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Assessment of Plasma Levels of Malondialdehyde, Zinc, Antioxidant Vitamins (A , E , C) , and Lipid profile in Sudanese patients With type 2 Diabetes Mellitus in Khartoum State

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Abstract

Diabetes mellitus (DM) is fast gaining the status of a potential epidemic

in Sudanese and it is associated with high incidence of morbidity and mortality. The pathogenesis of diabetes complications remains elusive, however oxidative stress seems to be most favorable linkage amongst factors suggested. A case control study conducted during the period from May 2013 to November 2015 to assessment the plasma levels of malondialdehyde (as a marker of lipid peroxidation), antioxidant vitamins (A, E, C), and zinc in addition to lipid profile in Sudanese with type 2 diabetes mellitus compared to healthy volunteers. Three hundred of diabetic patients who attended to Advanced Diagnostic Centre for routine follow up and a control group of 100 healthy subjects (non-diabetic). Blood specimens were collected from both groups, and plasma levels of Malomdialdehyde, antioxidant vitamins (A, E, C), and zinc, in addition to glycetaed hemoglobin (HbA_{1c}) were determined. Age and gender of the test group were matched with the control group.

The results of the study indicate a significant raised in the means of the plasma levels of malondialehyde, cholesterol, LDL, triglyceride, and HbA_{1c} of the test group when compared with healthy control group subjects, whereas the means of the plasma levels of antioxidant vitamins (A, E, C),HDL and zinc showed significant reduction when compared with that of control group.

The results of the present study indicate also significant elevations of the mean of the plasma levels of antioxidant vitamins (A, E, C), HDL and zinc of the control diabetic patients when compared with uncontrol diabetic patient, and there is significant reductions of means of plasma levels MDA, TG, Total cholesterol, LDL and HbA1c of the control diabetic patients with when compared uncontrol diabetic

Insignificant differences were found in the means of antioxidants (A, C, E), MDA, Zinc, HbA_{1c} and lipid profile between diabetic patients on hypoglycemic drug and those on diet control.

The results of this study indicate significant modrate positive correlation between HbA_{1c} and malondialdhehyde , and significant strong negative correlation between HbA_{1c} and plasma zinc, whereas there is significant strong positive negative correlation between HbA_{1c} and plasma levels of, vitamin A,E, and C .

The current study indicate significant strong positive correlation between the BMI and the plasma level of MDA,and modrate negative correlation with vitamins (A,E,C) and zinc.

The results of current study show modrate positive correlation between the duration of disease (in years) and the plasma level of MDA and show strong negative correlation with plasma levels of vitamin A, E, C and zinc.

In conclusion, the present study indicate that the plasma levels of MDA, antioxidant vitamins (A, E, C) and zinc, lipid profile and HbA_{1c} are important markers for evaluation of oxidative stress, antioxidant status, and glycemic control of diabetic patients respectively. Accordingly, these indicators can be used as prognostic markers for prediction of oxidative stress, antioxidant state, and glycemic control of diabetic patients especially in patients with complications such as lipid abnormalities and uncontrolled diabetes.

مرض السكري من الأمراض سريعة الاكتساب بالسودان ويرتبط بمعدلات عالية من الحالات المرضية والوفيات. تظل مسببات ومضاعفات السكري متداخلة، إلا أن الإجهاد التأكسدي يبدو أكثر الروابط ضمن العوامل وضوحاً. أجريت هذه الدراسة (دراسة الحالات والشواهد) في الفترة ما بين مايو إلى نوفمبر لتحديد وتقييم مستويات البلازما من المالون ثنائي الألدهيد، والفيتامينات مضادة الأكسدة (أ، ج، هـ)، وعنصر الزنك في المرضى السودانيين المصابين بمرض السكري النوع الثاني. شملت عينة الدراسة من مرضى السكري السودانيين النوع الثاني من المترددين علي المركز التشخيصي المتطور بحري للمتابعة الروتينية، إضافة إلى مجموعة ضابطة من من الأصحاء (غير المصابين بالسكري). تم جمع عينات الدم من المجموعتين، تم قياس مستويات البلازما من المالون ثنائي الألدهيد، والفيتامينات مضادة الأكسدة (أ، ج، هـ)، وعنصر الزنك إضافة إلى مستوي السكر التراكمي. تم مطابقة العمر والنوع بين مجموعتي الدراسة.

أظهرت نتائج الدراسة ارتفاع جوهري دال إحصائيا في متوسطات مستوى الدم من المالون ثنائي الألدهيد ، الكوليستيرول، الكوليسترول ذو الكثافة الخفيفة، ثلاثي الجلسريد، والسكر التراكمي للمجموعة المختبرة مقارنة بالمجموعة الضابطة. في حين أن مستويات البلازما من الفيتامينات مضادة الأكسدة (أ، ج، هـ)، الكوليستيرول ذوالكثافة العالية وعنصر الزنك أظهرت انخفاض دال في المجموعة المختبرة مقارنة بالمجموعة الضابطة.

