Lipid Peroxidation in Iraqi Men Newly Diagnosed with Non – Insulin Dependent Diabetes Mellitus (NIDDM)

Hana A. Ali
Chemistry Department, College of Science, Kufa University

(NJC)

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Abstract

This study was designed to investigate Lipid profile pattern and Lipid peroxidation in 40 Iraqi men newly diagnosed with non – insulin dependent diabetes mellitus (NIDDM) compared to 40 healthy non- diabetic control. The results showed that blood glucose and lipid parameters were significantly increased ($p < 0.01$) with the exception of HDL-c, which was significantly decreased ($p < 0.01$). On the other hand, a significant elevation in malonedialdehyde level and a decrease in glutathione content were observed in newly diagnosed NIDDM in comparison with controls.

These findings indicate that the increase in Lipid peroxidation and decline in antioxidant defences, may appear early in newly diagnosed NIDDM, before the development of secondary complications and might play an important role in initiation and progression of diabetic complications.

الخلاصة

تم تصميم الدراسة الحالية لمعرفة النموذج الخاص بمجموعة الدهون وكذلك الإجهاد التأكسدي للدهون عند (٤٠) مريض بداء السكري من الذكور الذين تم تشخيصهم حديثاً مقارنة مع (٤٠) شخصاً سوياً. بينت النتائج زيادة ملحوظة في مستوى سكر الدم ومجموعة الدهون ما عدا HDL–c الذي يقل بشكل ملحوظ . ومن جهة أخرى حصلت زيادة ملحوظة في مستوى مالون داي ألديهايد وقلة ملحوظة في مستوى الكلوتاثايون في مصل الدم للمرضى المشار إليهم عند مقارنتهم مع أقرانهم الأصحاء.

تؤكد النتائج أن الزيادة في الإجهاد التأكسدي للدهون والنقصان في مضادات التأكسد قد يظهر مبكراً لدى مرضى داء السكري المشخصين حديثاً قبل حصول المضاعفات الثانوية للمرض وربما يلعب دوراً مهماً في تطور مرض السكري ومضاعفاته.

Introduction

Diabetes mellitus is a chronic syndrome affecting carbohydrate, protein and fat metabolism. It is characterized by relative or absolute insufficiency of insulin secretion (type 1 diabetes or Insulin dependent diabetes mellitus (IDDM)) or concomitant insensitivity resistance to metabolic action of insulin or target tissues (type 2 diabetes or non – insulin dependent diabetes mellitns (NIDDM)) , both resulting in hyperglycemia[1]. Type 2 diabetes is a common disorder with prevalence that rises markedly with increasing degrees of obesity. The prevalence of Type 2 diabetes has risen alarmingly in the past decade, in large part linked to the trends in obesity and secondary the lifestyle.[2] Type 2 diabetes is increasing in incidence as a result of change in human behavior and increased body mass index[2].

Diabetes mellitus is considered to be one of a rank of free radical diseases which propagates complications with increased free radical formation [3]. Oxidative stress is increased in diabetes mellitus owing to the increase in the production of oxygen free radicals and a deficiency in antioxidant defense mechanisms[4].Diabetes produces disturbances of lipid profiles especially an increased susceptibility to lipid peroxidations [5].

Lipid peroxidation of cellular structures, a consequence of increased oxygen free radicals, is thought to play an important role in atherosclerosis and microvascular complications of diabetes mellitus[6]. To overcome the toxic effect of reactive oxygen species the body utilizes several antioxidant defense systems including both enzymatic and non-enzymatic components[7]. However, if these damaging species are ineffectively scavenged they can interact with biological molecules like DNA, lipids , proteins with potential threat to cellular function [8 , 9].

In the present study the following parameters were assessed to elucidate the oxidant–antioxidant status in Iraqi men newly diagnosed to have non insulin dependent diabetes mellitus (NIDDM). Serum glucose, lipid profile, MDA which serves as an index extent of lipid peroxialation and reduced glutathione (GSH) serves as non enzymatic antioxidant parameter levels were measured.

Patients and Methods

Fourty Iraqi men newly diagnosed non–insulin dependent diabetes mellitus patients, with age range of (38–70 years), from AL- Sadder teaching hospital , in Al-Najaf city, Iraq, were included in this study. No medication and any other hypoglycemic agents was taken by those patients. The patients did not have intercurrent illness, hypertension, liver, renal and other endocrine diseases. Heavy smokers were excluded from this study. Fourty healthy non diabetic men, with age range of (36–68 years), were selected as control group. Blood samples were collected after an overnight fast of 12–14 hours for the determination of serum glucose and serum lipid concentrations in addition to MDA and glutathione .

Serum glucose was determined by the glucose oxidase method (Randox , U.k). Serum concentrations of total cholesterol and triglycerides were determined by enzymatic methods (Biomeiurex, France). The serum concentration of high density lipoprotein cholesterol (HDL–c) was also determined after precipitation of very low density lipoprotein cholesterol (VLDL–c) and low density lipoprotein cholesterol (LDL–c) with phosphotungstate and magnesium [10]. Serum concentration of LDL–c was estimated using the formula reported by friedewald [11]. Lipid peroxidation product, MDA , was measured by the method outlined by Draper [12]. The reduced glutathione level was measured by adopting the method described by Beutler[13].These biochemical parameters were measured spectrophotometrically. All values were expressed as the mean ±SD. And all statistical comparisons were made by applying student's t test and $p < 0.05$ was considered as a significant value between two groups.

