

Blood lipid peroxidation (Malondialdehyde), thiol, taurine levels and oxidative stress in Saudi diabetic patients

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ABSTRACT

Diabetes mellitus is associated with derangements in the serum levels of several biochemical parameters, and type 2 *Diabetes mellitus* (T₂DM) is a risk factor for cardiovascular diseases (CVD). The existence of hyperglycaemia enhances oxidative stress. The depletion of antioxidants (taurine) as a defensive body mechanism may augment the risk of diabetic complications. This study aims to investigate the levels of antioxidants and oxidants in T₁DM, in T₂DM patient and T₂DM patients with cardiovascular diseases (CVD) among female Saudi diabetic patients.

Our study included 130 female subjects divided into four groups, group I (T₁DM), group II (T₂DM), group III (T₂DM with CVD) and group IV (Control). Fasting blood samples (six ml) were collected. Glucose, glucosylated haemoglobin (HbA_{1c}), cholesterol (C), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triacylglycerol (TAG), malondialdehyde (MDA), thiol, uric acid and nitric oxide (NO) levels were determined.

The results of this study showed that taurine levels were significantly lower in all patient groups as compared to controls ($p < 0.05$ for all parameters). Thiol level was significantly high in GIII. Both NO and uric acid were also significantly higher in all patient groups as compared to controls. Hypercholesterolemia, hypertriglyceridemia, high levels of LDL-c and MDA were detected in patients groups compared to control. Serum insulin level was significantly high in GII and GIII. All patients groups had significant hyperglycaemia compared to control.

The female Saudi diabetic patients in this study have a higher oxidative stress status due to the high level of the production of free radicals (nitric oxide) and lipid peroxidation (malandialdehyde) and lower level of antioxidants (taurine and uric acid) in concomitant with dyslipidemia which may be due to taurine and uric acid deficiency.

Key words: *Diabetes mellitus*, lipid peroxidation, oxidative stress.

INTRODUCTION

Diabetes mellitus (DM) is emerging as a major public health problem in Saudi Arabia in parallel with the worldwide diabetes epidemic, which is having a particular impact upon the Middle East and the third world. DM, especially type 2 is a polygenic disorder and the high consanguinity rate among Saudis may play a significant role in its prevalence. It has been reported that Saudis have unique genetic characteristics, which may explain in part the dramatic rise in the prevalence of diabetes (El-Hazmi *et al.*, 1995). The change in dietary habits consequently with regular consumption of large quantities of high caloric content food coupled with

more sedentary lifestyle and the traditional way of life has led to high obesity. Obesity is a strong risk factor for diabetes, especially in high-risk population (Elhadd *et al.*, 2007). *Diabetes mellitus* (DM) is characterized by hyperglycaemia which leads oxidative stress. DM is a risk factor for cardiovascular diseases and is also associated with derangements in oxidative status (Soliman, 2008). Depletion of body antioxidants may increase the risk of diabetic complications. Lipid peroxidation of cellular structures coupled with elevated oxygen free radicals generation, is thought to play an important role in atherosclerosis and microvascular complications of diabetes mellitus (Velazquez *et al.*, 1991). Cellular thiols have emerged as playing an

important role in the development of diabetic complications. The oxidation of the thiol groups in several peptides or proteins is specifically coupled with the reduction of other molecules. These thiol antioxidative peptides or proteins, play an important role in the cellular antioxidative defense as well as the regulation of cellular functions involving the thiol disulfide exchange (Liang and Pietrusz, 2007).

Taurine, 2-amino-ethane sulfonic acid $C_2H_7NO_3S$, plays an important role in stimulating glucose mediated insulin secretion and glucose metabolism (Militante *et al.*, 2000). In addition, taurine has been reported to protect against pathological conditions including cardiomyopathy (Redmond *et al.*, 1998). Intracellular depletion of taurine could disturb carbohydrate metabolism and promote chronic complications of diabetes (Militante *et al.*, 2000).

The present study aims to investigate the levels of antioxidants (taurine, uric acid and thiol) and oxidants (lipid peroxidation MDA and NO) in T_1DM and in T_2DM patient and T_2DM patients with cardiovascular diseases (CVD) among Saudi diabetic patients.