أوضحت نتائج الدراسة الحالية إلى وجود ارتفاع واضح في متوسطات مستويات البلازما من الفيتامينات مضادة الأكسدة (أ، ج، هـ) ، الكوليستيرول ذوالكثافة العالية وعنصر الزنك لمرضى السكري ذوي السكر المضبوط مقارنة بذوي السكر غير المضبوط. وهناك انخفاض واضح في متوسطات البلازما من المالون ثنائي الألدهيد ، وثلاثي الجلسريد، الكولستيرول، الكوليستيرول ذو الكثافة المنخفضة والسكر التراكمي لمرضى السكري ذوي السكر المضبوط مقارنة بذوي السكر غير المضبوط.

لم توجد فرق ذات دلالة إحصائية في متوسطات الفيتامينات مضادة الأكسدة (أ، ج، هـ)، المالون ثنائي الألدهيد، الزنك، سكر الدم التراكميو دهون الدم بين مرضى السكري الذين يتناولون أدوية سكر الدم، والذين يستخدمون الحمية الغذائية.

تشير نتائج هذه الدراسة إلى علاقة ارتباطية طردية قوية موجبة بين قياسات السكر التراكمي و المالون ثنائي الألدهيد ، وعلاقة ارتباط عكسية دالة بين السكر التراكمي ومستويات البلازما

من عنصر الزنك. كما توجد علاقة عكسية قوية بين السكر التراكمي والفيتامينات مضادة الأكسدة (أ،ج ،ه).

أشارت نتائج الدراسة الحالية إلى وجود علاقة ارتباط طردية قوية بين منسب كتلة الجسم مستويات البلازما من المالون ثنائي الألدهيد،وعلاقة عكسية متوسطة مع الفيتامينات مضادة الأكسدة (أ، ج ،ه) وعنصر الزنك.

أوضحت نتائج الدراسة وجود علاقة طردية متوسطة بين مدة المرض (سنوات) ومستويات الامصال من المالون ثنائي الألدهيد إضافة إلى، وجود علاقة عكسية قوية مع مستويات البلازما من فيتامينات(أ، ج، ه) وعنصر الزنك.

خلاصة القول، دلت نتائج الدراسة الحالية على أن مستويات البلازما من المالون ثنائي الألدهيد، والفيتامينات مضادة الأكسدة (أ، ج، هـ)، وعنصر الزنك، سكر الدم في حالة الصيام، الدهون، والسكر التراكمي من المؤشرات المهمة لتقييم الإجهاد التأكسدي، والحالة مضادة الأكسدة، والتحكم في سكر الدم لمرضى السكري على التوالي، بناءً على ذلك فإن هذه المؤشرات ذات أهمية قصوى كمؤشرات على التحسن والتنبوء بوضع المواد المضادة للأكسدة، والتحكم في نسبة السكر في الدم خاصة لدى مرضى السكري الذين يعانون من ارتفاع الدهون ونسبة مستوى السكر غير المضبوط.

1. Introduction

Reactive oxygen species (ROS), in particularly free radical induced lipid peroxidation, cause tissue damage that have been implicated in the

pathogenesis of various disease including diabetes [1,2].

Diabetes mellitus is a disorder with many complications including, cardiovascular disease, nephropathy, retinopathy which affects severely the quality of life [3].

Diabetes mellitus is an important risk factor for atherosclerosis, and coronary- heart disease, is nowadays the most frequent cause of mortality in these patients [4]. One of the pathogenic mechanisms that can explain this increased risk in diabetes is the imbalance between oxidants and antioxidants, which results in oxidative stress (os)[5].

Hyperglycemia result in-glucose auto-oxidation, nonenzymatic glycation and monocyte dysfunction, which lead to increased production of free radicals[6]. This is further aggravated by the decreased levels of antioxidants and leads to oxidative damage, illustrated by the high levels of lipid and DNA peroxidation products found in these patients"[7]. All these diabetes-related abnormalities can intensify the endothelial dysfunctions, oxidation of LDL and foam cell formation, which ultimately lead to atherorma plague[8,9]. Although of these several complication mechanisms of diabetes, the pathphysiology of these complications are still needed to be investigated. Recent reports indicate that free radicals have important roles in the pathogenesis of diabetes and a relationship between oxidative stress and secondary complications of diabetes exists [10, 11].

Subsequently, free radicals change lipid/protein ratio of membranes by affecting poly unsaturated fatty acids and lipid peroxidation causes functional irregularities of several cellular organelles [12,13].

Lipid peroxides are disintegrated quickly and form reactive carbon compounds, among these, malondialdlehyde (MDA) is an important reactive carbon compound which is used commonly as an indicator of lipid peroxidation, and has become one of widely reported analytes for the purpose of estimating oxidative stress effects on lipids [14,15].

