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Study of some biochemical parameters for patients with Type II Diabetes Mellitus in Thi-Qar Governorate, Iraq

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Abstract

Background: Diabetes mellitus is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin. Current study was aimed to observe the lipid profile, malondialdehyde, antioxidant and electrolyte levels in type 2 diabetes mellitus patients.
Methods: Serum glucose, total cholesterol, triglycerides, high density lipoprotein, very low density lipoprotein and low density lipoprotein, malondialdehyde (MDA), ceruloplasmin, uric acid, sodium, potassium and chloride levels were determined in 75 patients with type II diabetes mellitus and 25 healthy subjects.
Results: The levels of serum glucose, total cholesterol, triglycerides, very low density lipoprotein, low density lipoprotein, malondialdehyde, ceruloplasmin, sodium, potassium and chloride showed significant increase in ype II diabetes mellitus patients as compared to control group whereas the levels of high density lipoprotein and uric acid showed a significant decrease in type II diabetes mellitus patients in comparison to control subjects ($P \leq 0.05$). In addition, current study demonstrated the characteristic diabetic dyslipidaemia which is characterized by low HDL and high triglyceride. Increased levels of MDA may be a useful marker of oxidative stress. Increased oxidative stress may result in consumption of antioxidants including ceruloplasmin. Also, there is significant decrease in serum uric acid levels in type II diabetes mellitus patients. It may be concluded from this study that dysregulation of glucose homeostasis may lead to electrolytes imbalance due to increase in sodium and potassium chloride levels.

Keywords: diabetes mellitus, lipid profile, antioxidants, malondialdehyde, serum electrolytes.

INTRODUCTION

Diabetes mellitus (DM) is a heterogeneous condition reflecting different metabolic disorders accompanied by a variety of complications. This is characterized by hyperglycemia due to absolute or relative deficiency of insulin [1]. Lack of insulin, whether absolute or relative, affects the metabolism of carbohydrates, proteins, fats, water and electrolytes [2]. Insulin affects many sites of mammalian lipid metabolism. It stimulates synthesis of fatty acids in liver, adipose tissue and intestine. Insulin has also been reported to increase cholesterol synthesis. The activity of lipoprotein lipase in white adipose tissue is also increased [3]. As many as 75% of patients visiting diabetes clinics report significant gastrointestinal symptoms [4]. The global figure of people suffering from diabetes mellitus is estimated to rise from current estimate of 415 million to 642 million by 2040. The number of people with Type 2 Diabetes Mellitus (T2DM) is increasing in every country and 75% of people with DM are living in developing countries [5]. With an increasing incidence worldwide, DM will likely be a leading cause of morbidity and mortality in the future. It is well established that dyslipidaemia is a major risk factor for macro-vascular complications in patients with T2DM and affects 10-73% of this population [6]. Dyslipidaemia in DM commonly manifests as raised low-density lipoprotein cholesterol (LDL-C), decreased high-density lipoprotein cholesterol (HDL-C) levels, or elevated triglyceride (TG) levels. Furthermore, data from the United Kingdom Prospective Diabetes Study suggested that both decreased HDL-C and elevated LDL-C predict CVD in diabetes. All national and international guidelines recommend aggressive management of lipids in this population [7].

DM a metabolic disorder characterized by hyperglycemia and associated with increased free-radical activity. The mechanisms of free-radical production include glucose auto-oxidation, protein glycation, advanced glycated end-products formation, and activation of polyol pathway. These events , ultimately, result in oxidative stress in a variety of tissues [8]. The absence of suitable compensatory mechanisms from endogenous antioxidant systems causes a redox imbalance and leads to activation of stress-sensitive intracellular signaling pathways [9]. Hence, oxidative stress may be implicated in the pathogenesis of diabetes.

Ceruloplasmin is an enzyme (E.C. 1.16.3.1) [10]. It is an acute-phase protein synthesized in liver and is a member of blue multicopper oxidase. The physiological functions of ceruloplasmin are uncertain, but ceruloplasmin has a role in copper transport, coagulation, angiogenesis, defense against oxidative stress, and iron homeostasis [10,11]. There has been conflicting data on serum ceruloplasmin in metabolic syndrome and T2DM. Some studies reported significantly increased serum level of ceruloplasmin in metabolic syndrome and DM [12,13]. Data available mainly explain the association between increased ceruloplasmin levels and cardiovascular diseases [14,15]. Few studies have also shown a decrease in plasma ceruloplasmin in T2DM [16.17].

