



Effect of Type 2 Diabetes Mellitus on Extracellular Superoxide Dismutase: Without Complications among Iraqi Patients

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Received in: 22/March/2016, Accepted in: 5/April/2016

Abstract

The current study includes (130) T2DM patients (group P) [51 males and 79 females with an ages range (35 to 55) and ages mean 49.89 years], they are sub-grouped into three categories according to their HbA1c value. patients with HbA1c less than 7 are considered as good controlled diabetic patients (30 patients) (group P1), while patients with HbA1c between 7 and 8 are considered as medium controlled diabetic patients (40 patients) (group P2), and the patient whom their HbA1c more than 8 are considered as uncontrolled diabetic patients (50 patients) (group P3). The patients group results are compared to control healthy subjects (35 subjects) (group C) [14 males and 21 Females with age range 45.51 years] matched for age, gender and BMI were included in the study. Patients and controls groups were characterized in terms of age (year), duration of DM (year), body mass index (BMI) (Kg/ m²), serum insulin (μ IU/ml), fasting serum glucose (FSG) (mg/dl), Homeostatic model assessment (HOMA) parameters using HOMA2 calculator, MDA (mmol/L) using TBA reaction method, and EC-SOD activity (U/ml), using riboflavin/NBT method. were measured for patients and control subjects. The HbA1c, FSG, FSI and I.R have been found to be significantly higher in diabetic patients group (P) in comparison to group C. The HOMA parameters (S% and β %) have been found to be significantly higher in group C as compared to diabetic patients group (group P), serum specific SOD activity, EC-SOD activity found to be significantly higher in control group C in comparison to patients group P. Serum MDA level showed a significantly higher value in diabetic patients group P in comparison to control group C. The FSG, FSI and I.R have been showed that they are increased as HbA1c increase, i.e. these parameter were higher in group P3 compared with group P2, group P1 and group C. HOMA parameters (S% and β %) have shown a significant decrease as HbA1c increase, i.e. these parameter were lesser in group P3 than group P2, and were higher in group P2 than group P1, although these parameters were lower in patients group P than control group C. and serum EC-SOD activity were decreased as HbA1c increase, i.e. SOD activity, specific SOD activity and serum EC-SOD activity were found to be significantly higher in group P1 comparing with group P2 and P3, while serum MDA level in group P3 was significantly higher than group P2, and P1. The serum MDA level in group P1 and group P2 showed a significant positive correlation with age. In group P3, MDA showed a significant negative correlation with serum Cr level, while, a significant positive correlation was observed with age, duration of DM, and HbA1c.

We can conclude that the T2DM patients have a risk of oxidative stress due to increasing the level of serum MDA and decreasing EC-SOD activity. The HbA1c value between 7 to 8 % can not be considered as an acceptable HbA1c value, due the severing of oxidative stress rising manifested clearly in this patients group.

Keywords: T2DM; SOD; EC-SOD; MDA; hyperglycemia.

1. Introduction

Diabetes mellitus (DM) is a metabolic disorder; the patients with DM are suffer from abnormally hyperglycemia. The cause of DM is either the pancreas dose not produces insulin or the cells do not response to the insulin secreted or both [1]. As these disorders are progresses that can be lead to many complications like cardiovascular disease, retinopathy, nephropathy and ulceration [2]. Symptoms hyperglycemia include thirst, polyuria, polydipsia, unexplained weight loss, sometimes with polyphagia, and blurred vision [3]. DM is likely to be underreported as a cause of death simply because diabetes leads to many complications that ultimately cause death. DM can be classified into four types [3]:

- I. Insulin-Dependent Diabetes Mellitus (IDDM) or Type I Diabetes Mellitus (T1DM): In T1DM patients there is no endogenous insulin Secretory capacity and they depend on injected insulin to prevent ketosis and sustain life.
- II. Non-Insulin-Dependent Diabetes Mellitus (NIDDM) or Type II Diabetes Mellitus (T2DM): In this type insulin levels may be normal, elevated, or depressed; hyperinsulinemia and insulin resistance characterize most patients. These patients do not need insulin treatment to survive. Most patients with this form of DM are obese, and obesity itself causes some degree of insulin resistance.
- III. Gestational diabetes mellitus (GDM): is a carbohydrate intolerance of variable severity with onset or first recognition during the pregnancy.