Since free radical production is increased whereas capacity of antioxidant system is reduced in diabetes, it has been proposed that diabetic patients may require more antioxidants compare to healthy individuals [16,17].

Since effect of free radicals in diabetes are now documented, it has been proposed to use antioxidant vitamins to block formation of free radicals and hence prevent development of diabetes complication [18,19]. While superoxide radicals are cleaned by enzymatic dismutation, compounds known as antioxidants clean free radicals in organisms.

Glutathione is a very important non enzymatic antioxidant together with antioxidants vitamins. Vitamin A, E and C are among these important non enzymatic antioxidants [20,21]. It has been proposed that in diabetic patients several abnormalities related with absorption develop in the absence of antioxidants vitamins[22]. Vitamin A functions as catalyzer of removal of singlet oxygen and as a result vitamin A inhibits singlet oxygen dependant reactions [23,24]. Vitamin C is also has role in activating vitamin E when it loses its antioxidant capacity by turning it into tocopherol.

Zinc, is an essential trace element, is useful in synthesis, storage and secretion of insulin .Zinc may play a crucial role in preventing molecular reactions that lead to the destruction of insulin – producing beta cells and the development of type2 diabetes. The combination of insulin with zinc increase the duration of its action and helps the immune system function properly .Its also needed for cell growth and division, wound healing ,and the breakdown of carbohydrate for energy. Zinc is needed to

maintain sense of taste and smell, too. Finally, zinc is an antioxidant, protecting cells from free radicals, or molecules that can possibly lead to heart disease and cancer[25].

Great sources of zinc are found in muscle meat, poultry, fish and seafood, while grains, nuts, eggs, seeds and brewers yeast also supply good quality zinc.

Zinc deficiency is associated with Malabsorption, chronic diarrhea, chronic liver disease, malignancy, chronic renal disease, diabetes mellitus, pregnancy and uses of contraceptive[26].

Lower serum plasma zinc levels in diabetics have been reported by [27]. Decreased gastrointestinal absorption of zinc may explain the hypozincemia seen in the diabetes population[28].

It is known that in people with type 2diabetes receiving Zn supplementation there is improvement in antioxidant status [29]. The potential antioxidant effects of zinc in diabetes could be related to several mechanism[30]. It has been suggested that zinc metallothionein complexes in the Islet cells provide protection against immune-mediated free-radical attack. Zinc could also play a role in protecting sulfhydryl groups against oxidation.

Therefore the aim of the present study is to asses the plasma levels of antioxidants vitamins (A, E, C), MDA and zinc addition to lipid profile in Sudanese patients with type 2 diabetes mellitus compared with healthy subjects and Further to asses possible relationship among antioxidant vitamins (A, C, E), zinc and malondialdehyde verus glycaemic control, body man index and duration of diabetes.

1.1 Rationale

During the past 20 years, major sociodemographic changes have occurred in Sudan, and changes in physical activity and dietary patterns have promoted the development of non-communicable disease, such as

diabetes mellitus. The micro vascular and neuropathic complications of diabetes mellitus are a major clinical and public health problem in Sudan. Recent studies suggest a possible relationship between lipid peroxidation and complications of diabetes mellitus[5, 6].

There is considerable evidence that hyperglycemia represents the main cause of complications of diabetes mellitus (DM), and oxidative stress resulting from increased generation of reactive oxygen species plays a crucial role in their pathogenesis. In fact, in the absence of an appropriate response from endogenous antioxidant mechanisms, the redox imbalance causes the activation of stress-sensitive intracellular signaling pathways. The latter play a key role in the development of late complications of DM. To date, many investigations have focused on the antioxidant status and oxidative stress in diabetes mellitus. It has been shown that an increase in free radicals production in type2 diabetes mellitus occurs due to lipid peroxidation or non enzymatic glycosylation of proteins or antioxidation of glucose. The current study may play an important role in determination of lipid peroxidation and monitoring diabetes through measuring malonaldehyde, lipid, lipoproteins and antioxidant vitamins, glaciated hemoglobin. Also to set group of data concerning complications and control of diabetes in Sudan.

1.2. Objectives

1.2.1 General Objective:

-To assess the plasma levels of malondialdehyde (as a marker of lipid peroxidation), antioxidant vitamins (A, E, C), and zinc in addition to lipid profile in Sudanese with type 2 diabetes mellitus.

1.2.2 Specific Objectives:

-To assess plasma lipid peroxidation (by measuring malondialdehyde) in Sudanese patients with type 2 Diabetes mellitus in comparison with a healthy control group.

-To measure the plasma levels of antioxidant vitamins (A, E, C) and zinc in Patients with type2 Diabetes mellitus in comparison with a healthy subjects control group.

-To assess the relationship between the plasma levels of Malondialdehyde, Antioxidant vitamins (A, E and C), lipid profile and zinc with:

a. Glycated hemoglobin (HbA1c).

b. Body mass index.

c. Duration of the disease.