Uric acid can act as a pro-oxidant and it may, thus, be a marker of oxidative stress, but it may also have a therapeutic role as an antioxidant [18]. Urate, the soluble form of uric acid, can scavenge the superoxide and the hydroxyl radicals and it can chelate transition metals [19]. Hyperuricaemia has been also added to the set of metabolic abnormalities which are associated with insulin resistance and/or hyperinsulinaemia in the metabolic syndrome [20]. While an increase in uric acid levels in pre-diabetes and diabetes was demonstrated by some studies, a declining trend of serum uric acid levels with increasing blood glucose levels was observed by other research workers [21].

Electrolytes imbalance is common in patients with diabetes, which could be the result of an altered distribution of electrolytes and it is related to hyperglycemia-induced osmotic fluid shifts or of total-body deficits brought about by osmotic diuresis [22]. Insulin-mediated glucose intake is impaired, but the potassium intake of cells remains normal. Hyperkalaemia occurs due to increase in plasma tonicity that results from redistribution of potassium from intercellular space to extracellular space in patients with T2DM. Moreover, DM produces dysnatremias via several underlying mechanisms [23, 24]. Thus, the aim of this study was to observe the lipid profile, malondialdehyde, ceruloplasmin, uric acid and measure the serum electrolytes (sodium, potassium and chloride) in patients with T2DM.

MATERIALS AND METHODS

This study is conducted at the Center of Diabetes and Endocrine Glands in Thi-Qar, Biochemistry Laboratory in the College of Sciences/ University of Thi-Qar, Iraq. The study included 125 subjects; 50 normal healthy subjects as controls and 75 patients with Type 2 Diabetes Mellitu (T2DM). .

A 5 mL-blood sample was drawn from each participant. Samples were allowed to clot at room temperature in empty disposable tubes, then centrifuged at 3000 r.p.m. for 10 minutes. The serum

samples were separated and stored at (-20ºC) until the time of assay.

The serum was used for the estimation of glucose. It was measured according to the method of Barham et al. [25], the used reagents were supplied by (Randox, UK), cholesterol (TC) was measured according to the method of Allan and Dawson [26], the used reagents were supplied by (Biolabo, france), triglycerides was measured according to the method of Tietz et al. [27], the used reagents were supplied by (Biolabo, france), high–density lipoprotein (HDL) was measured according to the method of Lopes-Virella [28], the used reagents were supplied by (Biolabo, france), very low-density lipoprotein (VLDL) and low– density lipoprotein (LDL) was measured according to the method of Friedwald et al. [29], malondialdehyde was measured according to the method of Fong et al. [30], ceruloplasmin was measured according to the method of Menden et al. [31], uric acid was measured according to method of Fossati et al. [32], the used reagents was supplied by (Biolabo, france), , Sodium and Potassium were measured according to Retiman and Frankel [33], the used reagents were supplied by (Randox, UK) and chloride was measured according to Florence and Farrar [34], the used reagents was supplied by (Biolabo, France).

RESULTS

The results showed a significant increase (P ≤0.05) in the concentrations of serum glucose, total cholesterol (TC), triglycerides (TG), very low density lipoprotein (VLDL) and low density lipoprotein (LDL) in DM group in comparison with control group. Also, there was a significant decrease (P ≤0.05) in the concentration of serum high density lipoprotein (HDL) in DM group in comparison with control group. (Table, 1).

Moreover, the results of current study showed a significant increase (P ≤0.05) in the concentrations of serum malondialdehyde (MDA) and ceruloplasmin (Cp) in DM group in comparison with control group. Also, there was a significant decrease (P ≤0.05) in the concentration of serum uric acid in DM group in comparison with control group (Table 2). Also, the current study revealed a significant increase (P ≤0.05) in the concentrations of serum sodium (Na^+), potassium (K^+) and chloride (Cl^-) in DM group in comparison with control group (Table 3).

