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Study Lipids Profile In Patients With Type 1 Diabetes Mellitus

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

{سَيَجْعَلُ اللَّهُ بَعْدَ عُسْرٍ يُسْرًا}

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Abstract

Dyslipidemia and hyperglycemia are metabolic anomalies ordinarily found in youthful patients with Type 1 diabetes mellitus (T1DM) and both increment the danger of cardiovascular illness

Background

Dyslipidemia is prevalent in adults living with type 1 diabetes, and it can worsen the presentation of microvascular complications such as retinopathy. This study aims to identify the pattern coupled with the frequency of dyslipidemia in diabetic adults who followed up at different clinics in Baqubah Teaching Hospital , and evaluate the associations with demographic and clinical characteristics.

Aim and objective

The study aim to evaluate serum level of triglycerides and cholesterol in patients with diabetes mellitus type 1.

PATIENTS OF METHODS

The study was under taken 10 patient with diabetes mellitus type1.

RESULTS

Type 1 diabetes patients showed elevated in level of serum triglycerides and cholesterol.

Conclusion

Diabetes is a disease of insulin which strictly regulates both glucose and lipid metabolism. Hyperlipidemia is the commonest complication of Diabetes Mellitus . Common lipid abnormalities in diabetes are raised Triglycerides and total cholesterol level .

Introduction

Type 1 Diabetes Mellitus (T1DM) is characterized by the destruction of immune-mediated pancreatic β - cells, leading to absolute insulin deficiency and thus the need for replacement therapy for survival. It is recognized as a serious health problem, supported by the epidemiological data, which reveals a 3% -4% increase in incidence rate per year globally. Furthermore, the age of onset keeps on reducing [1] according to surveys conducted in both developed and developing countries [1,2]. Over the last 40 years, the incidence rate of T1DM has increased in Saudi Arabia [3]. The prevalence of the disease is highest in Riyadh Provinces (126 cases per 100,000) and lowest in Eastern Provinces (48 cases per 100,000) [4].

One of the main aspects of the assessment of T1DM patients is the association of the disease with chronic complications that represent a burden not only to the public healthcare system but also to individuals who cope with them daily. Moreover, it is frequently associated with disabling and life-threatening complications linked to several modifiable risk factors, including an abnormal amount of lipids or Dyslipidemia (DLD) [5].

Lipid abnormalities are common in diabetes mellitus (DM) patients and unquestionably contribute to the increased risk of Atherosclerotic Cardiovascular Disease (ASCVD). The American Diabetes Association (ADA) encourages lipids screening at the time of diagnosis and every five years subsequently for diabetic patients under the age of 40 years, and more often for older patients [6]. DLD is notably seen in people with diabetes irrespective of insulin resistance or deficiency [7]. Low-density lipoprotein (LDL) is the most critical risk factor for ASCVD, in particular Coronary Artery Diseases (CAD), which is the leading cause of death in DM patients [8]. The major classes of DLD are classified according to the Fredrickson phenotype [9], categorized into various defects, and some are familial. It can also result from underlying 'nonlipid' causes other than a primary disorder of lipoprotein metabolism. The secondary causes of DLD are DM, cholestatic liver disease (CLD), nephrotic syndrome, chronic kidney disease (CKD),

hypothyroidism, obesity, smoking, alcohol consumption, and some medications such as thiazide diuretics, beta-blockers, and hormonal therapy. Lipids that are routinely measured in clinical practice are LDL, high-density lipoprotein (HDL), total cholesterol (Chol), and triglycerides (Trig).

Due to the lack of sufficient data locally in this regard, the study aimed to assess the pattern and frequency of lipids profile in T1DM Saudi adults following up at King Abdulaziz Medical City, Riyadh, (KAMC-RD), and to identify the associations with demographics and clinical characteristics. This would, in turn, aid in better understanding and awareness of the disease that could change our management practices.

How lipoprotein metabolism happen in DM ?

Lipoproteins, which transport non-water soluble cholesterol and triglycerides in plasma, are spherical particles composed of a central core of non-polar lipids (cholesterol esters, triglycerides) and a surface monolayer of phospholipids, free cholesterol and apolipoproteins. Lipoproteins are generally classified according to their density as chylomicron, Very Low Density Lipoprotein (VLDL), Intermediate Density Lipoprotein (IDL), Low Density Lipoprotein (LDL) and High Density Lipoprotein (HDL).

