Dyslipidemia: A Frequently Missed Disorder in Type 2 Diabetes Mellitus

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Abstract

Background: Dyslipidemia and type 2 diabetes mellitus a deadly combination need early diagnosis, proper management, and regular follow up.**Aims of the study**: Is to find the proportion, pattern, and factors related to dyslipidemia in patients with type 2 diabetes mellitus.**Methodology:** A cross sectional study on 74 patients with Type 2 diabetes mellitus attending the diabetes clinic in Al-Hindeya General Hospital to evaluate them for the prevalence of dyslipidemia. The patients underwent a series of investigations including serum lipid profile, fasting blood sugar, and glycated hemoglobin among others.**Results:** Dyslipidemia reported in 73% of the studied group. Elevated low density lipoprotein, triglycerides, total cholesterol, and reduced high density lipoprotein were noted in 28, 22, 16, and 16 patients, respectively. Patients' age above 50 years significantly associated with elevated mean TG (P-value=0.04), TC (P-value=0.001), and reduced mean HDL-C (P-value=0.004). Poor glycemic control significantly associated with elevated mean TG (P-value=0.04). Disease duration more than 5 years adversely affects mean TG level (P-value=0.01). Obesity showed highly significant correlation with elevated mean TG (P-value=0.001), TC (P-value=0.006), and LDL-C (P-value=0.001). Insulin therapy showed highly significant association with elevated mean TC (P-value=0.006) and reduced mean HDL-C (P-value=0.001). Patient gender did not affect the prevalence of dyslipidemia. **Conclusions:** Dyslipidemia detected in 73% of the patients and manifested by variable combinations of elevated low density lipoproteins, triglycerides, total cholesterol, and reduced high density lipoprotein. Older age, poor glycemic control, longer disease duration, obesity, and using insulin therapy are significantly associated with dyslipidemia.

Keywords: Type 2 diabetes mellitus, dyslipidemia, triglycerides, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol.

Introduction

Type 2 diabetes mellitus (T2DM) is a common metabolic disease accounting for 90-95% of the reported diabetes mellitus (DM) cases (1). It is prevalence increasing worldwide in an epidemic pattern with an estimation of 592 million patients by the year 2035 (2).

Dyslipidemia is a medical problem that frequently associated with T2DM, as a result of insulin resistance with relative insulin deficiency and obesity, because insulin is the cornerstone hormone in controlling lipid metabolism (3). Insulin resistance or deficiency result in lacking lipoprotein lipase activity and over production of triglyceride rich lipoproteins in addition to the increased release of free fatty acids from adipose tissue. Both factors resulted in dyslipidemia with an accelerated atherosclerosis and macrovascular complications (4). Furthermore, Simmons R K *et al.* (5) noted an increased risk of T2DM, elevated TG level, and reduced HDL-C level in 25% of the apparently normal nonobese, nondiabetic individuals with insulin resistance similar in it is extent to that seen in T2DM.

The IV Adult Treatment Panel guidelines define dyslipidemia as a variable combinations of elevated serum triglycerides (TG), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), and reduced high density lipoprotein cholesterol (HDL-C) levels.

T2DM increases the risk of cardiovascular disease (CVD) by tow to fourfold and with the presence of dyslipidemia the morbidity and mortality will be higher (6,7). In recent studies, they found a relation between diabetic dyslipidemia and malignancies like prostate, colorectal, and breast (8-10). Furthermore, in addition to the CVD risk of insulin resistance and hypercholesterolemia, the hallmarks of T2DM and dyslipidemia, they found to predispose to Alzheimer's disease (11).

In a meta-analysis of 14 randomized trials on statin use in 18000 patients with T2DM they found for each one mmol/L decrease in LDL-C level there will be 9% decrease in all-cause mortality and 13% decrease in vascular mortality (12). Thus, early diagnosis and proper treatment of diabetic dyslipidemia has the same importance as good glycemic control (13,14).

The study aims to find the prevalence of dyslipidemia in T2DM patients, define the pattern of dyslipidemia in this group of patients, and to discover the factors associated with dyslipidemia.

Patients and methods

A prospective cross sectional study involving 74 patients (26 males and 48 females) with T2DM was performed at the diabetes clinic, Al-Hindeya General Hospital, Karbala, Iraq from January to April 2015. All participants were above 37 years and randomly selected.

A detailed record of the patients, history and a thorough clinical examination was done to them. The

patients, records included age, gender, duration of disease, residence, and type of anti-diabetic medication (insulin, or oral anti-diabetics, or both). Blood pressure measurement in sitting and standing positions, height, and weight were estimated for each patient. The body mass index (BMI) of the patients was calculated by dividing the weight in kilograms over the height in meter squared. According to the results of BMI the patients were categorized into three groups including normal (< 25 kg/m^2), overweight (25-29.9 kg/m^2), and obese ($\geq$30kg/m^2).

