# EVALUATION OF LIPID AND LIPOPROTEIN PROFILE IN PATIENTS WITH TYPE 2 DIABETES

**Lamia M. Al-Naama[1], Salman K. Ajlan[2] & Mariam S. Mahmood[3]**

## ABSTRACT

*Objective:* To evaluate the pattern of lipid and lipoprotein profile in patients with type 2 diabetes (T2D).

*Methods:* In this prospective study, which was carried out in Basrah, Southern Iraq, serum concentrations of glucose "fasting blood sugar" (FBS), total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), triglycerides (TG) and very low density lipoprotein-cholesterol (VLDL-C) were measured in 92 patients (43 males and 49 females) with T2D and 120 control subjects (35 males and 85 females).

*Results:* Patients with T2D have significantly higher serum concentrations of TC, LDL-C, TG, VLDL-C and LDL-C/HDL-C ratio (P<0.001) and significantly lower HDL-C serum concentration (P<0.001) compared to control subjects. Male patients with T2D showed significantly higher TC, LDL-C serum concentrations and LDL-C/HDL-C ratio in comparison to control subjects (P<0.001), while serum HDL-C concentration was significantly lower among T2D patients compared to controls (P<0.001). No significant differences were seen in serum TG and VLDL-C concentrations between male patients and control subjects (P>0.05). In females, serum levels of TC, LDL-C, TG, VLDL-C, and LDL-C/ HDL-C ratio were significantly higher (P<0.001), and serum HDL-C level was significantly lower (P<0.05) in patients with T2D than in control subjects.

*Conclusion:* T2D has marked effects on lipid and lipoprotein profile causing a diversity of dyslipidaemia, that might lead to atherosclerosis, and hence, increasing the risk of coronary heart disease.

## INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by impaired metabolism of glucose, protein and fat, as well as the late development of vascular (involving small and large blood vessels) and neuropathic complications.[1,2] DM consists of a group of disorders involving distinct pathogenic mechanisms in which hyperglycaemia is the common denominator.[2] Genetic and environmental factors often interact leading to absolute or relative insulin deficiency[1,3] which plays a key role in the metabolic derangement occurring in DM.[2] DM is a global public health problem, especially among elderly. Diabetics are at high risk for dyslipidaemia, cardiovascular disease (CVD), coronary heart disease (CHD) and mortality.[4-7] DM has a world-wide distribution and the incidence of both types of primary diabetes, type 1 diabetes (T1D) and type 2 diabetes (T2D), is rising. However, the prevalence of both types varies considerably in different parts of the world.[1,2,4-7] It increases the risk of cardiac, cerebral and peripheral vascular disease two- to seven folds and as a major contributing factor to neonatal morbidity and mortality.[2]

Also, DM is associated with early indicators of functional decline.[8] DM and dyslipidaemia constitute major independent and modifiable risk factors of CHD.[9-11] In addition, DM enhances the effects of the other major cardiovascular risk factors; smoking, hypertension and hypercholesterolemia.[1] Dyslipoproteinaemia has been found to be a significant independent predictor of CHD in patients with T2D[12], and also linked to complications of DM.[13,14] In Basrah, Southern Iraq, changes in lipid and lipoprotein profile in several important medical diseases like CHD[15] and thyroid dysfunction[16,17] have been studied. The aim of this study was to determine the pattern of lipid and lipoprotein profile in patients with T2D in Basrah.

## PATIENTS AND METHODS

*Patients:* In this prospective study, which was carried out in Basrah, Southern Iraq, 92 patients with T2D were included. They were 43 males and 49 females, their age ranged from 30-70 years. They were already diagnosed as having T2D. They were on oral hypogylcaemic drugs (sulphonylureas and biguanides), apart from two

[1]PhD, Department of Biochemistry, College of Medicine, University of Basrah,
[2]MBChB, MSc, Department of Biochemistry, College of Medicine, University of Basrah,
[3]Supervisor, Clinical Laboratory Department, Basrah Health, Directorate, Basrah, IRAQ.
E-mail: lamia_alnaama@yahoo.com

patients were on just dietary/lifestyle modification.

**Controls:** One hundred-twenty apparently healthy subjects (35 males and 85 females) were included as a control group, their age ranged from 31-76 years.

**Methods:** Venous blood specimens were withdrawn after overnight fasting (12-14 hours) from patients and controls. Sera were separated and either analyzed immediately or stored for later analysis within 2 days. FBS was estimated immediately, and was determined enzymatically using kit from bioMerieux. France. The other parameters (TC,HDL-C, TG) were determined using kits from bioMerieux, France. LDL-C and VLDL-C were estimated using Friedwiald equation:[18]

> **LDL-C= TC - (HDL-C+TG/5)**
> **VLDL-C=TG/5**

(provided that TG concentration is not exceeding 400 mg/dl).