Free radicals are atoms or molecules with an unpaired electron and they are produced by living organisms as a result of normal cellular metabolism pathways and environmental factors, such as cigarette smoke or air pollutants [4 & 5]. The most common free radicals are superoxide ($O_2^{\cdot-}$), hydroxyl ($\cdot OH$) and peroxynitrite ($ONOO^{\cdot-}$). Free radicals are important intermediates in many natural processes such as cytotoxicity, neurotransmission and phagocytosis [6]. Due to their electron pair, free radicals are highly reactive and can react fastly with other molecules to capture the needed electron and thus gain stability. That leads to chain reaction, once when it is started it can cascade and finally leads to a disruption of the living cells [7].

Antioxidants are the molecules capable of stabilize or deactivate free radicals before they attack living cells. Antioxidants can be considered a critical molecules for maintaining optimum health and wellbeing. The most common antioxidant systems are enzymatic antioxidant system like superoxide dismutase and glutathione reductase, and nonenzymatic antioxidants system such as C and E vitamins [8].

From the above we can say free radicals are normally formed in the living cells and the body response to the harmful effect of these radicals by its antioxidant systems, so in the ordinary state there is a balance between oxidants and antioxidants, any shift from this equilibrium regardless increasing production of radicals or any defect in the AO systems may be present, that leads to produce a condition known as “oxidative stress” [9]. That plays important role in the development of vascular complications in DM particularly T2DM [10]. Free radical formation in DM by non-enzymatic glycation of proteins, glucose oxidation and increased lipid peroxidation lead to damage of AO enzymes [11].

Extracellular-superoxide dismutase (EC-SOD) is a secretory glycoprotein located in blood vessel walls at high levels and may be important in the antioxidant ability of vascular walls [12].

EC-SOD has been studied in low extent in DM, some studies have been reviewed:

In a genetic study presented by Fumiaki Kimura et al, 2003, serum EC-SOD has been evaluated in T2DM patients to assess whether increased EC-SOD concentration is associated with the development of diabetic vascular complications, they found a strong relationship between the serum level of EC-SOD and the severity of both microvascular and macrovascular diabetic complications [13]. EC-SOD has been studied in T2DM with a correlation to insulin resistance, by T Adachi *et al*, 2004, they found the EC-SOD level was strongly and positively associated to homeostasis model assessment-insulin resistance (HOMA.IR) [12]. W. Ajam et al, 2012, introduced a work involves estimating the oxidative Status in post-menopausal women with T2DM and the EC-SOD was one of the oxidative stress markers, they found an elevation of (EC-SOD) concentrations [14]. According to proteinuria the patients in study of Armin Rashidi, *et al*, 2009, has been classified into groups, to evaluate the oxidative status in T2DM, EC-SOD levels was both significantly associated with proteinuria [15]. EC-SOD levels were in GDM by S. Kharab, 2010, And it was significantly decrees in those women [16]. So our study was aimed:

Studying the effect of T2DM on the oxidative stress by measuring:

Serum MDA level as an oxidants marker and EC-SOD as an antioxidants in patients of T2DM Iraqi patients (without any complications).

2. Subjects, Materials and methods

2.1 Study population

Patients enrolled in the present study were subdivided into Iraqi T2DM (130) subjects, they clinically diagnosed with T2DM, all of them were diagnosed proven under the supervision of specialists, and (35) healthy subjects as a control. All subjects were selected from the National Diabetes Center for Treatment and Research, Al-Mustassryia University, Baghdad, Iraq during the period from November, 2014 to May, 2015.

2.2. Sampling

After an overnight, fasting venous blood samples were collected aseptically from the subjects via venipuncture, (5ml) was collected and divided into two parts, (4ml) was kept in plain tubes without any anticoagulant at room temperature for half hour. The tube then was centrifuged ($3000 \times g$) for 15min. The clear serum was pipetted into clear dry eppendorfs and stored at (-20 C°) until used for different investigations, while (1ml) of the whole blood was kept in tube with EDTA anticoagulant and used in the estimation of HbA1c.

2.3. Exclusion criteria

Any known disease except DM including T1DM and GDM, also patients T2DM and treat with insulin are excluded. The patients who take any supplement are excluded.