Blood samples after an overnight fasting for 12 hours was collected to assess for serum lipid profile (TG, TC, HDL-C, and LDL-C), fasting blood sugar, and glycated haemoglobin (HbA1c) levels. Furthermore, tests for renal function, liver function, thyroid function, and electrocardiogram were also done to the patients.

Participants with history of coronary heart disease, thyroid disease, diabetic nephropathy, and lipid lowering medications were excluded from the study. Women with gestational diabetes and diabetic women with pregnancy were also excluded from the study.

The American Diabetes Association (ADA) guidelines were used to define abnormal lipid values as $\geq$1.7 mmol/L for TG, $\geq$6.2 mmol/L for TC, $\geq$3.38 mmol/L for LDL-C, and <1.0 mmol/L for HDL-C.

Verbal consent was taken from the patients to use their medical records in the study. SPSS version 22 software was used for statistical analysis and data were expressed by means ± stander deviation. ANOVA was used to examine the differences between different groups and within groups in continuous data Chi-square test for discrete data. The statistical difference was considered to be significant when P-value <0.05 and highly significant when P-value <0.001.

Results

As shown in table 1, out of 74 patients with T2DM involved in the study, 48 (64.9%) were females and 26 (35.1%) were males. The age of patients ranges from 37 to 71 years with a mean of 53.28 ± 8.78 years. The disease duration ranges from 3 to 25 years with a mean of 9.39 ± 4.54 years and about two thirds of the patients with history of T2DM less than 5 years. The majority of the participants were of urban origin constituting 67.6% of the studied group. The body mass index of patients ranges from 19 to 42.56 kg/m^2 with a mean of 29.63 ± 4.99 kg/m^2.

Table 1 Demographic features of the studied group

Variables	Age, year		Gender		Duration of disease, year		Residence	
	<50	≥50	Male	Female	<5	≥5	Rural	Urban
No.	38	36	26	48	44	30	24	50
%	51.4	48.6	35.1	64.9	59.4	40.6	32.4	67.6

The serum lipid profile of the patients revealed an increased LDL-C in 28 (38%) patients, TG in 22 (30%) patients, TC in 16 (21.6%), and reduced HDL-C in 16 (21.6%) patients (fig. 1). Further analysis of the data showed the presence of mixed dyslipidemia, having more than one abnormal lipid value in the same patient, in 18% of the participants.
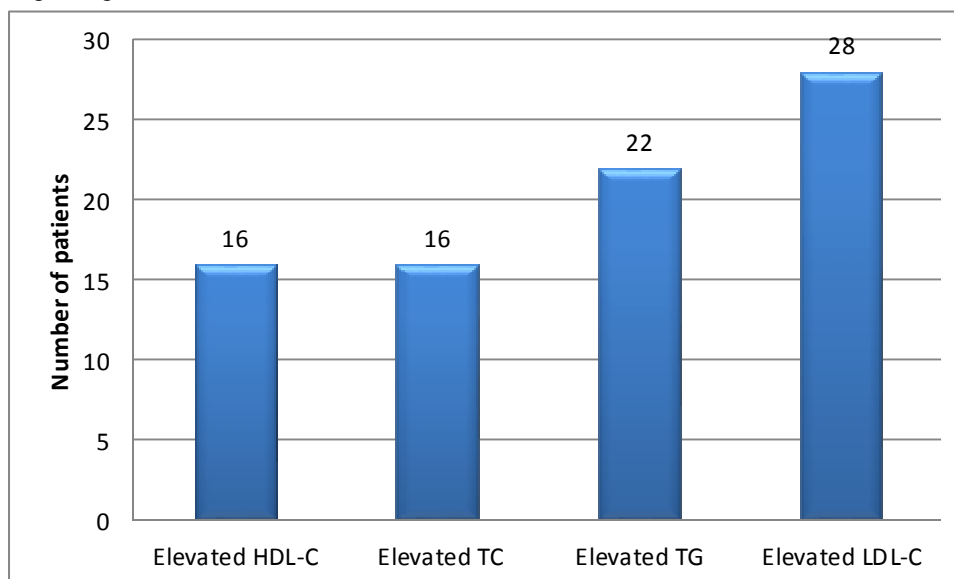
(TG = triglycerides, TC = total cholesterol, HDL-C= high density lipoprotein cholesterol, LDL-C= low density lipoprotein cholesterol).

