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CORRELATION BETWEEN OXIDATIVE STRESS AND GLYCATED HEMOGLOBIN AND LP (A) IN PATIENTS WITH DIABETES MELLITUS

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ABSTRACT

Oxidative stress (OS) is well defined as an imbalance between free radicals and antioxidants defense in human body which can be lead to inflammation across the body and its serious particularly in heart and brain. In this cross-sectional study, blood samples were collected from 40 type 1 diabetes (T1DM) and 60 type 2 (T2DM) compared with 50 healthy subjects as controls, glycation and lipids profiles were measured, GPx and SOD antioxidants enzymes were measured as well as MDA and Lp(a) were measured and compared across study groups. Glycemic, Lp(a), GPx, SOD and MDA were high in patient than controls ($p<0.001$). In addition, Lp(a), GPx and MDA were higher in T2DM than in T1DM ($p<0.05$). Moreover, GPX and MDA correlates with FPG and HbA1c in T1DM and T2DM ($p<0.05$), and SOD was significantly correlated with FPG and HbA1c in T2DM ($p<0.05$). furthermore, Lp(a) correlates with FPG, HbA1c, GPx, SOD MDA in T1DM and T2DM ($p<0.01$). In conclusion, antioxidant levels were lower in patients with diabetes compared to healthy subjects, patients with diabetes have a high risk of developing and progression of different vascular diseases correlated with hyperglycemia, hyperglycemia and high lp(a) were correlated with low antioxidants levels.

KEYWORDS: Oxidative stress, OS, T1DM, T2DM.

INTRODUCTION

Oxidative stress (OS) is considered as an imbalance between increasing levels of reactive oxygen species (ROS) and antioxidant levels, leading to possible damage in many tissues.[1] Excess ROS can cause increased OS stress, which has been linked to inflammation and other diseases such as cancer, neurological disease, and atherosclerosis.[2] Because diabetes is associated with increased production of ROS and free radicals, as well as decreased antioxidant levels, enhanced oxidative stress is well recognized as a major component in the development and progression of diabetic problems. OS can have substantial repercussions, especially in T2DM patients with high insulin resistance, by disrupting the insulin-signaling pathway and impairing beta cell function in the pancreas. As a result, OS is assumed important in the evolution of diabetic problems.[3,4]

The generation of reactive oxygen-free radicals have been suggested with different mechanisms. The main source of free radicals production was suggested glucose oxidation pathway, so in the diabetes, free radicals levels were higher than in healthy subjects. In the other hands, the defense mechanisms with antioxidants include both enzymatic and non-enzymatic pathway were lower in diabetes because of high free radicals. Vitamins A, C, and E, glutathione, and the enzymes superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase are all examples of antioxidants. They operate together to combat distinct types of free radicals in a synergistic manner. [5,6]

This study was undertaken to investigate the level of two antioxidant enzymes in T1DM and T2DM compared to healthy subjects, because it was hypothesizing that free radicals and ROS were increased in diabetes.

METHODS

This is a cross sectional study processed in different hospitals and diabetes centers around Khartoum, Sudan. A 60 T2DM (34 males) and 40 T1DM (27 males) were enrolled and compared with 50 healthy subjects (30 males) as control group. Inclusion criteria: diabetes selected as fasting plasma glucose (FPG) ≥ 7.7 mmol/l and HbA1c ≥6.5%. exclusion criteria: patients with acute illness like severe liver or kidney diseases, endocrine interfere with diabetes, anemic, and who use antioxidants supplements. Ethical clearance was taken from ministry of health, research ethical committee. An informed consent was signed by all contributors before sample collection.

Biochemical parameters: Fasting blood samples were collected from participants and FPG and lipid profiles (Total cholesterol, triglyceride, HDL, and LDL) were measured with a Hitachi 704 autoanalyzer. Lp(a) were measured based on the immunoturbidimetric method using same automated analyzer.[7-10] Malondialdehyde (MDA) measured same to protocol mentioned before.[11] GPx and SOD enzymes were measured.[12]

Statistical analysis: To analysis of data, SPSS version 19 was used. Analysis includes ANOVA, t-test and chi-square. $p<0.05$ consider significant.

RESULTS

Table shows comparison of demographic and biochemical profiles between study groups, in which, age, gender, and lipid profiles there were no significant differences ($p>0.05$).In addition, the period of diabetes was increased in T1DM than T2DM ($p<0.001$). Moreover, FPG, HbA1c, Lp(a), GPx, SOD and MDA were high in patients both groups (T1DM & T2DM) than in controls ($p<0.001$). Furthermore, Lp(a), GPx and MDA were higher in T2DM compared to T1DM ($p<0.05$).