Results and Discussion

Blood glucose and lipid profile of type 2 diabetes mellitus patients and control group is shown in table (1). The body mass index (BMI) of type 2 diabetic group was significantly higher ($p<0.01$). compared to control group. The levels of fasting serum glucose, triglycerides, total cholesterol, LDL–c and VLDL–c were found to be significantly elevated ($p<0.01$), while the level of HDL–c showed a significant decrease ($p<0.01$) in type 2 diabetic patieuts compared to control group.

Table 1 : Biochemical parameters of control and newly diagnosed NIDDM

Parameter	Control N=40 Mean ±SD	Newly dignosed NIDDM N= 40 Mean ±SD
Age (years)	42.5 ± 9.8	43.1 ± 8.8 **
BMI (kg/m^2)	22.8 ± 1.6	25.2 ± 3.6*
Glucose (mg /dl)	92.7 ± 7.2	230.8 ± 42.1 *
Triglycerides (mg / dl)	129.6 ± 12.3	189.2 ± 4.8 *
Total cholesterol (mg/dl)	177± 23.6	231.8 ± 29.4 *
HDL-c (mg/dl)	53.7 ± 8.04	33.3 ± 5.1 *
LDL–c (mg/dl)	97.4 ± 25.6	160.7 ± 28.4 *
VLDL–c (mg/dl)	25.3 ± 3.1	37.7 ± 7.1 *

*significant : $p < 0.01$

** non – significant : $p > 0.01$

Table 2 : MDA, glutathione levels blood serum of Newly diagnosed NIDDM patients controls.

Parameter	Control Mean ±SD	Newly diagnosed NIDDM Mean ±SD
MDA(µM mole/L)	3.2 ± 0.4	4.9 ± 0.6 *
Gluathione (% mg)	8.2 ± 0.61	5.7 ± 0.1 *

* significant : $p < 0.01$

Results shown in table 2 reveals that the serum MDA level, a product of lipid peroxidation, increased significantly ($p<0.01$) in Newly diagnosed NIDDM patients in comparison to non diabetic healthy controls.

Major disturbances in lipoprotein metabolism in type 2 diabetic individuals are reflected by an increase in plasma triglycerides and low HDL-c with normal or near normal LDL–c levels[14]. Okubo and Murase[15] reported hypertriglyceridaemia and low HDL-c levels in Japanese patients with type 2 diabetes mellitus. U.K Prospective Diabetes Study 27 [16] showed higher levels of total cholesterol and LDL–c in type 2 diabetes at diagnosis . Agboola – Abu et al [17] noticed raised triglycerides, total cholesterol , LDL–c and lower HDL–c in newly diagnosed type 2 diabetes mellitus patients. Our results show like the forementioned workers, elevated levels of triglycerides , total cholesterol , LDL–c , VLDL–c and decreased levels of HDL– c in type 2 newly diagnosed diabetic patients compared to control subjects. The mechanisms responsible for hypertriglyceridaemia may be increased hepatic secretion of VLDL–c and delayed clearance of total glyceride rich lipoproteins which might be due to increased levels of substrates for triglycerides production , free fatty acids and glucose . the latter could be secondary to decreased activity of lipoprotein lipase , a key enzyme for lipoprotein – triglyceride[18]. Hypertriglyceridaemia usually accompanies decreased HDL-c which is also a feature of plasma lipid abnormalities in diabetic subjects [19].

Many investigators reported that oxidative stress may be associated with the pathogenesisof NIDDM complications [20-22]. Free radicals are formed disproportionately in diabetes mellitus by glucose degradation , non – enzymatic glycation of proteins and the subsequent oxidative degradation, which may play an important role in the development of complications in diabetic patients.

The generation of radicals may lead to lipid peroxidation and formation of several damage in diabetes mellitus. In the present study MDA levels, a lipid peroxidation product and a marker of oxidative stress, were elevated significantly in newly diagnosed NIDDM patients compared to controls as shown in table(2). Other researchers have also reported elevated lipid peroxidation products in blood samples of type 1 and type 2 diabetic patients[23,24].

Abnormally high levels of free radicals , lipid peroxidation, and simultaneous declines in antioxidant defence mechanisms can lead to damage of cellular organelles and enzymes. Antioxidant enzyme–dependent defences play an important role in scavenging free radicals produced under oxidative stress [25,26]. Our data reveal that, glutathione, an antioxidant of blood serum of newly diagnosed NIDDM patients were significantly low (table2) , indicating decreased scavenging capacity of glutathione antioxidant defensive system against elevated lipid peroxidation processes in these patients,

The results suggest that increase in lipid peroxidation and decline in antioxidant defences may appear early in newly diagnosed NIDDM patients before the development of secondary complications and might play an important role in the initiation and progression of diabetic complications.

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