Figure 1 Frequency of abnormal individual serum lipids in the studied group

Dyslipidemia was found in 54 (73%) patients with deferent patterns of presentation, while normal

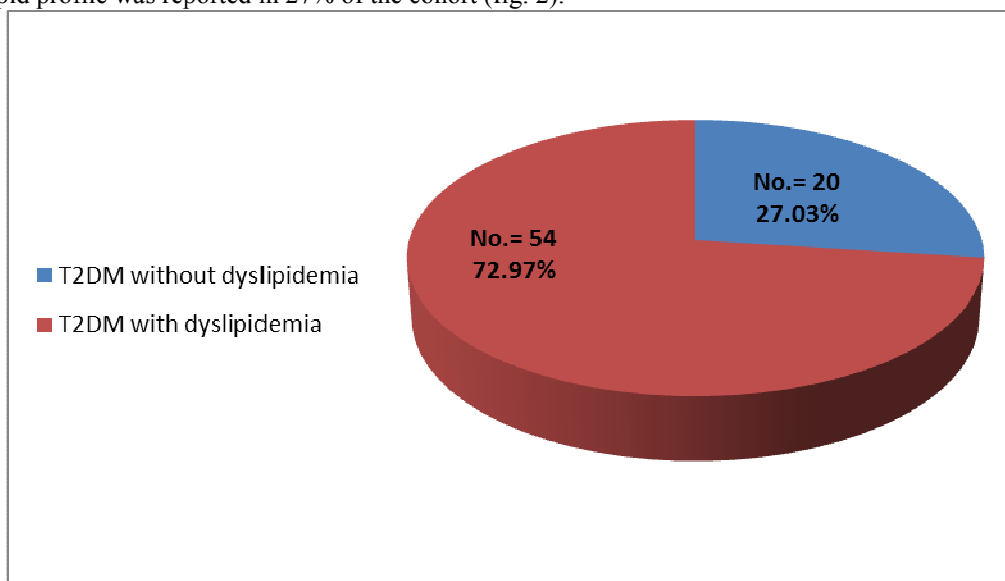serum lipid profile was reported in 27% of the cohort (fig. 2).

Figure 2 Proportion of dyslipidemia in the studied group

In multivariate analysis we assessed gender, age, HbA1c level, duration of disease, BMI, and anti-diabetic medications with mean serum lipid values (table 2). The factors significantly associated with different patterns of dyslipidemia include age ≥50 years, poor glycemic control, disease duration ≥5 years, obesity, and insulin therapy. Patients' gender did not show significant relationship with dyslipidemia. Mean TG, TC, and HDL-C were significantly deranged from normal levels in patients more than 50 years of age as compared with those below 50 years with a P-value of 0.04, 0.001, and 0.001, respectively. Poor glycemic control (HbA1c levels ≥7%) showed significant relationship with elevated mean TG level with a P-value of 0.04. Disease duration more than 5 years adversely affects mean TG level with a P-value of 0.01. Obesity (BMI ≥ 30 kg/m^2) showed highly significant effects on mean TG, TC, and LDL-C levels with a P-value of 0.001, 0.006, and 0.001, respectively. Patients using insulin therapy showed a highly significant elevation in mean TC and reduction in HDL-C with a P-value of 0.006 and 0.001, respectively.

Discussion

In our study we find elevated LDL-C, TG, TC and reduced HDL-C levels in 28%, 22%, 16%, and 16% of the patients, respectively. These results consistent with the findings of an Iranian and Indian studies (15,16). Elevated LDL-C, TG and reduced HDL-C levels are independent risk factors for coronary heart disease raising the risk of CVD seen in T2DM. Almost similar results have been documented by studies done in India and Pakistan (17, 18). Dyslipidemia reported in 54 out of 74 patients involved in the study constituting about 73% of the total number. Similar studies done in India, Nigeria, and South Africa found the proportion of dyslipidemia in T2DM about 82.5%, 89.1%, and 90.3%, respectively (19-21). Our result was lower than that of the aforementioned studies because more than 50% of the patients involved in our study were below 50 years and it is well known that dyslipidemia incidence increases with age especially in those beyond 60 years.

In this study mean TG, TC, and HDL-C were significantly outside the normal range in patients with an age above 50 years. This result in contrast to a study done in Saudi Arabia showed younger age significantly related to higher mean TC and LDL-C levels (22). However, Hetal Pandya *et al.* (19) did not report a significant relation between age and dyslipidemia. The explanation to our result is that older age per se is an unmodifiable risk factor for both dyslipidemia and T2DM (23).

In the present study higher HbA1c was significantly associated with elevated mean TG level. Aljabri *et al.* (22) found the higher HbA1c levels significantly correlated with elevated mean TG and TC levels. Another study done on Pakistani patients with T2DM detected the positive correlation between poor glycemic control (HbA1c level ≥ 7%) with elevated mean TC, LDL-C, and reduced HDL-C levels (24). Dyslipidemia was expected in this group of patients because poor glycemic control adversely influences serum lipids as mentioned above.