DISCUSSION

Glucose is the major source of energy used by the cells. However, glucose cannot enter the cell unless insulin is there. In a normally functioning pancreas, an adequate amount of insulin is produced to move glucose into cells. In an abnormal pancreas, little or no insulin is produced or the body cells do not respond to insulin that is produced. As a result, glucose accumulates in the blood and its concentration is elevated and causes diabetes mellitus [35].

The results of this study showed significant increase of glucose in T2DM when compared with control subjects. The reasons of this state which usually appears after the age of 40 years may include weakness of β-cell, modicums of insulin production and/ or function and increasing insulin resistance [36,37]. The results of this study showed statistically significant increase in total cholesterol in diabetes patients when compared with control subjects. This finding could be attributed to decrease in muscular exercise or inhibition of cholesterol catabolism [38]. However, it could be attributed to an increase in plasma concentration of VLDL-C and LDL [1] which may be due to hepatic production of VLDL or decreased removal of VLDL-C and LDL from the circulation. Moreover, triglycerides level was found to be significantly increased in diabetic patients when compared with controls. This is attributed to insulin deficiency causing hyperglycemia and mobilization of fatty acids from adipose tissue [39]. The fatty acids from adipose tissue are mobilized for energy purpose and excess fatty acids are accumulated in liver and are converted to triglyceride [39]. The VLDL cholesterol of diabetic patients was significantly increased when compared with controls. This increase maybe result from hyperinsulinemia and resultant increase in triglycerides, LDL and VLDL cholesterol. It is known that insulin and growth hormone promote the production of VLDL cholesterol by increasing the production of Apo-E and Apo-B 48 and by stimulating lipolysis in the adipose tissues and triglycerides in the liver [40].

Compared with control individuals, participants with T2DM exhibited significantly increased plasma LDL cholesterol levels. The latter could be attributed to the fact that, insulin increases the number of LDL receptors so chronic insulin deficiency, as found in T2DM, might be associated with a diminished level of LDL receptor and subsequent rise in plasma LDL cholesterol levels [41].

Table 1: Serum glucose and lipid profile of DM patients and their controls.

Groups	No.	Glucose (mg/dL)	TC (mg/dL)	TG (mg/dL)	HDL (mg/dL)	VLDL (mg/dL)	LDL (mg/dL)
control	50	99.33± 5.24 ^{b}	176.39± 7.00 ^{b}	124.22± 5.72 ^{b}	47.00± 3.52 ^{a}	24.84± 1.15 ^{b}	104.64± 8.60 ^{b}
DM	75	296.66± 38.16 ^{a}	233.61± 8.46 ^{a}	160.89± 6.96 ^{a}	34.22± 3.48 ^{b}	32.18± 1.39 ^{a}	166.79± 8.48 ^{a}
LSD		15.51	4.49	3.59	2.00	1.18	4.93

Each value represents Mean±SD values with non-identical superscript (a , b or c …etc.) were considered significantly different (P ≤ 0.05).

Table 2: Serum MDA and antioxidants of DM patients and their controls

Groups	No.	MDA (µmol/L)	Cp (mg/dL)	Uric acid (g/L)
control	50	3.83±0.24 ^{a}	3.03±0.30 ^{b}	7.24±0.48 ^{a}
DM	75	2.06±0.27 ^{b}	4.12±0.32 ^{a}	4.82±0.28 ^{b}
LSD		0.15	0.18	0.32

Each value represents Mean±SD values with non-identical superscript (a , b or c …etc.) were considered significantly different (P ≤ 0.05).

Table 3: Serum electrolytes of DM patients and their controls

Groups	No.	Na^+(mmol/L)	K^+(mmol/L)	Cl^-(mmol/L)
control	50	138.72±4.40 b	4.15±0.72 b	98.77±2.35 b
DM	75	164.14±10.77 a	5.41±0.88 a	117.22±5.80 a
LSD		4.79	0.47	2.57

Each value represents Mean±SD values with non-identical superscript (a , b or c …etc.) were considered significantly different (P ≤ 0.05).

