.8 ± 10.3	57.5 ± 10.0	5.92	0.56
Weight (kg)	66.9 ± 12.6	65.9 ± 9.9	0.42	0.68
Height (m)	1.52 ± 0.03	1.54 ± 0.06	1.92	0.06
BMI (kg/m²)	28.9 ± 5.3	27.9 ± 3.8	1.16	0.25
Systolic (mmHg)	137.2 ± 21.4	118.2 ± 10.8	5.61	0.00
Diastolic (mmHg)	81.8 ± 10.4	73.0 ± 6.5	5.07	0.00

BMI - Body Mass Index

The cases had statistically significant higher mean plasma glucose and LDL-C but a statistically significant lower mean plasma HDL-C levels compared to the control group. There was no significant difference in the mean plasma total cholesterol and triglyceride levels of the cases and the control groups as shown in Table II.

Table II: Comparison of the mean plasma concentrations of biochemical parameters of the subjects

Parameters	Cases Mean ± SD	Controls Mean ± SD	t- test	p-values
Glucose (mg/dL)	182.7 ± 60.2	85.6 ± 12.8	11.2	0.00
T. Cholesterol (mg/dL)	188.0 ± 59.3	184.4 ± 29.4	0.38	0.70
Triglyceride (mg/ dL)	86.6 ± 48.9	96.4 ± 49.0	1.00	0.32
HDLC (mg/dL)	51.0 ± 14.8	66.2 ± 14.8	5.11	0.00
LDLC (mg/dL)	119.7 ± 52.8	98.9 ± 30.7	2.40	0.02

In addition, the mean plasma magnesium, zinc and selenium levels in the cases were significantly lower compared to the levels in the control subjects (Table III).

There were significant negative correlations between triglycerides and the micronutrients (magnesium, zinc and selenium) (r = - 0.36, r = - 0.43, r = - 0.51 respectively). However, these micronutrients showed no significant correlation with fasting blood glucose, cholesterol, HDLC and LDLC.

Table III: Comparison of the mean plasma concentrations of micronutrients among the subjects

Parameters	Cases Mean ± SD	Controls Mean ± SD	t- test	p-values
Mg (mg/dL)	1.57 ± 0.5	2.1 ± 0.5	5.23	0.00
Zn (mg/dL)	0.21 ± 0.08	0.38 ± 0.12	7.90	0.00
Se (µg/ dL)	0.25 ± 0.09	0.34 ± 0.12	4.38	0.00

Table IV: Pearson Correlation of the plasma concentrations of glucose, lipid profiles and micronutrients in subjects with Type II Diabetes mellitus

Parameters	SBP	DBP	FBG	Total Chol	Trig	HDLC	LDLC	Mg	Zn	Se
Systolic BP	1									
P value	-									
Diastolic BP	0.79*	1								
P value	0.00	-								
FBG	-0.33*	-0.21	1							
P value	0.02	0.15	-							
Total Chol	0.26	0.38*	-0.16	1						
P value	0.07	0.01	0.28	-						
Trig	-0.16	-0.09	-0.06	0.39*	1					
P value	0.26	0.54	0.67	0.01	-					
HDLC	0.32*	0.31*	-0.09	0.43*	0.14	1				
P value	0.02	0.03	0.55	0.00	0.34	-				
LDLC	0.23	0.36*	-0.21	0.94*	0.22	0.15	1			
P value	0.11	0.01	0.15	0.00	0.13	0.30	-			
Mg	0.28	0.30*	-0.04	0.01	-0.36*	0.03	0.08	1		
P value	0.05	0.04	0.80	0.97	0.01	0.85	0.57	-		
Zn	0.16	0.07	-0.02	-0.14	-0.43*	-0.14	-0.04	0.73*	1	
P value	0.28	0.63	0.90	0.35	0.00	0.35	0.79	0.00	-	
Se	0.20	0.10	0.09	-0.25	-0.51*	-0.09	-0.15	0.58*	0.72*	1
P value	0.17	0.50	0.55	0.09	0.00	0.55	0.31	0.00	0.00	-

*Statistical significance p<0.05

SBP = Systolic Blood Pressure; DBP = Diastolic Blood Pressure; FBG = Fasting blood glucose; T Chol = Total cholesterol; Trigly = Triglyceride; HDLC = High density lipoprotein; LDLC = Low density lipoprotein; Mg = Magnesium; Zn = Zinc; Se = Selenium.

Discussion

The importance of micronutrients (zinc, magnesium, selenium, chromium, vanadium, molybdenum and manganese) in metabolic processes had been established by different studies which addressed insulin action and carbohydrate metabolism. [16] The effect of DM on micronutrients and the role of these micronutrients in the pathogenesis and

progression of DM are unclear. [17] Variations in the status of these micronutrients in individuals with DM have been noted, and this is attributable to the observed hyperglycaemia and increased protein glycosylation in the diabetic state. [18]

The observed distribution of the duration of the illness suggested that a remarkable proportion of the cases were relatively newly diagnosed as they had the disease for less than two years. It is plausible that any abnormality in the plasma micronutrients concentrations might have started early and could progress arithmetically or geometrically depending on the underlying general conditions in the patients.