Table 2 Relation between mean serum lipid values and demographic features of the studied group

Variables No. (%)		Mean serum lipid values (mmol/L)			
		TG	TC	HDL-C	LDL-C
Gender	Male 26 (35.1)	2.18±1.34	5.01±1.60	0.96±0.17	4.17±1.16
	Female 48 (64.9)	1.98±1.05	5.33±1.22	0.95±0.20	4.03±1.07
	P-value	0.07	0.34	0.42	0.17
Age	<50 years 38 (51.4)	1.87±0.93	5.12±1.05	1.02±0.14	3.93±1.04
	≥50 years 36 (48.6)	2.51±1.61	5.75±1.41	0.90±0.18	4.42±1.24
	P-value	0.04*	0.001**	0.004**	0.06
Glycated hemoglobin	<7% 18 (24.3)	1.72±1.16	4.75±1.21	1.02±0.10	4.24±1.08
	≥7% 56 (75.7)	2.33±1.37	5.37±1.39	0.94±0.18	4.15±1.19
	P-value	0.04*	0.097	0.096	0.77
Duration of disease	<5 years 44 (59.4)	1.73±0.84	5.12±1.05	0.9±80.12	4.09±1.01
	≥5 years 30 (40.6)	2.26±1.46	5.28±1.46	0.93±0.22	4.17±1.44
	P-value	0.01*	0.63	0.44	0.84
Body mass index	<25 kg/m^2 8 (10.8)	1.52±0.73	3.80±0.85	0.95±0.053	2.90±0.64
	25-29.9 kg/m^2 34 (45.9)	2.51±0.92	5.36±1.03	0.9±10.21	4.11±0.84
	≥30 kg/m^2 32 (43.3)	3.45±2.85	5.42±1.59	1.01±0.12	4.55±1.33
	P-value	0.001**	0.006**	0.087	0.001**
Anti-diabetic medication	OAD 56 (75.6)	1.94±1.33	5.16±1.29	0.99±0.12	4.11±1.27
	Insulin 4 (5.4)	3.40±0.00	7.00±0.00	0.60±0.00	1.20±0.00
	Mixed 14 (19)	2.26±0.76	4.80±0.83	1.20±0.00	3.70±0.00
	P-value	0.077	0.006**	0.001**	0.39

(TG = triglycerides, TC = total cholesterol, HDL-C= high density lipoprotein cholesterol, LDL-C= low density lipoprotein cholesterol, OAD= oral anti-diabetes, *= significant relationship, **= highly significant relationship).

We found a significant positive relationship between elevated mean TG level and disease duration, while Hetal Pandya et al. (19) study did not notice such a relationship. The longer duration of DM associated with progressive pancreatic beta cell destruction as a result of the toxic effect of hyperglycemia on these cells leading to pancreatic failure and insulin deficiency with it is unfavorable effects on lipid metabolism.

This study showed a significant relationship between elevated mean TG, TC, and LDL-C levels with obesity (BMI ≥30 kg/m^2). Aljabri et al. (22) and Hetal Pandya et al. (19) also noticed the direct relationship between weight and mean TG, TC, and LDL-C levels. Obesity associated with insulin resistance and increased adipose tissue mass. Both factors are the main features of diabetic dyslipidemia as mentioned earlier.

In our study we found a highly significant relationship between insulin therapy with elevated mean TC and reduced mean HDL-C levels. The need for insulin therapy in this group of patients indicates the presence of an aggressive disease resulted in severe hyperglycemia and insulin resistance with inadequate insulin secretion. Such a constellation of problems are usually the triggers for diabetic dyslipidemia. Proper glycemic control with adequate insulin therapy improve serum lipid profile and reduce lipid deposition in different body tissues, the long term consequences of dyslipidemia (25).

The present study did not show a significant effect of gender on dyslipidemia. This result consistent with the findings of studies had been done by Subbash S Pujari (3) and Vinter-Repalust et al. (26). However, female gender was significantly associated with different patterns of dyslipidemia as shown by Aljabri et al. (22),

Yuthika Agrawal *et al.* (16), Gustafsson *et al.* (27), Syed Gilani *et al.* (28), and Nakhjavani *et al.* (15). Others noted the increased incidence of CVD in diabetic females in addition to the elevated prevalence of dyslipidemia (29-31). Many theories were postulated for the increased incidence of dyslipidemia in diabetic women. The most accepted theory suggests the adverse effect of diabetes on female sex hormones resulting in reduced estrogen related protective effects on body fat distribution and insulin action (32). Another theory regarded the different pattern of obesity between females and males as the possible cause for the increased incidence of dyslipidemia in females (33).

The limitations to our study are the younger patients, age and the small sample size.

Conclusions
Dyslipidemia marking 73% of the patients and elevated LDL-C and TG levels are the most common patterns. It was significantly associated with older age, poor glycemic control, longer disease duration, obesity, and using insulin therapy.

Recommendations
All T2DM patients should have serum lipid profile assessment on diagnosis and at least annually thereafter.

Acknowledgment

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