What's Chylomicrons?

Chylomicrons, the largest lipoprotein particles, are responsible for the transport of dietary triglycerides and cholesterol. Chylomicrons are composed of triglycerides (85-90%), cholesterol esters, phospholipids and apolipoproteins (mainly apoB48 but also apoA-I and apoA-IV). The formation of chylomicrons takes place in the enterocytes, and the process associating the lipid components (triglycerides, cholesterol esters, phospholipids) and the apoB48 is performed by the MTP

(Microsomal Transfer Protein). Chylomicrons are secreted into the lymphatic circulation before entering the bloodstream. In plasma, triglycerides of chylomicrons are hydrolyzed by the lipoprotein lipase leading to the formation of smaller, triglyceride-poorer particles known as chylomicron-remnants. Chylomicron-remnants are cleared by the liver through LDL B/E receptor or LRP receptor (LDL-receptor related protein).

What is cholesterol?

Cholesterol is a type of blood fat (blood lipid) that forms the membrane of each cell of the body. Cholesterol is carried in the blood by proteins called lipoproteins and it is these that are measured when you have a **cholesterol test**.

These are:

- High Density Lipoprotein (HDL)
- Low Density Lipoprotein (LDL)

LDL is often referred to as ‘bad cholesterol’, because it is this form of cholesterol that can build up in blood vessels.

HDL is often referred to as ‘good cholesterol’, because it helps to clear excess LDL out of the blood.

Symptoms of high cholesterol

High cholesterol does not usually present any symptoms in itself, however, people that have high or unbalanced cholesterol levels over a number of years are more likely to develop problems conditions such as heart disease, stroke and **peripheral arterial disease (PAD)**.

What causes high cholesterol?

High or unhealthy cholesterol levels may be brought on by:

- High-calorie diet
- High-carbohydrate diets
- Low physical activity
- **Obesity**
- Smoking
- High alcohol intake

High cholesterol levels may also result from the following:

- Hypothyroidism – an underactive thyroid
- Kidney disease
- Liver disease
- Familial hypercholesterolaemia – a genetic condition that affects around 1 in 500 people

What's normal level of cholesterol in dm?

The total cholesterol is the sum of the cholesterol in LDL, HDL and triglyceride particles. For LDL, or low-density lipoprotein, a healthy reading for someone with diabetes is 100 mg/dl or less. If you have diabetes and heart disease, the desired number is 70 mg/dl or less

Pathophysiology of diabetic dyslipidaemia

The most common lipid abnormalities are hypertriglyceridaemia associated with increased concentrations of triglyceride (TRG)-rich lipoproteins, mainly those consisting of large very-low-density lipoprotein (VLDL1) and their remnants. Decreased HDL cholesterol (mainly due to decreased HDL2 particles secondary to an increased rate of HDL catabolism) and normal or slightly increased LDL cholesterol levels with a predominance of atherogenic small, dense LDL (sd LDL) particles are the greater contributors to atherogenic disease. Such particles cannot be detected in routine measurements of LDL. Increased glycation and oxidation of these particles also occurs. These alterations are related to CVD risk and are the major treatment target in diabetic patients .

Insulin plays an important role in regulating lipid metabolism. It acts on the liver by inhibiting the production of VLDL, increases LDL receptors, and reduces free fatty acids and the production of ApoB. In addition, it inhibits the hormone-sensitive lipase in adipocytes, activates lipoprotein lipase in the circulation and increases the catabolism of chylomicron remnants.

What are triglycerides?

Triglycerides are blood fats that are a flexible source of energy.

The body can convert triglycerides into glucose and triglycerides can also be stored in adipose tissue (fat cells).

The process of converting triglycerides into glucose is known as gluconeogenesis and is performed by the **liver**.

Are there symptoms of raised triglyceride levels?

High triglyceride levels will not usually result in symptoms but, if you have diabetes and live in the UK, you should be given a cholesterol test at least once each year which will test your triglycerides in addition to **cholesterol**.

