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Assessment of Plasma Trace Elements, Uric Acid, Malondialdehyde, and Glycated Haemoglobin among Sudanese Patients with Types 2 Diabetes Mellitus in Khartoum State.

A thesis submitted for fulfillment of PhD degree in Clinical Chemistry

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ABSTRACT

Diabetes mellitus (DM) is of a major and increasing global public health importance. The global burden of diabetes as per the International Diabetes Federation 2013 amounts to 381.8 million and is fast gaining the status of a potential epidemic in Sudan and it is associated with high incidence of morbidity and mortality. This is a case control study conducted during the period from September 2013 to December 2015 to assess plasma trace elements, uric Acid, malondialdehyde (as a marker of lipid peroxidation), and glycated hemoglobin in Sudanese with type 2 diabetes mellitus compared to healthy volunteers. Two hundred fifty patients with type 2 diabetes mellitus were selected as a test group was compared with the control group which included 150 apparently healthy volunteers (non diabetics). Blood specimens were collected from both groups, and plasma levels of malondialdehyde, copper, zinc, uric acid and fasting blood glucose were analyzed using spectrophotometric methods. HbA1c was estimated by method based on boronate affinity chromatography by using NYCOCARD. Age and gender of the test group were matched with the control group.

The results of the study indicate a significant rise in the means of the plasma levels of malondialehyde, zinc, uric acid, fasting plasma glucose, and HbA1c of the test group when compared with healthy control group subjects, whereas the means of the plasma levels of copper were raised but no significant difference was found when compared with that of control group.

The results of the current study also indicate significant elevations in the means of the plasma levels of malondialehyde, copper, zinc and uric acid of the uncontrolled diabetic patients when compared with control diabetic patients.

The results of current study indicate positive correlation between the BMI and the plasma level of malondialehyde and significant strong negative correlation between the BMI and plasma levels of FPG.

The current study indicate positive correlation between the duration of disease (in years) and plasma malondialehyde, moreover the results of current study indicate moderate positive correlation between the HbA1c and the plasma level of copper and moderate negative correlation between the HbA1c and the plasma level of uric acid.

In conclusion, the present results demonstrate that the plasma levels of malondialehyde, copper, zinc, uric acid, FPG, and HbA1c are important indicators which can be used as prognostic markers for the prediction of oxidative stress which plays pivotal role in progression and development of diabetes and its complications. And also can be used to assess the situation in controlled and uncontrolled diabetic patients.

الدراسة مستخلص
عام للسكري الدولي للاتحاد ووفقا ,بالغة بأهميه السكري مرض يحظي العالمي الصعيد علي سريعة الأمراض من السكري مرض .مليون 381.8 السكري بمرض المصابين عدد بلغ 2013 الدراسة هذه أجريت .والوفيات المرضية الحالات من عالية بمعدلات ويرتبط بالسودان الاكتساب وتقييم لتحديد 2015 ديسمبر إلى 2013 سبتمبر بين ما الفترة في (والشواهد الحالات دراسة) وحامض الألدهيد ثنائي والمالون (الزنك ,النحاس) النادره العناصر من البلازما مستويات .الثاني النوع السكري بمرض المصابين السودانيين المرضى التراكميفي والسكر اليوريك مجموعة إلى إضافة ، الثاني النوع السودانيين السكري مرضى من 250 الدراسة عينة شملت المجموعتين، من الدم عينات جمع تم .(بالسكري المصابين غير) الأصحاء من 150 من ضابطة الألدهيد، ثنائي المالون ومن (الزنك ,النحاس) النادره العناصر البلازما مستويات قياس تم الطيف قياس جهاز طريق عن الصيام حالة في الدم سكر مستويات إلى إضافة اليوريك وحامض العمر مطابقة تم .الانجذابي الكروماتوجرافي التحليل طريق عن التراكمي السكر الضوئي، .الدراسة مجموعتي بين والنوع
ثنائي المالون من الدم مستوى متوسطات في إحصائيا دال جوهري ارتفاع الدراسة نتائج أظهرت التراكمي والسكر الصيام، حالة في الدم سكر ,اليوريك حامض ,الزنك عنصر الألدهيد، البلازما مستويات متوسطات ان حين في .الضابطة بالمجموعة مقارنة المختبرة للمجموعة المختبرة المجموعة في احصائية دلالة ذات علاقة علي العثور يتم لم لكن مرتفع النحاس لعنص .الضابطة بالمجموعة مقارنة
مستويات متوسطات في احصائيا دال واضح ارتفاع وجود إلى الحالية الدراسة نتائج أوضحت السكري لمرضى اليوريك وحامض الزنك ,النحاس , الألدهيد ثنائي المالون عنصر من البلازما .المضبوط السكر بذوي مقارنة المضبوط غير السكر ذوي
ومستويات الجسم كتلة منسب بين موجبة ارتباط علاقة وجود إلى الحالية الدراسة نتائج أشارت الجسم كتلة منسب بين قوي عكسي ارتباط بينت كما الألدهيد، ثنائي المالون من البلازما .الصيام حالة في الدم سكر من البلازما ومستويات
ثنائي المالون ومستويات بين قوية موجبة ارتباط علاقة وجود الي الدراسة نتائج اوضحت بين متوسطه طردية ارتباط علاقة اوضحت كما ,(بالسنه) السكر مرض فترة وبين الالدهيد عكسية ارتباط علاقة ايضا اوضحت كما ,النحاس عنصر وبين التراكمي السكر مستويات .اليوريك وحامض التراكمي السكر مستويات بين متوسطه
الألدهيد ثنائي المالون من البلازما مستويات أن على الحالية الدراسة نتائج دلت ، الخلاصة التراكمي والسكر الصيام حالة في الدم وسكر اليوريك وحامض الزنك وعنصر النحاس وعنصر تلعب والتي للأكسدة المضادة المواد بوضع التنبوء كمؤشرات قصوى أهمية ذات المؤشرات من في الوضع لتقييم استخدامها وايضا .ومضاعفاتة السكري مرض وتطور تقدم في محوري دورا بين مرضى السكري المضبوط وغير المضبوط.

