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RESEARCH ARTICLE

ASSESSMENT OF SERUM LEVELS OF CHROMIUM AND COPPER AMONG SUDANESE PATIENTS WITH TYPE 2 DIABETES MELLITUS

[1]Siddig Mustafa Mohammed Suliman, *,[1]Suhair A. Ahmed and [2]Omer Fadl Idris

[1]Department of Clinical Chemistry, Faculty of Medical Laboratory Science, University AL Neelain University
[2]Department of Biochemistry and Molecular Biology, Faculty of Science and Technology, AL Neelain University

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ABSTRACT

Backgrounds: Diabetes Mellitus is a metabolic disease characterized by hyperglycemia due to defective insulin secretion or action. There is increasing evidence of the involvement of trace elements in the pathogenesis of diabetes mellitus and its complications.
Objectives: The aim of this study was to compare the serum levels of copper and chromium in Sudanese patients with type 2 Diabetes with that of non-diabetic healthy controls.
Methods and Results: A case-control study was conducted at Alsheifa specialized hospitals in Khartoum state, Sudan, during the period from December 2015 to January 2016.Included 60 type 2 diabetic patients and 40 non diabetic subjects (male and female) as controls were enrolled in this study. Written consent will be obtained from all participants whom will be asked not to alter their usual diets and physical activities throughout the study. Both groups were matched for age and gender. The serum levels of copper and chromium were measured using atomic absorption spectrophotometry technique. SPSS was used for analysis of data. In the diabetic group, the mean of the serum levels of chromium was significantly reduced, whereas the mean of the serum levels of copper also was significantly reduced when compared with the control group show in Table (1). The serum levels of chromium in the diabetic group had asignificant inverse correlation with HBA1c, Age and glycemic status ($P \leq 0.05$) show in Table (3), whereas the serum levels of Copper had insignificant inverse correlation with HBA1C%, Age and glycemic status ($P > 0.05$) show in Table (2).
In conclusion: The results of this study showed significantly reduced serum levels of chromium and significantly reduced serum levels of copper in Sudanese patients with type 2 diabetes.

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INTRODUCTION

Diabetes mellitus is currently emerging as an important health problem in Sudan, especially in urban areas. It is the comment cause of hospital admission and morbidity in Sudan due to a non-communicable disease (Ahmed and Ahmed, 2001). In Sudan type 2 diabetes constitutes 93.7%, whereas type 1 constitutes 6.3% of the diabetic population (Mahdi *et al*., 1989). some metals e.g. copper (Cu), zinc (Zn), iron (Fe) and manganese (Mn), chromium (Cr) etc. are neededin the body in very small amounts, less than 100 parts per million (ppm), hence, these are called trace elements ormicro-nutrients, Trace elementare involved in a range of physiological processes such as prosthetic groups of manyproteins, water balance, cofactors of many enzymes etc (Grivetti, 2000). According to the International Diabetes Federation (IDF), the cost for the Treatment of diabetes globally in 2010 was about $ 376 billion (11.6 percent of total health spending). The IDF predicts that these costs will increase by 2030 to $ 490 billion and it puts considerable strain on health systems. Type 2 diabetes can be prevented or delayed through healthy diet, regular physical activity, maintaining a normal body weight, and avoiding smoking (International Diabetes Federation, 2013). The proposed mechanism of trace elements enhancing insulin action includes activation of insulin receptor sites, serving as cofactors or components for enzyme systems involved in glucose metabolism (Kruse-Jarres and R¨ukgauer, 2000), increasing insulin sensitivity, and acting as antioxidants