Whilst it is less common, some people may develop fat deposits under the skin called xanthomas.

Complications of hypertriglyceridemia

Having high triglyceride levels over a long period of time raises the risk of conditions such as **heart disease** and **stroke**.

Higher than recommended triglyceride levels have also been linked with higher incidence of **diabetic neuropathy [151]**

Having very high triglyceride levels is associated with increased risks of **pancreatitis** and **fatty liver disease**.

How are triglycerides measured?

Triglyceride levels are measured with a fasting blood test called a lipid panel, which also measures LDL, HDL, and total cholesterol levels.

, the standards for fasting triglyceride levels are as follows:

- Normal: Less than 150 milligrams per deciliter (mg/dL), or less than 1.7 millimoles per liter (mmol/L)
- Borderline high: 150 to 199 mg/dL (1.8 to 2.2 mmol/L)
- High: 200 to 499 mg/dL (2.3 to 5.6 mmol/L)
- Very high: 500 mg/dL or above (5.7 mmol/L or above)

While being tested for triglyceride levels, don't forget to check other blood lipids (such as HDL, LDL, and total cholesterol), too.

Management of diabetic dyslipidaemia

Detailed and specific reviews of the management of hyperlipidaemia in diabetics have been written.^{8,9} The management of dyslipidaemia encompasses both lifestyle and pharmacological measures. Patients with multiple risk factors need more intensive treatment. The factors that should be considered in every patient include:

- Diet. The amount of total fat, particularly saturated fat, should be limited in tandem with the general recommendations of a diabetic diet.
- Weight control. Even a 10% weight reduction may be associated with significant metabolic benefits (reduction in triglyceride, elevation of HDL cholesterol and improvement in insulin sensitivity).
- Regular exercise. Exercise improves insulin sensitivity and the lipid profile (HDL rises), and enhances weight loss. The exercise should be individualised and appropriate to the person's cardiovascular status and fitness.
- Monitoring other vascular risk factors. Blood pressure should be controlled and people should stop smoking.
- Optimising glycaemic control. Some improvement in the lipid levels (especially hypertriglyceridaemia) often follow stabilisation of glycaemic control, but many patients with type 2 diabetes will show a sustained high triglyceride low HDL pattern. There do not appear to be any lipid profile differences when using sulphonylureas, metformin or insulin.

Drug therapy

If the lipid profile remains suboptimal after 3 months of lifestyle measures and attempted glycaemic control, drug treatment is indicated. The Pharmaceutical Benefits Scheme provides practical guidelines .

- Statins. All statins have a dose-dependent effect on lowering total cholesterol and LDL cholesterol as well as moderate triglyceride lowering effects. They are recommended for patients with predominant raised LDL cholesterol.
- Fibrates (gemfibrozil). Reduce hypertriglyceridaemia and are associated with improvement of HDL cholesterol. A 3-6 month trial is recommended as there may be a transient rise in the LDL cholesterol concentrations.
- Oestrogen replacement in postmenopausal women. Hypercholesterolaemia and HDL cholesterol may improve, but triglycerides may worsen.
- Fish oils (omega-3 fatty acids). May be used as second-line agents in treating hypertriglyceridaemia.
- Bile acid binding resins. These are often unpalatable and can raise triglyceride levels. They are less useful in diabetes.
- Nicotinic acid. Although a potent lipid modifying agent, it is poorly tolerated and can increase insulin resistance. It is also less useful in diabetes.