2.4. Inclusion criteria

Any known disease other than T2DM including T1DM and GDM, also T2DM patient and treated with insulin are excluded. The patients who take any supplements are excluded.

2.5. Design

The patients were subdivided into three groups according to their HbA1c test value. Patients with (HbA1c value less than 7) were considered good controlled T2DM according to universal guide, while, patients with (HbA1c value from 7-8) were involved within middle controlled T2DM. Patients with (HbA1c value more than 8) were included within uncontrolled T2DM.

2.6. Methods

The medical history of each patient was taken regarding, age, duration of DM and body mass index (BMI), and if the patient was smoker or alcoholic was reported.

Glycated hemoglobin (HbA1c) was determined by using Stanbiom Glycohemoglobin kit, Germany. Fasting serum glucose level was measured using an enzymatic colorimetric method, using spinreact kit, Spain. Fasting serum Insulin level (FSI) was measured spectrophotometrically. HOMA index were measured by HOMA-2 program. EC-SOD activity was assayed in serum by quantifying the inhibition of NBT transformation to formazan, after pooling the collecting serum. The EC-SOD activity was calculated by estimating the amount of generated superoxide anions which scavenged by SOD (the inhibitory level of formazan color development) [17]. The results were expressed as U/ml. Serum MDA was estimated using the thiobarbituric acid (TBA) reaction [18]. Determination of chromium has been done using atomic absorption spectrophotometry [GBC 933 Plus, Japan].

2.7. Statistical analysis

"IBM SPSS (Version 20) has been used for the analysis and presentations of data. Quantitative data were presented as form of Mean and Standard Deviation (SD). Differences in means between study groups were tested for statistical significance with independent samples t-test. One-way analysis of variance (ANOVA) was used to compare the parameters among groups followed by post hoc test.

3. Results

The patients group (P) has shown a highly significant increase in FSG, HbA1c, (FSI) level, HOMA2-IR, and serum MDA when comparing to control group (C), while no significant increase in BMI between P and C groups (Table 1).

Group P has been shown a significant decrease in HOMA- β %, HOMA_S%, serum Cr level and EC_SOD in comparison to group C (Table 1).

FSG, FSI, HOMA2-IR, and serum MDA were increased as the HbA1c increased, i.e. these parameters were higher in group P3 than group P2, in group P2 and were higher than group p1, although these parameters were higher in patients group P than control group C.

HOMA- β %, HOMA_S%, serum Cr level and EC_SOD were decreased as the HbA1c increased, i.e. these parameters were lesser in group P3 than group P2, and were higher in group P2 than group p1, although these parameters were lower in patients group P than control group C.

EC-SOD was assayed in serum of patients and control subjects using pooling method and the results revealed that the EC-SOD activity in control group was higher than patients group (12.43 vs. 10.05 U/ml) (Table 3). Also, EC-SOD activity was decreased as HbA1c increase in the groups, i.e. EC-SOD activity in controlled patients group was higher than medium controlled group and both were higher than uncontrolled group (11.78, 10.5 and 7.86 U/ml), Table (3).

T2DM is a chronic disease characterized mainly by a disorder in the metabolism of glucose associated with a lowering of the ability of tissues to respond to insulin secreted (insulin resistance). The resulting hyperglycemia damages nerve cells and blood vessels through the body, leading to micro-vascular diseases such as nephropathy, neuropathy and retinopathy. Furthermore, the risk for cardiovascular disease (CVD) is considerably elevated in patients with T2DM compared to the general population. As a consequence, T2DM represents a major public health problem [19]. DM is an endocrinological disease associated with a severe metabolic and oxidative stress problem. In the presence of free radicals, glucose can undergo a process called auto-oxidation. Studies show that oxidative stress has the greatest role in developing complications [20].