METHODS

Chemicals

Chemicals used for determination of plasma lipid peroxide (MDA) and serum thiol were purchased from Sigma-Aldrich (St Louise, MO, USA). Kits for determination of serum levels of glucose, HbA_{1c}, uric acid, total cholesterol (TC), TAG, LDL-C and HDL-C were purchased from Dade Behring (Buckinghamshire, UK). Insulin kit was purchased from Roche Diagnostics, GmbH, Mannheim, Germany). Nitric oxide kit was purchased from (Assay Designs, Ann Arbor, Michigan, USA).

Experimental Design

A total of 100 middle class female patients (40-60 years) attending Hypertension and Diabetes Hospital in Jeddah, Saudi Arabia were involved in this study. All controls and patients were diagnosed by the hospital physicians. They were divided into three groups: Group I (GI) included 27 female patients with type I diabetes (mean age \pm SE; 43.3

\pm 8.3 years, duration 8.5 \pm 0.5). Group II (GII) included 28 female patients with type II diabetes (mean age \pm SE; 47.3 \pm 2.2 years duration 8.0 \pm 0.8). Group III (GIII) included 45 female patient with type II diabetes and suffering of Cardio Vascular Disease (CVD) which was characterized by hypercholesterolemia and hypertension (mean age \pm SE; 49 \pm 3, duration 9.1 \pm 0.6). Also a control group was included consisting of 30 healthy age matching female subjects (mean age \pm SE; 45.6 \pm 3.2). All patients and controls were not suffering of high blood pressure. Exclusion criteria for patients included cardiomyopathy, serious organ disease, systemic illness, serious psychiatric illness and anticonvulsant therapy. The NIDDM patients were not taking any medicines other than oral anti-diabetic pills.

All these groups (female patients and control subjects) were examined, diagnosed and classified by the hospital physicians. All the patients gave written, informed consent and the study was approved by the Ethics and Research Committee.

Fasting blood samples (Six ml) were collected in two tubes, one with anticoagulant added. Blood samples were used for the determination of HbA_{1c}. Plasma samples were stored at -30° C, if not used immediately, until analysis. The plasma samples were thawed once and used for determination of taurine level using modified high-performance liquid chromatography (HPLC) (Frank and Powers, 2007), lipid peroxidation (malondialdehyde; MDA), glucose using Randox kit (Randox Laboratories, San Francisco, CA, USA). Plasma samples were subjected for determination of total thiol, insulin and nitric oxide (NO) levels. HbA_{1c} was determined using HPLC (John, 2003). Total TAG was determined using the Bicon kit (Bicon Diagnostik, Marienhagen, Germany). Serum TC, HDL-C and serum LDL-C were respectively determined using the bioMérieux kit (bioMérieux, Marcy l'Etoile, France).

Plasma levels of fasting blood sugar (FBS), HbA_{1c}, cholesterol, TAG, LDL-C, HDL-C, uric acid, plasma total thiol, plasma MDA and NO were estimated. Taurine was measured by a modified method using HPLC separation of the derivatised amino acids (Frank and Powers, 2007). It required

two mobile phase, mobile phase A consisted of 30 mmol / L potassium dihydrogen phosphate buffer with 0.4 % tetrahydrofuran adjusted to pH 7.0 with 4 mol / L KOH, and mobile phase B consisted of 50 % HPLC grade acetonitrile mixed with HPLC grade water. Derivatised amino acids were prepared as follows: Three-hundred μ l of plasma samples were prepared by adding 15 μ l of precipitating reagent (0.5 mol /L perchloric acid). After protein precipitation, the samples were vortexed for 3 min and stored at room temperature for 10 min then centrifuged at 1200 rpm for 5 min. To 135 μ l of cleared supernatant, 15 μ l of internal standard (norvaline 62.5 μ mol / L, Sigma) were added. The derivatised amino acids were separated on C18 column (100 mm \times 4.6 mm i.d, 5 μ m particle size) and C18 guard column (3.9 mm \times 20 mm, 5 μ m particle size). The chromatographic separation was performed at room temperature (22°C) and the flow rate of the mobile phase was 1.2 ml/ min throughout the analysis. Ultra Violet detection was used (instead of fluorescent) at 334 nm.