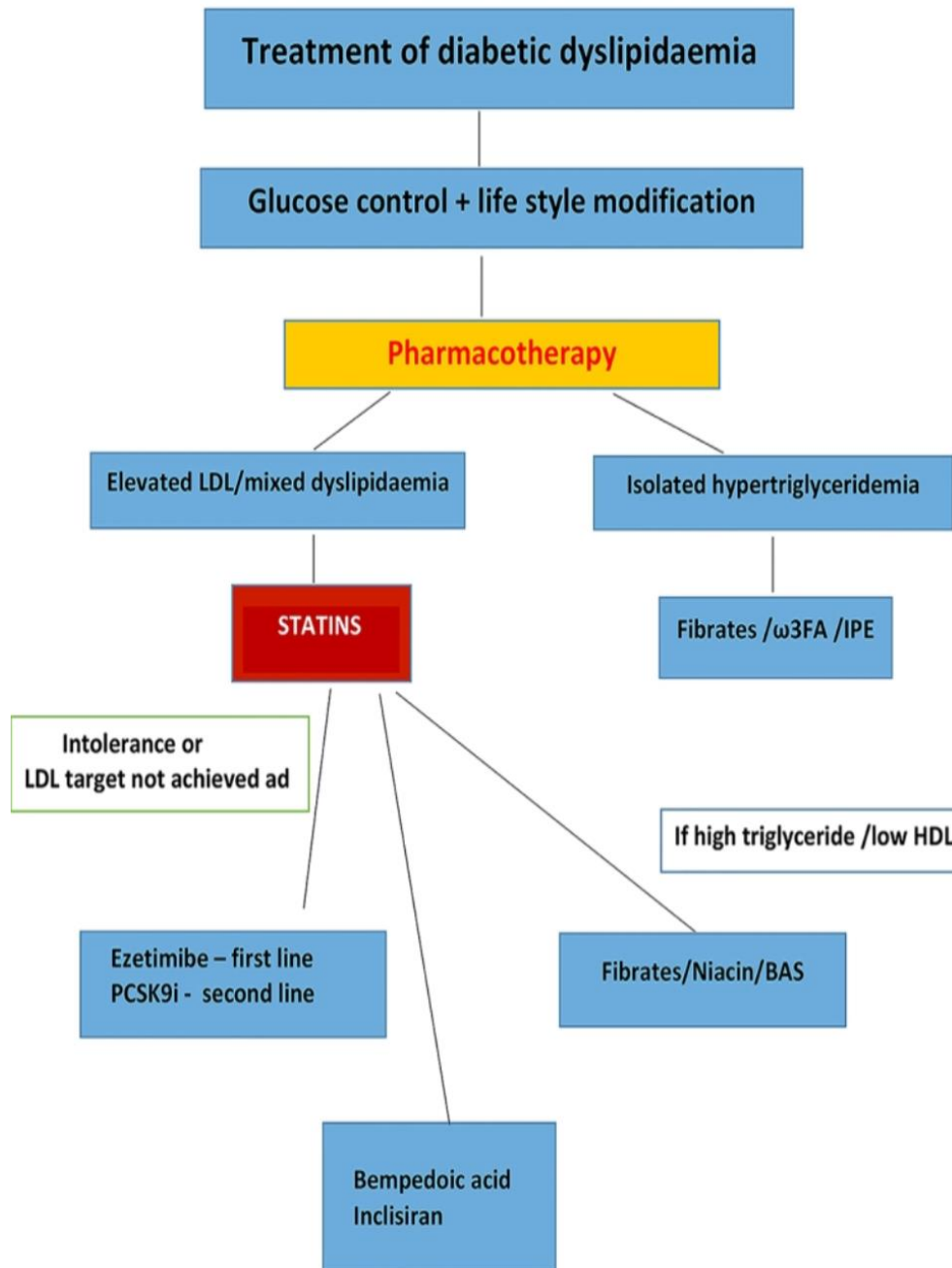


Figure 1. Treatment algorithm for diabetic dyslipidaemia. Statins are the cornerstone of the treatment. Combination therapies may be considered in patients at very high risk

Patients and Methods

Patients with Dm type 1 and patients with newly diagnosed dm type1 as 10 people, male and females

The detail history was taken; relevant clinical examination and all routine investigations were performed. An informed consent was taken from every patient after full explanation of procedure. Every patient was advise for at least 12-14 hours overnight fasting and the 5ml venous blood sample were collected in a disposable syringe on next morning (before breakfast) for the serum lipid profile and fasting blood sugar (for the assessment of blood glucose level).