Results showed in Table (1), indicated significant increase in HbA1c, FSG, FSI, and HOMA2-IR in group (P) in comparison with group (C). These findings are in agreement with previous study of Arie Srihardyastutie *et al*, 2015 [21]. There are many studies also has pointed out that the increase in the level of blood glucose is associated with an increase in incidence of cardiovascular disease and the high level of glucose, (hyperglycemia) leads to increase the generation of free radicals and then activates oxidative stress and would be an important cause of heart and blood vessels disease [22]. Insulin is a peptide hormone secreted by β -cell of the pancreatic islet of Langerhans for maintaining normal blood glucose level by facilitating cellular glucose uptake [23]. The main pathophysiological feature of T2DM is impaired insulin secretion and increased insulin resistance [24]. Insulin resistance is defined as reduced sensitivity of target organ to the insulin biological effects or a condition in which the body's muscle, fat, and liver cells do not use insulin effectively [25]. Insulin resistance has a correlation with the decrease of fasting insulin value. Because of insulin function keeps maintain the glucose blood homeostasis by facilitating cellular glucose uptake, so the increase of serum glucose will induce β -cell pancreatic to increase insulin secretion, but unfortunately, pancreatic Langerhan fail to process proinsulin as precursor to be mature insulin [21 and 26]. This will affect the increase of blood glucose value. The more FSG value increases, the more HbA1c value increase. Some researchers report that the glycation occur over span of 90-120 red blood cell day life, so HbA1c test is a biochemical test that reflects the average level of glucose in the blood over a three month period by measuring the proportion of hemoglobin that has become glycosylated [27]. It indicates that the increase of serum glucose values contributes to bind glucose-hemoglobin more (glycation reaction) and

gives consequently to make higher value of glycosylated hemoglobin (HbA1c) [21], that can explain the results obtained in the current study, the increase of FSG and FSI as HbA1c increase, i.e. FSG and fasting serum insulin in group P3 was higher than group P2 and that higher than group P1, Table (2). As shown in Table 1 HOMA2-S (%) and HOMA2- β cell (%) showed significant decrease in group (P) in comparison with group (C). These findings are in agreement with previous study of Al-Hakeim *et al.*, 2012; [28].

β -cell mass adapts to an increased metabolic load which caused by obesity and the inherent insulin resistance. T2DM in humans models is accompanied by a progressive decrease in beta cell mass. As a result, the body can no longer able to adapt to any increase in metabolic load, including insulin resistance related with obesity. This β -cell loss elevates from a marked increase in β -cell apoptosis, which far outweighs modest increases in β -cell replication [29]. As the T2DM state progresses, the situation worsens; the incidence of β -cell replication decreases and the β -cell population declines. The increased β -cell apoptosis in T2DM is further exacerbated by the formation of amyloid plaque deposits in islets [30]. Eventually, in the most severe cases, a "point of no return" β -cell mass can be reached and a permanent T2DM state arises that should be treated with insulin replacement therapy [31]. The brain processes information from adiposity signals such as insulin and leptin, which circulate in proportion to body fat mass, and integrates this input with signals from nutrients such as FAs then sends in response signals to control feeding behavior and substrate metabolism in ways that promote homeostasis of both energy stores and fuel metabolism. Misalignment of food intake with the expression levels of neuroactive peptides, such as leptin, could create metabolic imbalances that alter insulin sensitivity [32 and 33].

The importance of chromium (Cr) for glucose metabolic regulation has been noticed in clinical states of relatively severe Chromium deficiency, which characterized by impaired glucose tolerance, hyperglycaemia and lipid disorders [34]. The current study shown a significant decreasing in chromium concentration in patient group as compared to control group, and this lowering was manifested as HbA1c increased (Table 1 and Table 2). Cr is one of the essential nutrients whose metabolism changes during DM. Cr is a co-factor in the action of insulin and it potentiates the insulin action. As such Cr may improve blood glucose concentrations in individuals with a tendency towards blood glucose fluctuations related with DM (hyperglycaemia). Thus, it may not be surprising to find an inverse relationship between serum Cr and blood glucose control [35]. Hyperglycaemia and high levels of insulin increase Cr excretion, so low serum concentration of Cr seen in the DM patients has been attributed to insulin resistance, hyperglycaemia and osmotic diuresis results to from glycosuria, which increase urine Cr excretion. Hyperinsulinemia and insulin resistance may be associated with a reduce in insulin receptors, reduced insulin binding, or post-insulin- receptor signaling defects [36].

MDA is a highly toxic by-product formed partly by oxidation derived from free lipid radicals, and studies shown considerably raised concentrations in DM. MDA reacts both irreversibly and reversibly with proteins and phospholipids with profound effects [37].