Quality control sera from bioMerieux, France were included in each assay batch for all analyses.

**Statistical analysis:** *Statistical analysis was carried out using t-test and ANOVA. P<0.05 was considered statistically significant.*

### RESULTS

(Table-1) presents the characteristics of diabetic patients and control subjects. Body mass index (BMI), (P<0.01), systolic blood pressure (SBP), (P<0.001), and diastolic blood pressure (DBP), (P<0.001), were significantly higher among patients with T2D compared to controls.

**Table 1. Characteristics of T2D patients and control subjects.**

| Variable | Patients (n=92) | Controls (n=120) |
|---|---|---|
| Age (years) | 54.1 (9.8)** | 35.5 (17.7) |
| Duration (years) | 10.2 (7.2) | --- |
| BMI (Kg / m$^2$) | 26.9 (4.7)* | 24.4 (4.7) |
| SBP (mm.Hg) | 139.6(25.8)** | 119.4 (19.1) |
| DBP (mm.Hg) | 84.5 (13.1)** | 79.3 (8.3) |

Values given as Mean (SD).
* : P < 0.01
**: P < 0.001

The concentrations of the determined biochemical parameters in patients with T2D and control subjects are shown in (Table-2).

**Table 2. Lipid profile and FBS in patients with T2D and controls.**

| Parameter (mg/dl) | Patients (n=92) | Controls (n=120) |
|---|---|---|
| FBS | 182.4 (86.5)** | 90.3 (15.4) |
| TC | 224.9 (44.7)** | 180.2 (47.6) |
| HDL-C | 41.6 (11.2)** | 47.4 (9.8) |
| LDL-C | 149.5 (41.1)** | 110.4 (45.1) |
| TG | 175.7 (91.0)** | 122.8 (77.0) |
| VLDL-C | 36.2 (19.0)** | 24.6 (14.4) |
| LDL-C/HDL-C | 4.2 (1.5)** | 2.4 (1.2) |

Values given as Mean (SD).
**: P < 0.001

Serum concentrations of TC, LDL-C, TG, VLDL-C and LDL-C/HDL-C ratio were significantly higher in patients with T2D compared to control subjects (P<0.001), while serum HDL-C concentration was significantly lower in T2D patients than in controls (P<0.001). With respect to gender, male patients with T2D (Table-3) have significantly higher serum levels of TC,LDL-C and LDL-C/HDL-C ratio (P<0.001) and significantly lower serum HDL-C level (P<0.001) in comparison to normal males. Serum TG and VLDL-C levels showed no significant differences between patients and controls (P>0.05).

## Table 3 . Lipid profile and FBS in males

| Parameter (mg/dl) | Patients (n=43) | Controls (n=35) |
|---|---|---|
| FBS | 189.5 (69.7)** | 95.1 (25.0) |
| TC | 223.9 (40.1)** | 186.8 (40.0) |
| HDL-C | 37.5 (8.0)** | 46.6 (9.6) |
| LDL-C | 160.8 (33.0)** | 109.5 (43.0) |
| TG | 195.6 (80.0) | 159.1 (99.8) |
| VLDL-C | 33.9 (19.2) | 32.0 (18.5) |
| LDL-C/HDL-C | 4.3 (1.8)** | 2.6 (1.5) |

*Values given as Mean (SD).*
***: P<0.001*

(Table-4) presents the results in females. Serum concentrations of TC, LDL-C , TG, VLDL-C and LDL-C/HDL-ratio were significantly higher (P<0.001) and serum HDL-C level was significantly lower (P<0.05) among female patients with T2D compared to female controls.

## Table 4 . Lipid profile and FBS in females.

| Parameter (mg/dl) | Patients (n=49) | Control (n=85) |
|---|---|---|
| FBS | 186.0 (64.9)** | 88.2 (12.8) |
| TC | 225.1 (41.0)** | 177.3 (50.8) |
| HDL-C | 43.3 (11.7)* | 47.7 (9.9) |
| LDL-C | 148.2 (44.2)** | 110.2 (49.7) |
| TG | 176.6 (93.2)** | 107.7 (54.9) |
| VLDL-C | 35.1 (2.4)** | 21.8 (11.0) |
| LDL-C/HDL-C | 3.6 (1.6)** | 2.4 (1.1) |