Statistical Analysis

Statistical analysis was performed using Social Package for Social Science (SPSS) software package (SPSS Inc, Chicago, IL, USA) for data analysis version 12 for windows. The data presented in this study are expressed as mean \pm SE. Student *t* test was used to determine the significance of the difference between groups. Data were also analysed using a one-way Analysis of Variance (ANOVA).

RESULTS

Table 1 and Fig. 1 show a highly significant low levels ($p < 0.01$) of plasma taurine level in GI and a significant low levels ($p < 0.05$) in both GII and GIII with a percent change of -66%, -40% and -39%, respectively as compared to control. Data shown in Table I and Fig 1 reveals a significant higher level ($p < 0.05$) of plasma thiol in T₂DM with CVD patients group (GIII) as compared to control. Also, data of Table I and Fig 1 demonstrated a significant high level ($p < 0.0001$) of NO concentration in all the studied groups compared to control. Also Table I and Fig 1 show a high level of uric acid by 22.3% in T₁DM group and a higher level (51.9% and 35.6%) in T₂DM and T₂DM with CVD groups respectively, as compared to control.

Data shown in Table 2 and Fig. 2 show an abnormal lipid profile, where TC is significantly high ($P < 0.05$) in GI and GII and a highly significant level ($P < 0.001$) in GIII compared to control. Serum LDL-C shows a higher levels (Table 2 and Fig 2) in GI, GII and GIII groups ($P < 0.02$, 0.05 and 0.001 respectively) as compared to control. The lipid pattern also showed a highly significant elevation in TAG (in GI and GIII $p < 0.005$ and GII $p < 0.05$) as compared to control. In addition, serum level of MDA showed a highly significant elevation ($p < 0.0001$) in all the studied groups compared to control.

As expected, fasting blood sugar and glycated hemoglobin (HbA1c) were significantly high in all the studied groups (Table 3 and Fig. 3) as compared to control. Meanwhile, insulin serum levels were significantly higher ($p < 0.001$) in both GII and GIII as compared to control.

The statistical analysis (Table 4) showed a highly significant low levels in taurine levels between control group ($p < 0.0125$) and GI and a significant lower levels between all the studied groups ($p < 0.025$) as compared to control.

DISCUSSION

Most people with diabetes in developed countries by 2025 will be aged 65 years or more and this disease affecting their productive years. Around 4 million deaths worldwide every year are attributable to complications of diabetes (Al-Nozha *et al.*, 2004). The most common secondary complications of diabetes are seen within the vascular system. Changes much like those seen with atherosclerosis in the brain and heart resulting in reduction of circulation to these areas and may result in stroke and heart attack respectively (Militante *et al.*, 2000). Saudi Arabia is among the top 10 diabetes suffering countries. The prevalence of diabetes in Saudi Arabia, according to the epidemiological survey of Al-Nozha and colleagues was 23.7% (Al-Nozha *et al.*, 2004).

Taurine, a free amino acid, found in high concentration in most types of animal tissues (Militante *et al.*, 2000) and in human tissues (Odetti *et al.*, 2003) has antioxidant properties. In the present study, plasma taurine level showed a highly

Table 1: Plasma Levels of Taurine and Serum Levels of Thiol, NO and Uric acid in all Groups

\ Groups	Parameters	Taurine umol/L	Thiol $\mu\text{mol/L} \times 10^{-4}$	NO $\mu\text{mol/L}$	Uric Acid mg/dl
Control n=30	Range	41.1-66.8	1.6-5.8	4.1-11.4	4.1-5.9
	Mean \pm SE	48.5 \pm 9.1	3.2 \pm 0.4	7.12 \pm 0.9	4.7 \pm 0.3
T ₁ DM (GI) n=27	Range	29.3-34.8	2.2-9.0	10.4-17.6	4.2-7.8
	Mean \pm SE	16.5 \pm 5.6	3.7 \pm 0.3	10.9 \pm 0.6	5.7 \pm 0.2
	P value <	0.01	NS	0.0001	0.05
T ₂ DM (GII)n=28	Range	17.8-33.8	1.4-8.0	9.6-17.4	4.30-10.10
	Mean \pm SE	28.8 \pm 1.7	3.8 \pm 0.3	13.5 \pm 1.0	7.1 \pm 0.3
	P value <	0.05	NS	0.0001	0.001
T ₂ DM+ CVD (GIII) n=45	Range	25.3-33.3	1.6-5.9	10.7-17.6	4.0-9.5
	Mean \pm SE	29.4 \pm 0.9	3.6 \pm 0.2	12.1 \pm 0.6	6.3 \pm 0.2
	P value <	0.05	0.05	0.0001	0.001