In this study we have observed that MDA levels as a lipid peroxidation product and a marker of oxidative stress, was highly statistically significant increase in between group P and control group (C) Table (1), these results are in agreement with the findings of Mahreen *et al.*, 2010 and A. Z. Hassan, 2011[38 and 39]. The most probable causes for the increased MDA levels in serum of diabetic groups may be due to the abnormal lipid metabolism. Hyperinsulinemia and hyperglycemia may enhance the production of free radicals such as MDA and induce oxidative stress that may also contribute to increased risk for coronary artery disease in diabetes [40].

Hyperglycemia can induce oxidative stress by several different mechanisms. Autooxidation of glucose and the non enzymatic glycation of proteins generate superoxide (O_2^-) [41]. Comparative evaluation of the serum levels of MDA was done in patients of diabetes mellitus

with and without complications by B.Mandal, *et al*, 2010. It was highly significant increase in cases of DM with complications in comparison to cases of diabetes mellitus without complications indicate more association of oxidative stress with diabetic complications [42]. Free radical interacts in arachidonic acid metabolism forming a toxic endoperoxidase. The lipid peroxide thus formed stimulates the synthesis of cyclooxygenase, prostaglandin and thromboxane which in turn causes increased platelets aggregation leading to vascular complications [43]. EC-SOD is a secretory glycoprotein located in blood vessel walls at high levels and may be important in the antioxidant capability of vascular walls [12]. EC-SOD with an affinity for heparan-like substances, and it is the principal enzymatic scavenger of superoxide in the extracellular space [44]. The vascular wall contains abundant amounts of EC-SOD, one of the SOD isozymes produced and secreted to the extracellular space by fibroblasts and smooth muscle cells [45].

In current study EC-SOD showed a highly significant decrease in T2DM as compared to healthy subjects, and this decrease was intensified as HbA1c increased (Table 3).

As shown in Table 4, MDA in group P1 and group P2 showed a significant positive correlation with age (table 4, figure 1 and figure 2).

In group P3, MDA showed a significant negative correlation with serum Cr level, while a significant positive correlation was observed with age, duration of DM, and HbA1c (Table 4 and Figure 3).

Conclusions

Based on the findings of the present study, it is possible to reach the following most important conclusions:

- ❖ T2DM have a risk of oxidative stress due to increasing the level of serum MDA and decreasing Extracellular superoxide dismutase activity.
- ❖ The HbA1c value between 7 to 8 % can not be considered as an acceptable HbA1c value, due the severing of oxidative stress rising manifested clearly in this patients group.

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Table (1): Mean \pm S.D in patients and control groups.

Parameter	Group (C) (n=35)	Group (P) (n=130)	P value
Age (years)	45 \pm 6.4	49 \pm 6.2	0.001
Duration of DM (years)	—	6.23 \pm 3.72	—
BMI (kg/m ²)	27.06 \pm 3.8	30.62 \pm 6.9	N.S.
FSG (mg/dL)	87.31 \pm 9.93	197.61 \pm 73.7	0.000
Insulin (μ U/ml)	11.89 \pm 1.9	16.86 \pm 4.1	0.000
HOMA2- β cell (%)	140.42 \pm 34.4	49.53 \pm 27.3	0.000
HOMA2-S (%)	67.36 \pm 17.0	40.29 \pm 13.1	0.000
HOMA2-IR	1.51 \pm 0.25	3.38 \pm 16.6	0.004
Cr (μ g/L)	0.44 \pm 0.03	0.034 \pm 0.01	0.000
MDA (mmol/L)	1.232 \pm 0.53	1.91 \pm 0.55	0.000

P < 0.05: Significant.