Lipid abnormalities were defined based on the modified ADA criteria [11] and the Third Report of the National Cholesterol Education Program (NCEP III) [12]. Lipids were categorized into normal and abnormal levels. Abnormal levels were defined as total Cholesterol >5.18 mmol/L, triglyceride >1.7 mmol/L, HDL <1.55 mmol/L, and LDL >2.59 mmol/L. Diagnosis of dyslipidemia was made when one or more lipid values were abnormal. HbA1c was classified as optimal if $<7\%$, suboptimal if $7\%-10\%$, and poor if $>10\%$. Moreover, the normal TSH range was 0.35-4.94 mIU/L. Subjects were also classified into < 25 years and ≥ 25 years of age groups. The diabetes duration was classified into ≤ 10 years and > 10 years.

The data was entered into a spreadsheet and analyzed using IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0.

Armonk, NY: IBM Corp. The categorical variables were presented as frequency and percentages, while the numerical variables were presented as mean \pm standard deviation. The independent samples t-test was used to compare the numerical variables between two groups, while the Chi-Square test was tested to compare the categorical variables. A p-value of < 0.05 was considered significantly different for all the statistical tests.

Results

The result of my research is the outcome of ten patients with type 1 diabetes, whom I gathered during the last period to conduct my study on the results of their laboratory analyzes. They were four women, two adolescents, and four young men. The mean \pm SD for age of patients with type 1 diabetes mellitus was $22.1 \pm$. The lipid profile of patients with type 1 are whereas the frequency of dyslipidemia in patients with diabetes mellitus as far as gender is concerned is shown in tables. The pattern of disturbance in lipid profile of diabetic patients is shown in table . Majority of hyperlipidemic dm patients had uncontrolled diabetes as raised fasting blood sugar level and HBA1C.

N.cases	Age	Hba1c	Sugar	TG	Cholesterol
Case1	24	7.46	348	180	230
Case2	20	7.1	242	160	210
Case3	23	7.5	305	175	230
Case4	19	6.96	180	178	218
Case5	23	6.6	160	172	205
Case6	25	7	330	166	215
Case7	17	6.8	245	170	216
Case8	21	7.2	336	177	212
Case9	26	7.1	300	166	211
Case10	22	7.3	344	173	228

Counting

Statistics							
		age	gender	Hba1c	sugar	TG	cholseterol
N	Valid	10	10	10	10	10	10
	Missing	0	0	0	0	0	0
Mean		22.00	1.60	7.1020	279.00	171.70	217.50
Std. Deviation		2.789	.516	.28071	68.670	6.273	8.923
Variance		7.778	.267	.079	4715.556	39.344	79.611
Range		9	1	.90	188	20	25

age					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	17	1	10.0	10.0	10.0
	19	1	10.0	10.0	20.0
	20	1	10.0	10.0	30.0
	21	1	10.0	10.0	40.0
	22	1	10.0	10.0	50.0
	23	2	20.0	20.0	70.0
	24	1	10.0	10.0	80.0
	25	1	10.0	10.0	90.0
	26	1	10.0	10.0	100.0
	Total	10	100.0	100.0	

gender					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	male	4	40.0	40.0	40.0
	female	6	60.0	60.0	100.0
	Total	10	100.0	100.0	

Hb1c					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	6.60	1	10.0	10.0	10.0
	6.80	1	10.0	10.0	20.0
	6.96	1	10.0	10.0	30.0
	7.00	1	10.0	10.0	40.0
	7.10	2	20.0	20.0	60.0
	7.20	1	10.0	10.0	70.0
	7.30	1	10.0	10.0	80.0
	7.46	1	10.0	10.0	90.0
	7.50	1	10.0	10.0	100.0
	Total	10	100.0	100.0	

sugar					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	160	1	10.0	10.0	10.0
	180	1	10.0	10.0	20.0
	242	1	10.0	10.0	30.0
	245	1	10.0	10.0	40.0
	300	1	10.0	10.0	50.0
	305	1	10.0	10.0	60.0
	330	1	10.0	10.0	70.0
	336	1	10.0	10.0	80.0
	344	1	10.0	10.0	90.0
	348	1	10.0	10.0	100.0
	Total	10	100.0	100.0	

TG					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	160	1	10.0	10.0	10.0
	166	2	20.0	20.0	30.0
	170	1	10.0	10.0	40.0
	172	1	10.0	10.0	50.0
	173	1	10.0	10.0	60.0