SE: Standard error.

% Change : Percent change from control.

P Value < 0.01 : highly significant.

CVD: Cardio Vascular Disease.

P Value < 0.05 : significant.

NS : non significant.

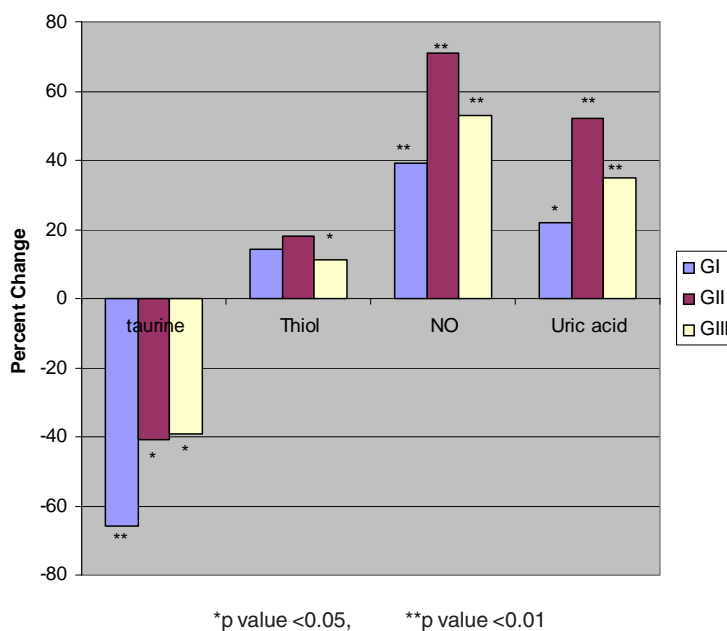
**Fig. 1: Percent change of taurine, thiol, NO and uric acid levels in all Groups**

Table 2: Serum Levels of Cholesterol, LDL, TAG, HDL and Lipid peroxide in all Groups

Parameters Groups	Cholesterol mg/dl	LDL mg/dl	TAG mg/dl	HDL mg/dl	MDA $\mu\text{mol}/\mu\text{L} \times 10^{-3}$
Control n=30 Range	151-176	100-110	165-179	30.9-45.5	2.11-6.9
Mean \pm SE	163.3 \pm 2.8	102.8 \pm 0.9	171.6 \pm 1.5	38.1 \pm 1.2	4.5 \pm 0.5
T ₁ DM (GI) n=27 Range	128-254	90-183	115-472	31-57	6.13-13
Mean \pm SE	183 \pm 8.0	130.3 \pm 8.3	272.1 \pm 39	42.6 \pm 1.9	8.3 \pm 0.7
P value <	0.05	0.02	0.005	NS	0.0001
T ₂ DM (GII) n=28 Range	138-250	91-175	114-400	31-64	7.98-14.9
Mean \pm SE	181 \pm 6.2	115.8 \pm 5.0	201.7 \pm 17.5	42.2 \pm 1.8	9.6 \pm 0.7
P value <	0.05	0.05	0.05	NS	0.0001
T ₂ DM+ CVD (GIII) n=45 Range	122-295	95-179	157-532	30-89	7.3-13
Mean \pm SE	200.6 \pm 5.9	132 \pm 4.9	267.2 \pm 26.2	41.5 \pm 1.7	8.7 \pm 0.5
P value <	0.001	0.001	0.005	NS	0.0001

SE : Standard error.

% Change : Percent change from control.

P Value < 0.02 : highly significant.