Table (2): Mean \pm S.D in controlled DM, medium controlled DM, uncontrolled DM, and control groups.

parameter	Group (C) (n=35)	Group (P1) (n=30)	Group (P2) (n=40)	Group (P3) (n=60)	P value
Age (years)	45 \pm 9.50	48 \pm 6.30	50.8 \pm 4.2	49 \pm 5.2	N.S
Duration of DM (years)	00.00	3.8 \pm 82	4.48 \pm 8.12	8.6 \pm 11.3	0.005
BMI (kg/m ²)	27.07 \pm 3.89	30.91 \pm 5.62	30.85 \pm 9.36	30.33 \pm 5.64	N.S
FSG (mg/dl)	87.31 \pm 9.93	153.90 \pm 35.11	163.83 \pm 47.70	241.98 \pm 77.52	0.000
Insulin (μ U/ml)	11.89 \pm 1.86	13.62 \pm 13.62	16.4 \pm 3.29	18.79 \pm 4.18	0.000
HOMA2- β cell (%)	140.42 \pm 34.42	57.35 \pm 23.66	62.00 \pm 30.23	37.29 \pm 21.61	0.000
HOMA2-S (%)	67.37 \pm 16.99	52.25 \pm 9.89	43.29 \pm 9.62	32.30 \pm 11.03	0.000
HOMA2-IR	1.51 \pm 0.25	1.97 \pm 0.35	2.42 \pm 0.52	4.73 \pm 10.41	N.S
Cr (μ g/L)	0.44 \pm 0.05	0.05 \pm 0.00	0.03 \pm 0.002	0.026 \pm 0.001	0.000
MDA (mmol/L)	1.23 \pm 0.53	1.88 \pm 0.57	1.92 \pm 0.43	1.92 \pm 0.61	0.000

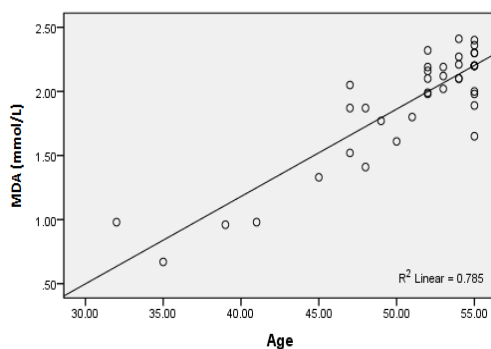
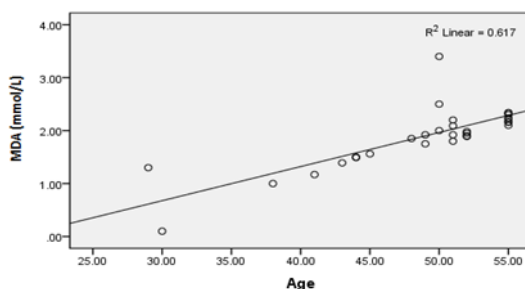
P* < 0.05; *P* < 0.01; ****P* < 0.001; no asterisk: *p* \geq 0.05.

Table (3): EC-SOD activity in total patients (P), controlled DM (P1), medium controlled DM (P2), uncontrolled DM (P3), and control groups (C).

Group parameter	Control group (C) (n = 35) (pooled)	patients group (P) (n = 130) (pooled)	Controlled DM (P1) (n = 30) (pooled)	Medium Controlled DM (P2) (n = 40) (pooled)	uncontrolled DM (n = 60) (pooled)
Ec-SOD (U/ml)	12.43	10.05	11.78	10.5	7.86

Table (4): Pearson correlation analysis of MDA in group P1, P2 and P3.

Parameters	MDA (mmol/L)					
	r value group (P1)	P value Group (P1)	r value group (P2)	P value Group (P3)	r value group (P3)	P value Group (P3)
Age (year)	.785**	0.000	.886**	0.000	.737**	0.000
Duration (year)	.128	0.176	.244	0.128	.401**	0.002
HbA1c	.016	0.450	-.119	0.464	.379**	0.003
FSG (mg/dl)	-.019	0.543	.080	0.625	.066	0.616
Insulin (μ U/ml)	.145	0.347	.250	0.120	.055	0.677
HOMA2- β cell (%)	.042	0.765	-.058	0.723	.005	0.972
HOMA2-S (%)	-.109	0.356	-.216	0.181	-.100	0.449
HOMA2-IR	.108	0.213	.270	0.091	.069	0.600
Cr (μ g/L)	-.017	0.076	.143	0.380	-.443**	0.000

**Figure (1): Significant correlation between MDA and age in group P1.****Figure (2): significant correlation between MDA and age in group P2.**

