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Copper, Magnesium and Selenium Levels in Serum Samples of Male Patients with Type 2 Diabetes Mellitus

Ifeanyichukwu Martin Ositadinma[1*] and Ngwu Amauche Martina[2]

[1]Department of Immunology, College of Health Sciences, Nnamdi Azikiwe University, Nnewi Campus, Anambra State, Nigeria.
[2]Department of Medical Laboratory Science, Faculty of Basic Medical Sciences, Enugu State University of Science and Technology, Enugu, Nigeria.

Authors' contributions

This work was carried out in collaboration between both authors. Author IMO designed the study, wrote the protocol and wrote the first draft of the manuscript. Author NAM performed the statistical analysis, managed the analyses of the study and managed the literature searches. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Trace elements are known to enhance the complete function of the immune system; avert uncontrolled expression and synthesis of inflammatory cytokines. The aim of this study was to determine the levels of Copper, magnesium, selenium in male individuals with type 2 diabetes mellitus.
Study Design: Prospective cohort study.
Place and Duration of Study: Medical outpatient clinic and Chemical Pathology Laboratory both of Enugu State University of Science and Technology Teaching Hospital, between January and December 2016.
Methodology: Forty male individuals with type 2 diabetes mellitus and forty apparently healthy male individuals within the age range of 45 - 75 years were recruited for this study. Glycated haemoglobin (HbA1c), fasting blood glucose (FBG), trace elements (copper, magnesium and selenium) was measured at six months interval.

**Corresponding author: Email: moifanyi@yahoo.co.uk;*

Results: The mean values of Cu, Mg, Se were significantly lower at pre-treatment compared to apparently healthy control values (*18.40 +/- 5.25* vs *95.16 +/- 30.32* µg/dl, *1.23+/- 0.16* vs *1.51+/- 0.09* mg/dl and *268.47+/-54.32* vs *349.63+/- 32.95* µg/l respectively) (p= <0.001, <0.001 and <0.001 respectively). At 6 month into treatment in comparison to pre-treatment values, there were significant decreases in HbA1c and Mg (*5.76+/-0.50* vs *9.74+/-1.25* %, *0.26+/-0.02* vs *1.23+/-0.16* mg/dl respectively) (p= <0.001, <0.001 respectively).
Conclusion: The levels of copper and magnesium were lower at pre-treatment, while magnesium was lowest at 6 month into treatment. In this study there is continuous increase in serum selenium levels during the treatment period.

Keywords: Diabetes mellitus; month; copper; magnesium; selenium.

1. INTRODUCTION

Diabetes mellitus (DM) is widespread metabolic disease affecting the people worldwide. There are more than 154 million diabetics globally and its commonness is on the increase in the low- and middle-income countries. Most people that suffer from this illness are from Africa and Asia. This may be due to genetic make-up and life style of people in these areas [1]. Diabetes mellitus is grouped into type I or the insulin-dependent diabetes mellitus (IDDM) and type 2 or the non-insulin-dependent diabetes mellitus (NIDDM). Type 2 diabetes is a lifelong disease that prevents someone body from using insulin the way it should. Person with type 2 diabetes are said to have insulin resistance [2]. So many studies have shown that copper (Cu) produces oxidative stress and functions as a pro oxidant and may engage in metal catalyzed creation of free radicals. The high production of free radicals is likely to be connected with development of type 2 DM. Copper is known as both a powerful enzyme catalyst and a hazardous reactant that produces hydroxyl radical [3]. Lack of copper results in glucose intolerance, reduced insulin response, and elevated glucose response. It is linked with hypercholesterolemia and atherosclerosis. Copper have an insulin-like property and encourage lip genesis [4]. Magnesium (Mg) is an essential mineral, involved in over 300 enzyme reactions in the human body. It is an important ion included in multiple levels in insulin's secretion. It is a cofactor in the glucose conveying mechanisms of the cell membrane [5]. It is also involved at multiple levels in insulin release, binding and promoting the capacity of insulin to produce tyrosine kinase. Magnesium deficiencies have been involved in insulin resistance, carbohydrate reaction, dislipidemia and development of diabetes [6]. Selenium, an important trace element, is involved in the composite system of protection against oxidative stress through selenium dependent glutathione peroxidases and other selenoproteins [7]. Because of its antioxidant effects, selenium might thus stop the development of diabetes. Lower serum levels of copper, magnesium and selenium have been reported in the diabetic patients [8]. The aim of the present study was to evaluate the serum levels of copper, magnesium and selenium in male patients with type 2 DM.