NS : Non significant.

P Value < 0.05 : significant.

P Value < 0.001: very highly significant.

CVD: Cardio Vascular Disease.

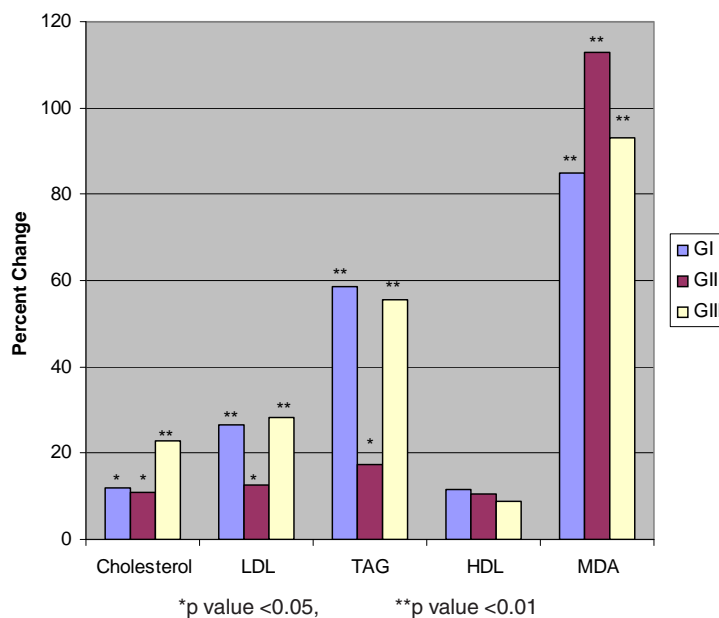
**Fig. 2: Percent change of serum cholesterol, LDL, TAG, HDL and lipid peroxide levels in all Groups**

Table 3: Levels of serum FBS, PPS, HbA_{1c}, Insulin and BMI in all Groups

Parameters Groups	FBS mg/dl	HbA _{1c} mg/dl	Insulin %	PPS μ U/ml
Control n=30 Range	75-111	91-130	5.9-9.5	3.99-8.3
Mean \pm SE	90.9 \pm 3.4	105.6 \pm 4.3	7.4 \pm 0.6	7.4 \pm 0.6
T ₁ DM (GI) n=27 Range	80-267	113-365	6.5-12.5	1.7- 8.9
Mean \pm SE	154.8 \pm 15.8	226.1 \pm 18.3	9.45 \pm 0.4	6.6 \pm 0.8
P value <	0.05	0.001	0.05	NS [†] !
T ₂ DM (GII) n=28 Range	78-187	129-416	6.5-13.2	15.7-68.9
Mean \pm SE	131.1 \pm 6.9	220.9 \pm 16.6	8.8 \pm 0.3	28.9 \pm 5.6
P value <	0.001	0.001	0.05	0.001
T ₂ DM+CVD (GIII) n=45 Range	78-297	90-348	6.7-13.8	15.4-52.9
Mean \pm SE	168.4 \pm 9.7	245.9 \pm 12.1	9.71 \pm 0.3	26.9 \pm 3.7
P value <	0.001	0.001	0.05	0.001

SE :Standard error.

% Change : Percent Change from control.

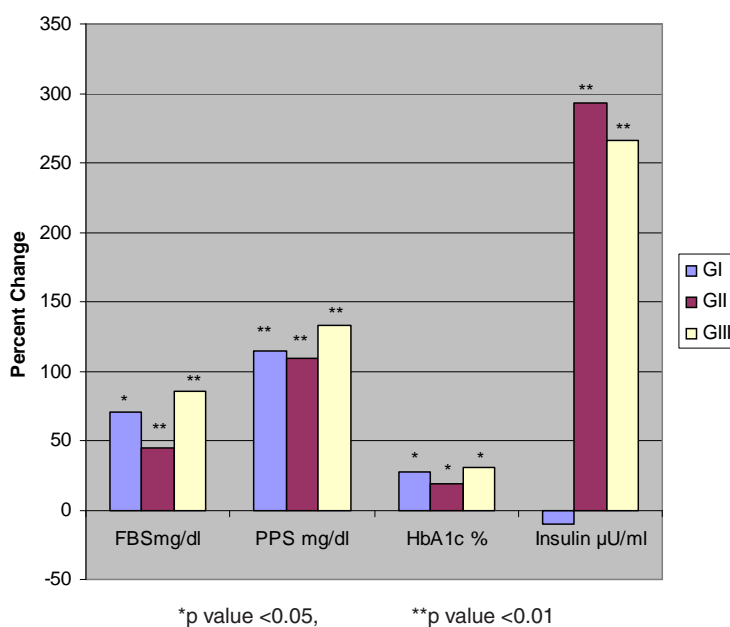
P Value < 0.01 : highly significant.