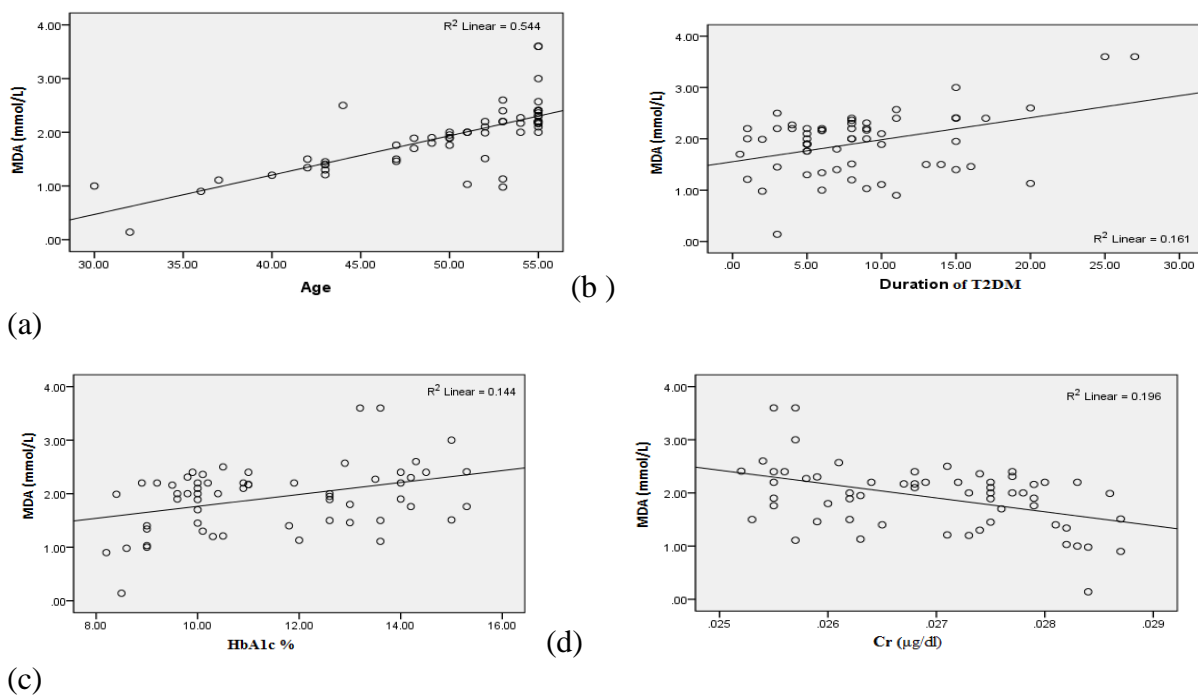


Figure (3): Significant correlation in group P3 between MDA and (a) age, (b) duration of DM, (c) HbA1c and (d) serum Cr level.

تأثير داء السكري النمط الثاني على السوبر أوكسيد ديسميوتيز بين المرضى العراقيين

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استلم في: 22/أذار/2016، قبل في: 5/نيسان/2016

الخلاصة

تتضمن هذه الدراسة (130) مريضاً بالسكري من النمط 2 المجموعة (71 ذكراً و 59 أنثى) تتراوح أعمارهم بين (30 - 55) سنة. تم تصنيفهم الى ثلاث مجاميع حسب نتيجة فحص السكر التراكمي لديهم، إذ المرضى الذين كانت نتيجة فحص السكر التراكمي لديهم أقل من 7% صنفوا على أنهم مجموعة مسيطرة (30) مريض، أما المرضى الذين كانت نتيجة فحص السكر التراكمي لديهم بين 7 الى 8% (40 مريض) صنفوا على أنهم مجموعة شبه مسيطرة على مستوى السكر و صنف المرضى الذين كانت نتيجة فحص السكر التراكمي لديهم أكثر من 8% (50 مريض) على أنهم مجموعة غير مسيطرة على مستوى السكري. النتائج المستحصلة من قياسات بعض المتغيرات في مصل مرضى السكري قورنت مع تلك المستحصلة من قياس ذات المتغيرات المقاسة في مصل مجموعة السيطرة التي تشمل (35) من الأصحاء (14 ذكر و 21 أنثى) الذين تتراوح أعمارهم بين (30 - 55) سنة.

تم جمع البيانات الديموغرافية للمرضى و الأصحاء وتمت مقارنتها و هي العمر (السنة)، مدة الإصابة بالمرض (السنة) و مؤشر كتلة الجسم (كغ/م²).