2. MATERIALS AND METHODS

This was a prospective cohort study carried out in the State Teaching Hospital Enugu, Enugu State, Nigeria, for a period of 12 months. Forty male individuals with type 2 diabetes, with fasting blood sugar level of ≥7.0 mmol/l and in the age range of 45 and 75 years were recruited for the study. They were diagnosed of type 2 diabetes mellitus at the chemical pathology laboratory of the Enugu State University of Science and Technology Teaching Hospital by glucose oxidase method. The approval for this study was given by the Research Ethics Committee of Enugu State University of Science and Technology Teaching Hospital (ESUTH) Enugu. Written informed consent was obtained from each patient. Those who were unable to sign inform consent form and had already started taken mineral supplement were excluded. Forty age matched male individual who do not have type 2 diabetes mellitus were recruited as controls. Participant's mobile phone numbers were collected and were used to follow them up.

2.1 Sample Collection

Six ml of overnight fasting blood sample was collected from the antecubital vein asceptically and dispensed into plain bottle for serum copper, magnesium and selenium estimation, ethylenediaminetetracetate (EDTA) bottle for glycated haemoglobin, fluoride oxalate bottle for glucose assay. Samples in the EDTA bottle were

refrigerated immediately at 4°c, while that in the flouride oxalate bottle were centrifuged at 3000 rpm for 5 minutes, and plasma separated into clean plain tubes and stored until time of analysis. Samples in plain bottle was allowed to clot and then centrifuged for 5 minutes, serum was separated and stored in clean plain tubes until time of analysis. Blood samples for the above mentioned tests were drawn from each patient before they started treatment, 6 months into treatment and 12 months of treatment.

2.1.1 Biochemical assay

Glycated haemoglobin was estimated with weak binding cation-exchange resin method. Serum copper, magnesium and selenium were assayed using atomic absorption spectrometer. Glucose was assayed by the Glucose oxidase method.

2.1.2 Statistical analysis

This was done using the SPSS version 21.0, means of variables are reported as mean ± standard deviation. Test of significant difference between means of variables was determined using the student "T" test and ANOVA. A value of ≤ 0.05 was considered significant.

3. RESULTS

Table 1 showed baseline values of serum copper, magnesium, selenium, glycated haemoglobin and FPG of male individuals with type 2 DM before treatment and control subjects. Before treatment, serum Cu, Mg and Se levels of DM patients were significantly lower (18.36±5.25 µg/dl, 1.23±0.16 mg/dl, 268.47±54.32 µg/l) compared with control (95.16±30.32 µg/dl, .51±0.09 mg/dl, 349.63±32.95 µg/l respectively) (p=<0.001, p=<0.001, p=<0.001 respectively), Before treatment, glycated haemoglobi and fasting blood sugar levels of DM patients were significantly higher (9.74±1.25%, 8.08+/- 3.22 mmol/l) compared with control (5.40±1.78%, 5.25+/- 0.35 mmol/l respectively) (p= <0.001, p=0.01). Table 2 showed mean +/- SD of serum Cu, Mg, Se, HbA1c and FBG of male diabetic patients before treatment, 6 months into treatment and 12 months into treatment. After initiating treatment, Mg significantly reduced from 1.23+/- 0.16 mg/dl to 0.26+/- 0.02 mg/dl at 6months (p= <0.001), Copper and Se significantly increase from (18.36+/-5.25 µg/dl, 268.47+/-54.32) to (28.04+/-3.80 µg/dl, 403.87+/-72.35 µg/l respectively) (p=<0.001, p=<0.001 respectively) at six months. Table 3 showed mean ±SD serum Cu, Mg, Se, HbA1c and FBG in male patients with type 2 DM between age group 45-64 years and >65 years before treatment, 6 months into treatment and 12 months of treatment. Before treatment, Copper significantly increased from 15.75+/-3.54 µg/dl in age group 45-64 years to 24.45+/- 1.09 µg/dl in age >65 years (p=<0.001).

Table 1. Comparison of baseline values of serum Cu, Mg, Se, HbA1c and FBG between individuals with type 2 DM and apparently healthy control

	Cu (µg/dl)	Mg (mg/dl)	Se (µg/l)	HbA1c (%)	FBG (mmol/l)
BT	18.36±5.25	1.23±0.16	268.47±54.32	9.74±1.25	8.08±3.22
C	95.16±30.32	1.51±0.09	349.63±32.95	5.40±1.74	5.25±0.35
P value	<0.001	<0.001	<0.001	<0.001	0.01

**Key = p < .05*

Abbreviation: BT= before treatment, C=control

Table 2. Mean values of serum Cu, Mg, Se, HbA1c and FBG of male subjects with type 2 DM (across treatment periods)