NS[†]! : non significant decrease.

P Value < 0.05 : significant.

P Value < 0.001: very highly significant.

CVD: Cardio Vascular Disease.

**Fig. 3: Percent Change of serum FBS, PPS, HbA_{1c} and Insulin levels in all Groups**

significant decrease in GI and a significant decrease in both GII and GIII as compared to control. In healthy subjects taurine acts as an antiglycative compound, providing free amino groups that may compete for the reducing sugars (Odetti *et al.*, 2003) and (Anuradha, 2009). In our study, the low in Saudi plasma taurine could be explained by higher consumption of taurine by some tissues was proposed as the cause of glucose reduced plasma levels. Other results showed a disturbed taurine content and release in platelets of T2DM patients (De Luca *et al.*, 2001). Also, Azuma *et al.*, (1992) suggested that diabetic patients have low level of taurine and that taurine could have beneficial effects in diabetic patients. Taurine could play a protective role as an antihypoxic (Franconi *et al.*, 1985) and antioxidant agent (Wolff and Dean, 1987). Hansen (2001) explained the low of taurine may be due to the intracellular accumulation of glucose forming sorbitol, which is suspected to be one of the key processes in the development of diabetic late complications. Sorbitol accumulation causes depletion in intracellular osmolytes including taurine.

Lu (2009) emphasized the importance of glutathione in preventing several diseases including diabetes. The result of our study showed a significant elevation in plasma thiol levels in T₂DM with CVD group as compared to control while a non significant increase was observed in T₁DM and T₂DM. In agreement with our results, Duman *et al.*, (2003) declared that serum of T₂DM patients had higher homocysteine (thiol) levels than control subjects. Also Ashfaq *et al.*, (2006) stated that plasma thiols (e. g glutathione redox), a marker of oxidative stress, may be helpful in identifying individuals at risk for early atherosclerosis, independent of traditional risk factor of assessment and presence inflammation.

Nitric oxide (NO) is a small lipophilic molecule which can travel freely through cell membranes by diffusion as well as by formation of S-nitrothiols by interaction with cellular proteins. Therefore, it can act on neighboring target cells (Guo *et al.*, 1995). Nitric oxide overproduction in diabetes has been documented in several animal models (Bank and Aynedjian, 1993) and clinical studies (Chiarelli *et al.*, 2000). The result of our study demonstrated a highly significant elevation in NO concentration in all the studied groups compared

to control. The reason for the greater NO production in patients with diabetes is unclear, but an increase in the expression of nitric oxide synthase (NOS) in these patients may play a role. Matata and Galiane (2001), found that NO_x (nitrite and nitrate) concentration were higher in the diabetic patients than control. NO_x was elevated in the diabetic patients with high HbA_{1c} compared with control subjects, but nearly normal in the well controlled diabetic patients. In agreement with our results Hoeldtke *et al.*, (2002) have found that NO over production occurs in patients with poorly controlled T₁DM and leads to increased peroxy nitrite and suppressed nitric oxide. Moreover, they revealed that hyperglycaemia was the stimulus to nitrosative stress and prompted this analysis to the relationship between NO overproduction and peripheral nerve function.