1. Introduction

Diabetes mellitus (DM) describes a metabolic disorder of multiple etiology, which is characterized by chronic hyperglycemia, with disturbances of carbohydrate, fat and protein metabolism, which results from defects in insulin secretion, insulin action, or both(1).Non-insulindependent
diabetes mellitus is one of the most widely spread and severe disorders currently, globally. The number of patients suffering from diabetes mellitus was reported to be over 381.8 million people worldwide (2).

Oxygen free radicals and lipid peroxides have been implicated in the pathogenesis of a large number of diseases such as Diabetes mellitus, cancer, rheumatoid arthritis, infectious diseases, and atherosclerosis (3). Growing evidence indicates that oxidative stress is increased in diabetes due to overproduction of reactive oxygen species (ROS) and decreased efficiency of antioxidant defenses. Oxidative stress, as well as nonenzymic
glycosylation, is now considered as a major factor contributing to the extent of chronic diabetes complications (4).

The increased oxidative stress in DM contributes to the development of diabetic complications. Oxygen derived free radicals and reactive oxygen species interact with the lipid bilayer of the cell membrane resulting in lipid peroxidation. Malondialdehyde (MDA) is a stable end product of lipid peroxidation. Elevated MDA levels alter the structural integrity of the cell membranes. Inactivation of membrane bound enzymes and surface receptor molecules leads to cell-regulating errors. The involvement of oxidized low density lipoproteins (LDL) in the foam cell formation leads to atherosclerosis (5).

There is accumulating evidence that the metabolism of several trace elements are altered in DM and that these nutrients might have specific roles in the pathogenesis and progression of this disease(6). A relationship between trace and macro elements with diabetes has been observed in many research studies. The proposed mechanism of trace elements enhancing insulin action includes activation of insulin receptor sites and serving as co-factors or components for enzyme systems involved in glucose metabolism(7). Alteration in the metabolism of trace elements like copper is associated with DM(8). Trace elements are accepted as essential for optimum health, because of their diverse metabolic characteristics and functions (9).

Trace elements participate in production of reactive oxygen species (ROS), which contribute to oxidative stress. Oxidative stress contributes to the pathogenesis of many diseases including DM. Previous studies have shown that copper causes oxidative stress(8, 10).Copper acts as a pro

oxidant and may participate in metal catalyzed formation of free radicals(8). The increased production of free radicals is likely to be associated with development of type 2 DM (8, 11). On the other hand some of these nutrients can directly modulate glucose homeostasis(12, 13).Deficiencies of certain minerals such as Zn have been shown to predispose a person to glucose intolerance and to promote the development of diabetic complications(14).It was reported that Zn is involved in the synthesis, storage, secretion, and conformational integrity of insulin monomers and that Zn assembles to a dimeric form for storage and secretion as crystalline insulin(15). Lower levels of Zn may affect the ability of pancreatic islet cells responsible for the production and secretion of insulin, such as in type-2 diabetes (16).
Hyperuricemia has been also added to the set of metabolic abnormalities associated with insulin resistance and/or hyperinsulinemia in metabolic syndrome (17, 18, 19). Hyperuricemia is a condition that is significantly associated with markers of metabolic syndrome such as dyslipidemia, glucose intolerance, high blood pressure, and central obesity, which are accepted as risk factors for developing cardiovascular disease. Hyperuricemia is probably associated with glucose intolerance due to various mechanisms, however, the most important is the association between insulin and renal resistance to absorption of urates (20, 21, 22).Recent studies have demonstrated that UA levels are higher in subjects with prediabetes and early Type 2 diabetes than in healthy controls(23, 24). Furthermore, an elevated serum UA level was found to increase chances for developing Type2 diabetes in individuals with impaired glucose tolerance (25).