The cases and controls were comparable regarding the mean height, weight and BMI. Therefore, observed variations in the lipid profiles may be attributable to the disease condition rather than strictly obesity or overweight. DM was also observed in the present study to coexist with hypertension. Hypertension was defined as systolic blood pressure greater than or equal to 140mmHg and diastolic blood pressure greater than or equal to 90mmHg. [19] The present study recorded a statistically significant increase in the mean values of the blood pressure (systolic and diastolic) among the cases compared with the control subjects. Similar coexistence of the two disease conditions had earlier been reported to occur among 40% to 60% of patients with Type II DM. [20] The observed increase in blood pressure could be an important aetiologic factor among individuals with DM or may be a complication of DM arising from the activation of the renin-angiotensin-aldosterone system (RAAS). The latter leads to hyperaldosteronism with consequent sodium retention and intravascular volume expansion. Other effects include increased activation of the sympathetic nervous system, atherosclerosis and impairment of the endothelial **nitric** oxide synthase activity. Similar coexistence of hypertension and DM had earlier been reported. [21, 22]

The relatively higher mean plasma glucose and LDL-C levels and lower plasma HDL-C levels among the cases compared with the control subjects agreed with the known dyslipidaemic state of patients with DM. [23] The mean plasma concentrations of magnesium, zinc and selenium were significantly lower among the cases compared to the mean concentrations among the control subjects. This finding corroborated the decrease in the serum levels of the micronutrients in Type II DM as earlier reported by Salem *et al*. [8] While Lichten and Cousins [24] reported a suboptimal level of serum zinc in Type II DM, Kljai and Runje [25] reported low serum selenium levels in the condition. On the other hand, Zargar *et al.* [15] reported comparable plasma copper and magnesium concentrations in Type II DM.

The observed relative deficiency in plasma magnesium in this study will cause changes in the enzymatic activities of several metabolic pathways where magnesium plays important cofactor roles. [23] Magnesium functions as a cofactor in glucose transporting mechanisms across the cell membranes and various enzymes involved in carbohydrate metabolism. It is involved at multiple levels in insulin secretion, binding to receptors and enhancing the ability of insulin to activate tyrosine kinase. [26] Therefore, the deficiency in plasma magnesium concentration can be linked to insulin resistance, carbohydrate intolerance, dyslipidaemia, complications of DM [27] and increased risk of Type II DM in general.

Zinc is involved in the synthesis, storage, release and maintenance of conformational insulin integrity. The observed low plasma zinc concentration in the present study will alter its status, affect central metabolic processes involving carbohydrate and lipids and potentiate the development of complications in DM. Selenium is a critical component of selenoproteins (glutathione peroxidase and thioredoxin reductase which contains selenocysteine in their active site). This basic principle suggests a protective role against diseases where oxidative stress is of an immense aetiological role such as DM and its

complications. [28] Selenium mediates some insulin-like actions, notably the stimulation of glucose uptake and regulation of metabolic processes such as glycolysis, gluconeogenesis, fatty acid synthesis and pentose phosphate pathway. [29]

In the present study, the mean plasma magnesium concentrations among the cases and the controls in the present study were 1.57 ± 0.5 mg/dL and 2.1 ± 0.5 mg/dL respectively (normal range: 1.8 - 2.4mg/dL). The mean plasma zinc concentrations among the cases and the control subjects were 0.21 ± 0.08 mg/dL and 0.38 ± 0.12 mg/dL (normal range: 0.8 - 1.1mg/dL). The corresponding mean values for plasma selenium were 0.25 ± 0.09 µg/dL and 0.34 ± 0.12µg/dL (normal range: 0.75 – 1.20µg/dL). Though plasma zinc and selenium were observed to be low in this study, the values were significantly lower among the subjects with DM compared to the control subjects. The observed reduction in the mean plasma concentrations of magnesium, zinc and selenium among the cases may probably be due to the high turnover rate of the ion in the course of the various compensatory metabolic processes involved in DM.

The present study showed that serum magnesium, zinc and selenium concentrations were inversely related to serum triglycerides. The inverse relationship between serum selenium and serum triglycerides suggests a protective role of selenium against oxidative damage and diabetic complications as selenium is an effective antioxidant. [30] However, the serum concentrations of these micronutrients showed no significant correlation with fasting blood glucose, cholesterol, HDL-C and LDL-C. This implies a lack of effect of the micronutrients on lipoproteins (HDL-C and LDL-C) and glucose metabolism. On the contrary, high serum selenium levels were reported to be positively associated with hyperglycaemia, dyslipidaemia and increased the prevalence of Type II DM among adult Americans. [27]

The probable mechanisms for the reduced plasma concentrations of the micronutrients in Type II DM include damage to intestinal absorptive surfaces, an affectation of tubular reabsorption of elements, increased urinary excretion of micronutrients and compensatory increased turnover rate of micronutrients due to the accompanying metabolic stress.

Conclusion

Type II DM is associated with derangements in serum magnesium, zinc and selenium concentrations. These micronutrient deficiencies will further complicate metabolic decompensations in carbohydrate and lipid metabolism. Dietary supplementation of magnesium, zinc and selenium in Type II DM may decrease the prevalence and the risks for the disease and its complications. Further studies may involve the estimation of urinary concentrations of the micronutrients and markers of diabetic nephropathy among patients with DM. Base on the results obtained from the present study, dietary supplementation with magnesium, zinc and selenium could improve the general health and well-being of patients with Type II DM. This should be carefully done to maintain a balance between the potential benefit of such micronutrient supplementation and potential harms.

Authors' Contributions: OWE designed and conducted part of the laboratory procedures and prepared the manuscript. IAT participated in the laboratory aspects of the research and manuscript drafting. OO recruited the subjects and participated in data collection and critical review of the manuscript. OOO participated in research design and critical review of the manuscript.

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