Uric acid is the end product of purine catabolism in humans (Kand'ar *et al.*, 2006) and it is also a potent non-enzymatic antioxidants (Bianchi *et al.*, 2007). In our study, the results of uric acid showed a significant increase in T₁DM group and a highly significant increase in T₂DM and T₂DM with CVD groups respectively, as compared to controls. Bianchi *et al.*, (2007) observed a positive association between serum uric acid and peripheral arterial disease appeared to be independent major CVD risk factors. The mechanism by which uric acid may be associated with atherosclerotic disease remain unclear, however uric acid may play an important role in free radical formation and oxidative stress. Therefore, high serum concentrations of uric acid may be seen as an adaptive response to oxidative stress induced by hyperglycaemia. Thus, whether uric acid is a true risk factor or a powerful marker of chronic oxidative stress, remains a marker of debate (Bianchi *et al.*, 2007).

Our data showed an abnormal lipid profile, where total cholesterol (TC) showed a significant increase in GI and GII and a highly significant increase in GIII compared to control. Hypercholesterolemia increases the risk of developing CVD. In our study the increase in serum TC level may be due to the decrease in taurine levels as explained by Militante and Lombardini (2000) and the overproduction of serum levels of NO causes also an elevation in cholesterol (Matata and

Galiance, 2001). The results of Pinto *et al.*, (2007) coincided with our results were they found a significant increase in cholesterol in T₂DM patients.

Also, Elvello *et al.*, (2008) suggested that the anti-hypercholesterol effects of taurine may be due to its ability to promote bile salt formation which in turn conjugates with cholesterol derivatives to form taurocholate. This is considered the major bile salt that extracts cholesterol from plasma in humans. Meanwhile, diminished taurine content is associated with a high blood cholesterol and increased risk of atherosclerosis. The anti-atherosclerotic effects of taurine have been studied in different hypercholesterolaemic and hyperlipidemic animals, but the exact mechanism of action is still unclear. It has been found that, the decrease in the cholesterol level in the serum by taurine is mainly due to the decrease in LDL. Taurine lowers cholesterol by repressing TAG secretion from the liver (Chen *et al.*, 2004).

The results of our study showed a significant increase in LDL-C serum levels in GI, GII and GIII groups as compared to control. LDL-C is a well-established risk factor for susceptibility to CVD (Chen *et al.*, 2004). It has been documented that high levels of cholesterol and LDL-C play a significant role in the development of arteriosclerosis and hence coronary heart disease, and as shown by the results of El-hazmi *et al.*, (1999) Saudi T₂DM patients with a higher prevalence of lipid abnormalities (dyslipidemia) constitute a moderate to high risk group for the development of coronary heart disease. Alizadeh *et al.*, (2008) stated that patients with T₂DM are known to suffer from high rates of cardiovascular disease. Hossein *et al.*, (2007) declared that diabetic patients are under high oxidative stress where hyperglycaemia plays an important role in LDL-C oxidation. Levels of acute and chronic hyperglycaemia correlate strongly with measures of LDL-C oxidation. It has been suggested that the oxidative modification of LDL-C could promote and accelerate the development of atherosclerosis. Bianchi *et al.*, (2007) highlighted that smaller LDL-C particle size is associated with increased intima-media thickness and with the presence of coronary heart disease in T₂DM.

In our study, the lipid pattern also showed a highly significant enhancement in TAG in GI and GIII and a non significant increase in HDL-C serum levels in all the studied groups as compared to control. These results may not show a typical dyslipidemic lipid profile but it showed a disturbance in lipid profile as a result of T2DM. The mechanisms responsible for hypertriglyceridemia may be an increased hepatic secretion of VLDL and a delayed clearance of TAG-rich lipoproteins, which might mainly be due to increased levels of substrates for TAG production, free fatty acids, and glucose. Hypertriglyceridemia usually accompanies decreased HDL-C, which is also a prominent feature of plasma lipid abnormalities seen in diabetic subjects (Howard, 1987) and (Yoshioka *et al.*, 1979). Other study performed by Valdivielso *et al.*, (2007) stated that, diabetic dyslipidemia, characterized by a fasting profile of high TAG levels, low HDL-C concentrations contributes to a greater incidence of arteriosclerotic disease in T₂DM. The low level of HDL-C, which exerts anti-atherogenic and antioxidative effects when present in sufficient amounts, is a key feature of T2DM. The reduced HDL-C levels, often accompanied by elevations in plasma TAG levels (Lamarche *et al.*, 1996) exerts anti-atherogenic and antioxidative effects when present in sufficient amounts, is a key feature of T2DM. Taurine plays an important role in lipid metabolism such as decreasing cholesterol by the enhancement of bile acid formation, and decreasing triacylglycerol which might improve lipid metabolism and insulin resistance in T₂DM in rat model (Nakaya *et al.*, 2000).