	Cu (µg/dl)	Mg (mg/dl)	Se (µ/dl)	HbA1c (%)	FBG (mmol/l)
BT	18.36±5.25	1.23±0.16	268.47±54.32	9.74±1.25	8.08±3.22
T6	28.04±3.43	0.26±0.02	403.87±72.35	5.76±0.50	6.05±0.57
T12	54.46±3.80	0.78±0.27	408.08±77.82	6.80±0.49	5.04±1.17
F (P) value	255.45 (<0.001)	125.60(<0.001)	25.35(<0.001)	46.10 (<0.001)	6.00 (0.01)
BT VS T6	<0.001	<0.001	<0.001	<0.001	0.19
BT VS T12	<0.001	< 0.001	<0.001	<0.001	0.03
T6 VS T12	<0.001	<0.001	0.99	0.02	0.03

Key = p < .05

Abbreviation: T6= 6 months into treatment, T12= 12 months into treatment

Table 3. Comparison of serum Cu, Mg, Se, HbA1c and FBG in age groups of individuals with Type 2 DM

	Cu (70-140µg/dl)	Mg (1.5-2.5 mg/dl)	Se (50-150µg/l)	HbA1c (6.6-8.6%)	FBG (4.2-6.4mmol/l)
Before treatment					
45-64 yrs	15.75±3.54	1.20±0.38	250.54±56.25	9.12±2.00	9.94±4.84
>65 yrs	24.45±1.09	1.34±0.19	261.46±70.81	10.17±1.29	8.25±2.50
p value	<0.001	0.27	0.65	0.42	0.53
6 month					
45-64 yrs	26.57±3.87	0.23±0.03	360.43±63.88	5.73±0.05	6.07±0.79
>65 yrs	28.89±1.75	0.25±0.01	371.14±38.49	6.16±0.63	6.06±0.53
p value	0.15	0.49	0.64	0.19	0.99
12 month					
45-64 yrs	56.08±7.12	0.80±0.31	421.20±21.08	7.02± 0.01	4.62±0.28
>65 yrs	53.46±4.86	0.55±0.03	419.46±17.55	7.01±0.01	4.51±0.42
p value	0.15	0.14	0.91	0.18	0.68

Abbreviation: yrs= years

4. DISCUSSION

Minerals in addition to being a structural component of body tissues are also included in various physiological processes, such as energy production and correct metabolism. The current study showed that the average level of serum copper is higher in normal controls than T2DM patients and also after initiating treatment, copper significantly reduced at six months in male diabetic patients. Human studies have shown that diabetic patients may have abnormal levels of serum copper [9]. Clinical studies of type 2 diabetes have demonstrated alterations in copper metabolism in this disease [10]. The present study results showed a decrease in serum copper level in diabetic individuals which is consistent with the findings of Hasan, [8]. It is not yet known, whether the reduction in serum copper levels noted in these subjects are a consequence of the disease or they play a role in the progression of the disease.

Magnesium is a cofactor for some enzymes involved in carbohydrate metabolism. There is a powerful relationship between magnesium and insulin action. Magnesium is crucial for the effectiveness of insulin. A decrease of magnesium in the cells increases insulin resistance [11]. The principal findings of the present study was a significant low serum Mg among diabetics than non-diabetics which is similar to the findings of Vikkorinova et al. [9] that showed decreased level of magnesium in cases as compared to controls. Though serum copper and magnesium were observed to be low in this study, the value of copper was significantly lower among the subjects between 45-64 years compared to those greater than 65 years. The observed reduction in the mean serum level of copper and magnesium among the subjects with type 2 diabetes mellitus may probably be due to the increase turnover rate of the ion in the course of the various compensatory metabolic processes involved in diabetes mellitus.

This antioxidant property of selenium stops the development of complications in diabetic patients. While in other studies increase serum selenium concentrations were associated with a high prevalence of diabetes [12]. In this study, after initiating treatment, Se significantly increased at six months in male diabetic patients. Recent epidemiological studies showed supranutritional selenium intake and increase in plasma selenium levels as possible risk factors for development of type 2 diabetes, indicating adverse effects of selenium on carbohydrate metabolism in humans. However, higher plasma selenium levels might be both a consequence and a cause of diabetes [13].

5. CONCLUSION

The levels of copper and magnesium were lower at pre-treatment, while magnesium was lowest at 6 month into treatment. In this study there is continuous increase in serum selenium levels during the treatment period. Also at twelve month, there is significant increase of serum copper, magnesium and selenium above its levels before the patients started their treatment.

ETHICAL APPROVAL AND CONSENT

The approval for this study was given by the Research Ethics Committee of Enugu State

University of Science and Technology Teaching Hospital (ESUTH) Enugu. Written informed consent was obtained from each patient.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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