Correlation between glycemic and lipid profiles and Lp(a) with antioxidant enzymes (GPx & SOD) and MDA were shown in table 2, GPX and MDA were significant correlates with FPG and HbA1c in T1DM and T2DM ($p<0.05$), in addition, SOD was significantly correlated with FPG and HbA1c in T2DM ($p<0.05$). Moreover, Lp(a) was significantly correlated with FPG, HbA1c, GPx, SOD MDA in T1DM and T2DM ($p<0.01$).

Table 1: Demographic and Biochemical characteristics of study groups.

	Type 1 diabetes n= 40	Type 2 diabetes n= 60	Controls n= 50	P value
Age (years)	45±3.5	46±7.2	45±3.4	0.53
Gender (male, female)	27, 13	34, 26	30, 20	0.55
Period (years)	22.8±8.2	6.1±3.3**	-	<0.001*
FPG (mmol/l)	9.1±2.5	9.2±3.2	4.5±1.4	<0.001*
HbA1c (%)	8.1±2.3	8.3±2.9	5.0±1.1	<0.001*
TC (mmol/l)	4.3±1.9	4.4±2.4	3.9±1.0	0.36
TG (mmol/l)	1.4±0.8	1.5±0.9	1.2±0.4	0.10
LDL (mmol/l)	2.4±1.0	2.5±1.1	2.1±0.5	0.06
HDL (mmol/l)	1.6±0.7	1.6±1.0	1.9±0.5	0.09
Lp(a) (mg/dl)	32.1±6.9	35.8±9.2**	19.1±9.5	<0.001*
GPx (U/l)	115.4±18.8	104.3±16.7**	131.8±19.9	<0.001*
SOD (U/l)	8.1±1.8	7.8±1.2	12.1±2.7	<0.001*
MDA (mg/dl)	0.9±0.2	1.1±0.4eeee	0.5±0.1	<0.001*

* significant compared to controls (p<0.001). ** significant compared to T1DM (p<0.05).

Table 2: Correlation between oxidative stress biomarkers with FPG and HbA1c.

	Type 1 diabetes			Type 2 diabetes		
	GPx	SOD	MDA	GPx	SOD	MDA
FPG (mmol/l)	0.41*	0.31	0.41*	0.49*	0.38*	0.42*
HbA1c (%)	0.43*	0.33	0.57*	0.47*	0.43*	0.68*
TC (mmol/l)	0.16	0.19	0.19	0.18	0.20	0.28
TG (mmol/l)	0.03	0.02	0.04	0.02	0.06	0.09
LDL (mmol/l)	0.04	0.03	0.09	0.10	0.09	0.11
HDL (mmol/l)	-0.09	-0.06	-0.05	-0.17	-0.14	-0.13
Lp(a) (mg/dl)	0.40*	0.39*	0.72**	0.5*	0.48*	0.78**

* significant (p<0.05). ** significant (p<0.01).

DISCUSSION

In this study, the correlation between OS selected biomarkers with Lp(a) and HbA1c was examined. MDA was significant correlated with Lp(a), HbA1c and FPG, moreover, GPx and SOD were correlated directly with Lp(a). According to diabetes trial researches, hyperglycemia is the main factor that can be lead to many complications including macrovascular and microvascular complications.[13]

It's well documented in clinical and experimental studies regarding OS in progression of diabetes complications; in diabetes, glucose oxidation, nonenzymatic glycation of proteins, and subsequent oxidative breakdown of glycated proteins produce a disproportionate amount of free radicals. Damage to cellular organelles and enzymes, increased lipid peroxidation, and the development of insulin resistance can all result from abnormally high amounts of free radicals and a concurrent drop in antioxidant defense mechanisms. These oxidative stress effects may contribute to the development of diabetes complications.[14-18]

In the present study, the antioxidant levels were lower in the patients with diabetes both types than in controls, this indicates the patients were at risk to develops a vascular complications especially cardiovascular diseases, because severity of oxidative stress support the pathogenesis of atherosclerosis and then diabetes chronic complications, tis finding agree with previous studies. This is supported by the results of Lp (a), because its significant high particularly in T2DM, and its well documented it is an independent risk factor indicating early developing of vascular disease.[19-31]

The patients with T2DM were more affect with the strongest of OS than T1DM, because the level of ROS increased in patients with diabetes was due to decrease in destruction by antioxidant enzymes levels, this agree with Pham-Huy and his team.[32]

The generation of these reactive oxygen-free radicals has been linked to a number of pathways. The main source of free radicals is thought to be glucose oxidation, so patients with diabetes especially T2DM need to control their glucose level and prevent hyperglycemia because it is play a critical role in the elevated levels of free radical like ROS.[4]

Among limitation of the current study, low sample size and monitoring of diabetes different stages, another study with large populations was recommended to cover different aspects of relation between antioxidants and free radical in patients with diabetes.

In conclusion, antioxidant levels were lower in patients with diabetes compared to healthy subjects, patients with diabetes have a high risk of developing and progression of different vascular diseases correlated with hyperglycemia, hyperglycemia and high lp(a) were correlated with low antioxidants levels.

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