*Values given as Mean (SD).*
* *: P < 0.05*
***: P < 0.001*

## DISCUSSION

DM is the most common endocrine disease, and is associated with vascular changes resulting in accelerated atherosclerosis.[19] This association exists in patients with T2D in whom plasma insulin levels may be low, normal or even high and is accompanied by changes in plasma lipids and lipoproteins regardless the mode of treatment.[20] T2D and the metabolic syndrome are both becoming more prevalent, and both increase the risk of CVD. Many patients are prone to atherogenic dyslipidemia, the so-called "atherogenic lipid triad" involving high serum TG levels, low serum HDL-C levels, and a preponderance of small, dense, LDL-C particles. All of the processes involved in atherogenesis can be exacerbated by insulin resistance and/or the metabolic syndrome.[21] One of the end points of atherosclerosis is CHD,[22] which remains the leading cause of morbidity and mortality in developed and developing countries.[23,24] Several novel risk factors for atherosclerosis have recently been proposed, with lipid parameters among these factors. They are suggested as potential criteria for improved detection of subclinical atherosclerosis.[25] The cholesterol that accumulates in atherosclerotic lesions originates primarily in plasma lipoproteins, mainly LDL. Several studies reported high levels of TC and LDL-C among diabetic patients,[26,27] a finding also observed in the present study. However, other studies couldn't report similar finding.[28] Furthermore, it has been found that loss of affinity for the Apo B receptors of the glycated LDL-C may contribute to the increased plasma TC level in diabetic patients.[29] T2D patients showed a low serum HDL-C level in comparison to controls. HDL turnover in patients with T2D appears to be accelerated resulting in low serum HDL-C level. Also, the higher insulin level in such patients may lower HDL-C concentration.[30] Low HDL-C levels are common in T2D patients, and this finding seems to be related to the increased mortality and morbidity in CHD.[31] The transport of cholesterol is reduced when HDL is glycated and the transfer activity of cholesteryl ester is increased.[32] In addition, low HDL-C level is frequently encountered in association with increased TG level, and both disorders may be

metabolically related.[33] Management of DM leads to favorable changes in HDL-C concentrations.[34] The present study revealed an increased serum LDL-C level in patients with T2D compared to control subjects. This is in agreement with the observation of others.[14,35] However, other studies found non-elevated LDL-C level among diabetic patients.[36] Several changes in LDL particles have been noted in T2D including non-enzymatic glycation[37] and oxidation[38] of LDL. Such LDL particles would be more susceptible for uptake by macrophage scavenger receptors leading to foam cell formation. Thereby, increasing the risk of atherosclerosis.[39] Moreover, diabetics have small, dense and glycated LDL particles[40] which are strongly associated with CHD.[41] Lowering of low-density lipoprotein cholesterol with statins is obviously effective in the prevention and treatment of CHD.[42] Treatment of high LDL-C levels should be initiated early during diabetic management to reach target levels and to minimize the cardiovascular risk and CHD risk.[34] Hypertriglyceridaemia is the most frequently recognized type of dyslipidaemia among T2D patients, and usually associated with an increased risk of CHD.[43] It has been proposed that increased plasma insulin levels promote VLDL synthesis resulting in elevated plasma TG levels, whereas, increased elimination of lipids and apolipoproteins from VLDL particles results in the increased production of intermediate density lipoprotein (IDL) and LDL.[44] Beneficial changes in TG levels occurs with the optimal management of diabetes.[34] Increased serum VLDL-C has been found among diabetic patients.[45] Glycated LDL and VLDL levels are markedly elevated in diabetics than in normal subjects. However, only glycated VLDL was markedly increased in diabetic patients with atherosclerosis than in those without evident atherosclerotic disease.[37] Moreover, Yegin et al[37] proposed that glycation of VLDL may be the reason behind the development of atherosclerosis in diabetic patients. Achievement of good metabolic control using different antidiabetic agents including exogenous insulin has been found to be associated with improvement of atherogenic lipid profile.[11,46,47] In addition, several lipid

lowering drugs have been shown to be effective in improving atherogenic lipid profile.[48-51] Combination lipid lowering therapy is more effective than statin monotherapy.[52] Control of diabetes results in reduction of not only morbidity and mortality, but also the economic burden of the disease.[53] Deterioration of the glycaemic control aggravates lipid and lipoprotein abnormalities[10], and thus, accelerate the atherosclerotic process. Thus, identifying patients with dyslipidaemia provide an opportunity to reduce the incidence of CHD.[54]

*In conclusion,* T2D has a profound effect on lipid and lipoprotein profile. Patients with T2D have a diversity of dyslipidaemia and also higher atherogenic (LDL-C/HDL-C) ratio. Thus, these patients might be at high risk of accelerated and diffuse atherosclerosis and would be at a greater risk of CVD and CHD.

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