On the other hand, plasma HDL cholesterol levels in patients with T2DM were significantly lower than those in healthy controls. This finding could be attributed to urinary loss of Lecithin: Cholesterol Acytransferase (LCAT) which leads to severe deficiency and limit the HDL-mediated uptake of surplus cholesterol from extra hepatic tissues [42]. This is also compounded by marked reduction of the hepatic HDL-C receptors. Low serum HDL-C levels contribute to structural and functional alterations which led to arterial rigidity

Increased serum level of MDA may be a useful marker of oxidative stress. The enhanced lipid peroxidation leads to an increase in free-radical activity in T2DM. The latter along with insulin resistance can lead to activation of stress-sensitive pathways which may play an important role in the complications of diabetes [43].

The increase in concentration of serum ceruloplasmin in diabetic patients, when compared with control subjects, maybe due to an increase in the proportion of younger red blood cells and the compensatory mechanisms after increased oxidative stress [4]. Besides, it maybe due to increased hepatic catalysis of Cp synthesis against iron overload status [44] and elevation in serum copper level [45] as a defiance function.

Nonetheless, uric acid (UA) is the final product of purines metabolism in humans. It is produced by conversion of hypoxanthine to xanthine and the latter to uric acid by the enzyme xanthine oxido-reductase. The latter uses molecular oxygen as an electron acceptor and generates superoxide anion and other Reactive Oxygen Species (ROS) [46,47,48]. UA is also a physiological scavenger of free radical and one of the major contributors to the plasma antioxidant capacity [49]. Thus, UA plays a dual role, both as a pro-oxidant and as an antioxidant [50,51]. T2DM is associated with oxidative stress by promoting generation of free radicals and by impairing the endogenous antioxidant defense system [52, 53,54]. Previous studies reported the association of hypouricaemia with T2DM [55.56]. A positive relationship between glucosuria and uricosuria had been described [57]. Furthermore, a higher degree of hyperglycaemia was observed to be associated with an increased rate of uric acid excretion and lowering of plasma uric acid levels [57]. Hypouricaemia and tubular transport of uric acid have been thoroughly reviewed [58]. It has been reported that increased urate clearance in T2DM is due to increased glomerular hyperfiltration as a result of abnormal handling of tubular urate [59].

Increased urination leads to loss of electrolytes and water and results in serum electrolytes disturbance, especially sodium and potassium. Studies suggest that uncontrolled DM can also induce hypovolemic hyponatraemia due to osmotic diuresis. Furthermore in diabetic ketoacidosis, urinary loss of electrolytes augments renal sodium loss [60,61]. In the present study it was found that sodium levels in diabetic patients were higher than in controls and sodium correlated negatively with glucose. Increased or normal plasma sodium concentrations in the presence of hyperglycemia indicate a clinically significant deficit in total body water. Poorly controlled DM was implicated in the development of hypernatraemia in few cases. Consequently, in patients with uncontrolled DM, serum concentration of Na+ is variable, reflecting the balance between hyperglycemia-induced water movement out of the cells that lowers [Na+] and the glucosuria-induced osmotic diuresis, which tends to raise [Na+]. Thus, hypernatraemia and hyperosmolarity may be considered as contributing factors to the occurrence of DM [62]. Present study showed that diabetic patients were more prone to mild hyperkalaemia when compared to healthy controls.

Previous studies reported that the exogenous insulin can induce mild hyperkalaemia, because it promotes the potassium influx into the skeletal muscles and hepatic cells which increases the activity of Na+ and K+ ATPase pump. Hyperkalaemia is also associated with impaired insulin secretion and decreased peripheral glucose utilization which results in carbohydrate intolerance and hyperglycemia [63]. Elevated serum Cl^- levels were found in diabetic patients and this might be due to diabetic ketoacidosis. The latter causes a reduction in blood pH which further disturbs acid-base balance and leads to elevation of serum chloride.

CONCLUSION

Diabetic dyslipidaemia is characterized by low HDL, high TG and high small dense LDL. Early screening of diabetic patients for dyslipidaemia and early intervention is required to minimize the risk of future cardiovascular mortality. In T2DM, which is associated with insulin resistance, there is an increase in free-radical production. Therefore, preventing the development of typical secondary complications would require strategies to normalize free-radical production. Moreover, assessment of serum electrolytes is important for monitoring the prognosis of patients with T2DM.

Ethical Clearance: It was obtained from Research Ethics Committee at College of Sciences/ University of Thi-Qar, Iraq.

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Conflict of Interest: None to declare.

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