Corresponding author: Suhair A. Ahmed,
Department of Clinical Chemistry, Faculty of Medical Laboratory Science, University, AL Neelain University

preventing tissue per oxidation (Kazi *et al*., 2008). The aim of this study was to compare the serum levels of chromium and copper in Sudanese with type 2 Diabetes with that of non-diabetic healthy controls and to assess the relationship of these elements with the glycemic status. Chromium is an essential trace mineral required by the human body for normal carbohydrate and lipid metabolism (Vincent, 2000). Chromium like all basic elements is not made in the body and a certain level is needed in the diet to maintain health. Nutritional chromium, also known as Chromium III (III indicates the state of oxidation), is found in foods and supplements. It is the most stable form of chromium, and is considered one of the least toxic nutrients (Jiang *et al*., 2004; Zargar *et al*., 2002). The normal range of chromium in whole blood is 0.04- 0.4 mg/dL and it appears to be most concentrated in the liver, spleen, kidneys and bones (Valko *et al*., 2005). Copper is considered as both a powerful enzyme catalyst and a dangerous reactant that generates hydroxyl radical. The normal level of total copper in the body0.7-1.4 mg/dL (11–22 μmol/L). It is well known that copper plays a vital role in oxidative stress (Tuvemo and Gebre-Medhin, 1983). Copper in its free form is a potent cytotoxic element because of its redox chemistry (Viktorínová *et al*., 2009). It readily participates in Fenton and Heiber Weiss reactions to generate reactive oxygen species (Evans *et al*., 2002). A high level of copper enhances the toxic effect of metal dependent free radicals. Moreover the increase in copper levels in patients with type 2 DM might also be attributed to hyperglycemia, which stimulates glycation and causes release of copper ions from copper binding sites of proteins. The release of copper ions into blood further accelerates the oxidative stress (Salem *et al*., 2011).

MATERIALS AND METHODS

A case-control and hospital-based study conducted at Alsheifa specialized hospitals in Khartoum state, Sudan, during the period from December 2015 to January 2016.The serum levels of chromium and copper were measured using atomic absorption spectrophotometry technique. Statistical analysis was performed using SPSS for Windows (version 14.0). The means and the standard deviations (SD) for variables of the test group and the control group were obtained showed in table (1). t -test was used for comparison between variables of the two groups and P-value $\leq$ 0.05 was considered significant. The study included 60 type 2 diabetic patients and 40 non diabetic subjects (male and female) as controls. Written consent was obtained from all participants whom were asked not to alter their usual diets and physical activities throughout the study. Blood samples were drawn with metal free, stainless steel needles into appropriately-coated tubes. Fasting plasma glucose was determined by the glucose oxidase method (Biocon). For estimation of serum Cu and Crashed serum was dissolved in diluted HCl and analyzed with atomic absorption spectrophotometer with air acetylene flame. HbA1C measured by I-CHROMA technique. The inclusion criteria for the case participants was as following: be suffering from type 2 diabetes for >1 year, age range 40-70 years, no treatment with insulin or any other drugs known to influence the glucose metabolism at least four weeks prior to sampling , no history of any recent acute illness or clinical evidence suggestive of kidney, liver, or endocrine diseases, absence of chronic diabetic complications (proliferative retinopathy, albuminuria, symptomatic neuropathy, coronary, and other vascular diseases). Patients taking vitamin and/or mineral supplements, thyroid hormones, estrogen, progesterone, diuretics, or antihypertensive agents were excluded from the study. The institutional ethical board granted the approval of the research protocol.

RESULTS

In this study, the test group included 60 Sudanese patients with Type 2 Diabetes (32% males, 28% females) and 40 healthy subjects (21% males, 19%females) as control group. No significant difference in age and gender between the Mean ±SD of the test group and the control group. Table 1: Shows a significantly reduced mean of the RBG, serum levels of chromium, and levels of copper in the test group when compared with the control group in Sudan.