	175	1	10.0	10.0	70.0
	177	1	10.0	10.0	80.0
	178	1	10.0	10.0	90.0
	180	1	10.0	10.0	100.0
	Total	10	100.0	100.0	

cholseterol					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	205	1	10.0	10.0	10.0
	210	1	10.0	10.0	20.0
	211	1	10.0	10.0	30.0
	212	1	10.0	10.0	40.0
	215	1	10.0	10.0	50.0
	216	1	10.0	10.0	60.0
	218	1	10.0	10.0	70.0
	228	1	10.0	10.0	80.0
	230	2	20.0	20.0	100.0
	Total	10	100.0	100.0	

Discussion

The present study discloses a high prevalence of dyslipidemia that reaches 70%. This high rate of dyslipidemia is consistent with other studies [13,14]. Many studies have shown similar findings in young and adolescents age groups [15-18]. In their study on dyslipidemia in Diyala adolescents and adults with T1DM, . Indicates that 80% of the subjects had dyslipidemia. Equivalently, reported a prevalence of 40% of lipid abnormalities upon evaluating selected adults with insulin-dependent diabetes.

However, distinct prevalence rates of dyslipidemia have also been reported [19,20]. Pérez et al [19] found a prevalence of dyslipidemia of 20% in Spanish adults, while Demirel et al. [20] found a prevalence of dyslipidemia of 30% in Turkish adolescents with T1DM. The differences in data presented by different studies are due to several factors such as differences in the reference ranges, targeted age, diabetes duration, treatment regimens, and glycemic control.

A study investigating cardiovascular risk factors in more than 11,000 children and adolescents with T1DM was conducted in the United States. Redondo et al. [21] reported a 3.8% prevalence of dyslipidemia, attributing the low prevalence to the fact that the majority of the subjects were neither young nor obese.

High LDL (70%) was the commonest dyslipidemia detected in our subjects, which is by far higher than the numbers from various studies [13-15].

Hypercholesterolemia has been recorded as the most prevalent type of dyslipidemia in various studies [18,20,22].

Dyslipidemia can lead to cardiovascular disease, which can be symptomatic.

High LDL cholesterol (bad cholesterol) levels are associated with coronary artery disease (CAD), which is blockage in the arteries of your heart, and

peripheral artery disease (PAD), which is blockage in the arteries of legs. CAD can lead to chest pain and eventually a heart attack. The main symptom of PAD is leg pain when walking.

There were 10 patients in this study out of which 60% of the patients were male and rest were female. 60% of total patients had dyslipidemia. According to the CDC, 97% of adults with diabetes have one or more lipid abnormalities while the prevalence of diabetic dyslipidemia varies from 25% to 60% in other studies [9]. This variation in prevalence may be due to differences in BMI and possibly genetic variation. A study showed that patients with type-1 diabetes had raised serum cholesterol ($>200\text{mg/dl}$) and 100% patients have raised triglycerides serum ($>150\text{mg/dl}$), The reason for difference in serum cholesterol values may be due to difference in the dietary habits of the people. In my study serum TG levels were found to be raised Equally between males and females, cholesterol was also high, but the risk of dyslipidemia during diabetes remains a greater risk for females than for males.

Conclusions

Diabetic dyslipidemia is a widespread condition, in which insulin resistance is considered the driving force behind the characteristic lipid abnormalities. All three components, namely hypertriglyceridemia, low HDL-cholesterol and high small dense LDL levels, are metabolically linked, with hypertriglyceridemia being the dominant feature.

Effectively managing diabetic dyslipidemia is significant in reducing the risk of CVD. Lifestyle and pharmacological interventions are the most important treatment strategies. Consequent treatment with statins is so far the most effective approach to decrease cardiovascular risk in diabetic patients. However, significant residual risk in statin-treated patients and statin intolerance in some patients still remain an unsolved problem. The role of statin in raising the risk for newly onset diabetes also warrants further research. In the quest for new therapeutic strategies, it is crucial to further promote the understanding of the underlying pathophysiology of lipid abnormalities in diabetic patients and to expand the existing knowledge on already established lipid-lowering drugs to clearly identify their role in the management of diabetic dyslipidemia.

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