On the other hand, Warren (2007) a researcher at the University of Kentucky suggested that, at least for people with diabetes, having high levels of HDL-C in the blood stream there might be an increase risk for cardiovascular disease. He explained, in people with diabetes, HDL-C molecules bind with a natural compound called myristic acid, which somehow causes the HDL-C to inhibit the body's natural production of NO, a substance known to protect against cardiovascular disease.

Lipid peroxidation is a free radical related process which is potentially harmful because it is

uncontrolled, self enhancing process causes disruption of membranes, lipids and other cell components. In our present study, serum level of MDA showed a highly significant increase in all the studied groups compared to control. It has been found to be connected with various disease processes, such as atherosclerosis and hypertension (Mahboob *et al.*, 2005). Duman *et al.*, (2003) and Hossein *et al.*, (2007), results coincided with our findings and they stated that plasma MDA levels were significantly increased in T₂DM. Mahboob *et al.*, (2005) revealed that the high levels of MDA clearly show that diabetic patients, irrespective of the gender, were exposed to an increased oxidative stress via lipid peroxidation. Harris (1992) found that a decreased level of glutathione (thiol) indicates reduced scavenging capacity of glutathione-dependent anti-oxidant defensive system against elevated lipid peroxidation processes in T₂DM patients.

Therefore, our previous results of plasma taurine level as well as serum thiol, NO, uric acid, abnormal lipids profile (dyslipidemia) and extensive lipid peroxidation showed that the Saudi diabetic and diabetic with CVD patients are under oxidative stress.

In our study, as expected, a significant high level of fasting blood sugar and PBS, glycated hemoglobin (HbA_{1c}) were found in all the studied groups as compared to control. Meanwhile insulin serum levels showed a highly significant increase in both GII and GIII and a non significant decrease in GI as compared to control. Insulin plasma levels were low in patients of T1DM patients of G1 could be explained as they are insulin dependent and traces of insulin might be still in their blood. On the other hand, Shanik *et al.*, (2008) revealed that hyperinsulinemia is often both a result and driver of insulin resistance. They recognized insulin resistance as a strong predictor of disease in adults which has become the leading element of the metabolic syndrome and renewed as a focus of research. The condition exists when insulin

levels are higher than expected relative to the level of glucose. Thus insulin resistance is by definition tethered to hyperinsulinemia (Rosenson, 2005). Resistance to insulin likely underlies the changes that occur in lipid parameters of T₂DM, and usually it is associated with higher concentrations of cholesterol and TAG, and lower concentrations of HDL-C (Garvey *et al.*, 2003).

In the present study, the relationship of taurine level between all the studied groups and control showed a significant decrease in taurine levels in all diabetic patients as compared to their respective controls. On the other hand, a non significant change in taurine level was detected between T₂DM and T₂DM+CVD patients. In the view of the results of Winiarska *et al.*, (2009) he concluded that taurine-induced increase in the activities of catalase and the enzymes of glutathione metabolism is of importance for antioxidative action of this amino acid and thus, taurine seems to be beneficial for the therapy of diabetes.

In conclusion, these results suggest that oxidative stress in Saudi female diabetic patients can be attributed to an increase in the production of free radicals (nitric oxide) and increased lipid peroxidation (MDA) and the decrease in antioxidants (taurine and uric acid) in concomitant with dyslipidemia which may be due to taurine and uric acid deficiency. So, our results suggest that there seems to be an imbalance between plasma oxidant and antioxidant systems in patients with NIDDM. Our results also suggest the possibility of a therapeutic protocol of giving taurine and other antioxidants as food supplements to Saudi patients, hoping that this may improve the obvious dyslipidemia, oxidative stress and decrease suffering from diabetes complications specially CVD.

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