Table 1. Means of the serum levels of RBG, copper, chromium and HbA1c of the diabetic group and the control group

Parameter	DM (Mean±SD)	Control (Mean±SD)	P-Value
RBG	297± 74.0 Mg/dl	99± 12.00 Mg/dl	0.000
COPPER	0.5 ± 0.21 Mg/dl	0.9 ± 0.2 Mg/dl	0.000
CHROMIUM	0.02 ± 0.01 Mg/dl	0.32 ± 0.1 Mg/dl	0.000
HbA1c	8.58 ± 1.41 %	5.05 ± 0.58 %	0.000

*Results Expressed as means ±SD *significance considerd as P.value ≤0.05

Table 2. Correlation of copper with study variables in diabetic patients

Parameter	R-value	P-Value
Age	-0.116	0.059
RBG	-0.048	0.056
HBA1c	-0.006	0.064

(P > 0.05).was considered insignificant.

Table (2): shows insignificant inverse correlation between the serum levels of copper and HBA1C% and Age of the diabetic group (P > 0.05).

Table 3. Correlation of chromium with study variable in diabetic patients

Parameter	R-value	P-Value
Age	-0.154	0.039
RBG	-0.029	0.024
HBA1c	-0.087	0.039

(P ≤ 0.05) was considered significant.

Table (3): Shows a significant inverse correlation between the serum levels of chromium and HBA1C% and Age among the diabetic group (P ≤ 0.05).

DISCUSSION

Several studies indicated that imbalance of some fundamental metals can adversely affect pancreatic islet that cause diabetes. However, imbalance of essential metals induced generation of some reactive oxygen species (ROS) during diabetes.

Hyperglycemia causes oxidative stress that can lead to a reduction of gene promoter activity and expression of mRNA in pancreatic islet cells. Assessment of trace elements such as Cu and Cr in various diseases including diabetes remains contradictory with a lot of unanswered questions (Khan and Awan, 2014). According to the results in the present study, patients with diabetic mellitus type 2 had lower serum concentrations of Cu and Cr than healthy individuals. Numerous studies reported the essential roles of trace elements in insulin action and carbohydrate metabolism (Zargar *et al*., 1998) Trace elements are such (selenium, copper, chromium, manganese, zinc, magnesium, vanadium, and molybdenum) important for human metabolic function. The actual role of these trace elements in the pathogenesis and progress of diabetes is still unclear (Schlienger *et al*., 1988). Changes of the plasma levels of these elements in diabetics have been attributed to hyperglycemia and increased protein glycosylation reported in this condition (Klevay, 2000). Chromium is required for normal carbohydrate metabolism and as a critical cofactor for insulin action (Kimora, 1996). In the present study the mean of the serum levels of chromium in the diabetic group was significantly reduced when compared with that of the control group ($P < 0.05$). This result agrees with the results of Kazi *et al*. (2008) who reported deficiency of chromium in patients with type 2 diabetes (Chwiej *et al*., 2008). The present study also showed significant inverse correlations of the serum levels of chromium with both; HbA1C% and duration of diabetes. In the present study there was a significant decrease in the serum levels of copper in patients with type 2 diabetes as compared to controls. (Schlienger and Sarkar) also reported elevated levels of copper in patients with type1 and type 2 diabetes when compared to controls (John *et al*., 2010). These studies were disagreeing with the present study. In the current study, the serum levels of copper showed insignificant correlation with HbA1C% in the diabetic group. Published data show that Cu deficiency is one of the reasons for the development of cardiovascular diseases. Other reports suggest that Cu is also beneficial to prevent arthritis associated inflammation and epilepsy (Eaton and Qian, 2002). More recently, it has been reported that disturbances in copper levels in various biofluids and tissues are associated with abnormalities implicated in metabolic pathways of diabetes and its complications. Copper play roles in order to protect oxidative Damage of body tissues (Zheng *et al*., 2006).

Conclusion

The Serum levels of chromium were significantly reduced in Sudanese with type 2 diabetes when compared with healthy control subjects, and showed a significant inverse correlation with HBA1C% age and glycemic status. The serum levels of copper were significantly reduced in Sudanese with type 2 diabetes when compared with healthy control subjects, and showed insignificant inverse correlation with HBA1C%, age and glycemic status that may be due to nutritional diet in study area.

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