تم قياس المتغيرات السريرية لمجاميع المرضى ومجموعة السيطرة و تشمل مستوى الكلوكوز في المصل بعد الصيام (ملغم / دل) بإستعمال العدد المتوفرة تجارياً، مستوى الإنسولين في المصل بعد الصيام (مايكرو وحدة دولية / مل) بأستعمال طريقة طيفية، نسبة خلايا بيتا (%) (بوساطة نموذج هومو)، نسبة حساسية الإنسولين (%) (بوساطة نموذج هومو، مقاومة الإنسولين (%) (بوساطة نموذج هومو، كما تم قياس فعالية السوبر أوكسيد ديسميوتيز الخارج خلوي بطريقة تفاعل الريبوفلافين و حامض النايترو بلو تترازوليوم كما تم تقدير تركيز المالونيلداي ألددهايد بوساطة تفاعل جامض ترائي باي بيوتيرك.

أظهرت الدراسة زيادة معنوية في قيم مستوى السكر التراكمي (HbA1c)، مستوى الكلوكوز في المصل بعد الصيام (FSG)، مستوى الإنسولين في المصل بعد الصيام (FPI)، مقاومة الإنسولين (IR)، و مستوى المالونيلداي ألددهايد (MDA) في مرضى السكري (مجموعة P) مقارنة مع مجموعة السيطرة C. بينما أظهرت الدراسة نقصاناً معنوياً في قيم نسبة خلايا بيتا (β%)، نسبة حساسية الإنسولين (S%)، مستوى الكروم (Cr) و السوبر أوكسيد ديسميوتيز الخارج خلوي (EC-SOD) في مرضى السكري (مجموعة P) مقارنة مع مجموعة السيطرة C.

إذا ما قورنت النتائج وفقاً للتقسيم الفرعي الذي تم تطبيقه على المرضى فإن المتغيرات التالية أظهرت تناسبا طرديا مع السكر التراكمي أي أن قيمها في المجموعة P3 كانت أعلى من قيمها في المجموعة P2 أو المجموعة P1 أو مجموعة السيطرة C، المتغيرات هي (مستوى الكلوكوز في المصل بعد الصيام (FSG)، مستوى الإنسولين في المصل بعد الصيام (FPI)، مقاومة الإنسولين (IR)، ومستوى المالونيلداي ألددهايد (MDA) في المقابل المتغيرات التالية أبدت تناسبا عكسيا مع السكر التراكمي (HbA1c) أي أن قيمها في المجموعة P1 أعلى من المجموعتين P2 و P3 بل حتى أن قيمها في مجموعة C هي الأعلى، هذه المتغيرات هي نسبة خلايا بيتا (β%)، نسبة حساسية الإنسولين (S%)، مستوى الكروم (Cr).

في مجموعة P1 و مجموعة P2 أظهر تركيز المالونيلداي ألددهايد (MDA) علاقة إرتباطية موجبة مع العمر. بينما في مجموعة P3 أظهر تركيز المالونيلداي ألددهايد (MDA) علاقة إرتباطية سالبة مع مستوى الكروم (Cr)، بينما أظهر علاقة إرتباطية موجبة مع العمر، مدة الإصابة بمرض السكري، و مستوى السكر التراكمي (HbA1c).

أعتمادا على نتائج الدراسة الحالية يمكننا إستنتاج بأن مرضى السكري معرضين لخطر الإجهاد التأكسدي، و ذلك لزيادة تركيز المالونيلداي ألددهايد (MDA) و إنخفاض فعالية إنزيم السوبر أوكسيد ديسميوتيز الخارج خلوي (EC-SOD). كما أن مرضى السكري الذين تكون نتيجة مستوى السكر التراكمي (HbA1c) لديهم بين 7 إلى 8% لا يعدون شبه مسيطرين على حدة المرض بل إنهم متضررين سريريا بشكل كبير و يجب عليهم خفض قيمة السكر التراكمي إلى ما دون الـ 7% من خلال العلاج و النظام الغذائي.

الكلمات المفتاحية: داء السكري النمط الثاني، سوبر أوكسيد ديسميوتيز الخارج خلوي، فرط السكري.