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Lipoprotein lipase levels in patients with Coronary Artery Disease with Type 2 Diabetes Mellitus

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Abstract
Introduction: *Diabetes mellitus is a common metabolic disease. Atherosclerosis being a risk factor is promoted by decreased LPL activity which leads to elevated TG levels and reduced high density lipoprotein cholesterol (HDL-C), both risk factors for the development of coronary artery disease (CAD). So we studied the Lipoprotein lipase levels in patients with Coronary Artery Disease and in patients with Type 2 Diabetes Mellitus and comparing it with non diabetic individuals.*
Objective: *To determine Lipoprotein lipase levels in patients with Coronary Artery Disease with Type 2 Diabetes Mellitus.*
Methodology: *We conducted a hospital based comparative cross sectional study by dividing the patients into three groups. We compared the lipoprotein lipase levels in controls and in patients with diabetes mellitus and coronary artery disease.*
Results: *The mean lipoprotein lipase levels in controls were 46.2 but in patients with diabetes mellitus the mean lipoprotein lipase levels were reduced to 27.5 and in patients with diabetes and coronary artery disease it was further reduced to 17.5 with p value <0.001 which is statistically significant.*
Conclusion: *Reduced levels of lipoprotein lipase levels were seen in patients with coronary artery disease establishing the possible role of lipoprotein lipase in the pathogenesis of atherosclerosis.*
Keywords: *Lipoprotein lipase level (LPL), Diabetes mellitus and coronary artery disease.*

Introduction

Diabetes mellitus, commonly known as diabetes, is a metabolic disease that causes high blood sugar.[1] A person with diabetes has a condition in which the quantity of glucose in the blood is too elevated (hyperglycemia). This is because the body does not produce enough insulin, produces no insulin or has cells that do not respond properly to the insulin the pancreas produces. Diabetes is known to accelerate the process of atherosclerosis.[2] Coronary artery disease is a major public health issue in developing countries. CAD develops when the major blood vessels that supplies the heart (coronary arteries) are occluded by cholesterol containing plaques. Eventually, the decreased blood flow causes myocardial tissue necrosis presenting as a spectrum of chronic stable angina, unstable angina, Non ST elevation

myocardial infarction and ST elevation myocardial infarction. [3]

Triacylglycerol (TAG) is transported in the circulation in the form of large multi-molecular lipoprotein particles. Dietary TAG and fat-soluble vitamins are packaged into chylomicrons by the intestine, whilst endogenously synthesized TAG is secreted by the liver as VLDL particles.[3] Both classes of lipoprotein enter the circulation in order to distribute TAG to tissues also preventing the dispersal of the lipid en route by exchange or diffusion, the lipoproteins also confer the ability to deliver lipids to specific target tissues. LPL plays a crucial role in lipid metabolism and transport by catalysing the rate-limiting step in the hydrolysis of the TAG component present in the circulation[3]. Endothelial dysfunction is widely regarded as the initial lesion in the development of atherosclerosis.LPL has also been found to play key roles in a number of physiological and pathophysiological conditions, with abnormal LPL expression or function being associated either directly or indirectly with atherosclerosis. [4]

Given the importance of LPL in physiological and patho-physiological changes there are various techniques available to measure lipoprotein lipase activity. Hence this study was done to know the lipoprotein lipase activity in patients with diabetes mellitus and coronary artery disease while comparing them with normal individuals.

Materials and Methods

Study area and design

This study was done at sri manakula vinayagar medical college and hospital from march to august 2019 for a period of six months after getting informed consent from patients. Sri manakula vinayagar medical college is a tertiary care hospital located at madagadipet, Puducherry. The study design employed was a hospital based cross sectional study.

Study Participants

Sample size was calculated to be 60 (20 in each group) using the software Open Epi version 3.0 taking into consideration from the previous study with 95% confidence interval and 80 % power. Study participants Study participants were categorised into three groups Group A Individuals of age group 30 to 65 years without Coronary artery disease, without Diabetes Mellitus. Group B Patients diagnosed to have Coronary Artery Disease in the age group of 30-65 years admitted as inpatients in Sri Manakula Vinayagar Medical College and Hospital, Puducherry. Group C Patients diagnosed to have Type 2 Diabetes Mellitus in the age group of 30-65 years admitted as inpatients in Sri Manakula Vinayagar Medical College and Hospital, Puducherry.

All patients with Type 2 Diabetes Mellitus with Dyslipidemia and Coronary Artery Disease aged between 30-65 years were included in the study.

Methodology

After identifying these patients, questionnaire would be used to collect data from them with proper informed consent. Blood sample of 5ml will be collected for estimation of fasting plasma glucose, post prandial glucose, HbA1C, renal function test, lipid profile and urine sample will be analyzed for urine routine examination. 12 lead ECG, 2D echocardiography and coronary angiogram. Serum lipoprotein lipase levels were measured using Elisa kit.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22m version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

MS Excel and MS word was used to obtain various types of graphs such as bar diagram, Pie diagram. SPSS version 22 **(**IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

Results

Table 1: Gender distribution of study participants

P value	Group 3		Group 2		Group 1		Gender
	%	n	%	n	%	n	
0.233	75.0	15	50.0	10	55.0	11	Male
	25.0	5	50.0	10	45.0	9	Female
		20		**20**		**20**	**Total**

Group 1-Controls, Group 2- Diabetes, Group-3 Diabetes with CAD

Table 2: Distribution of study participants by diabetes

P value	Group 3		Group 2		Group 1		Diabetes
	%	n	%	n	%	n	
<0.001	100.0	20	100.0	20	0	0	Yes
	0	0	0	0	100.0	20	No
		20		**20**		**20**	**Total**

Group 1-Controls, Group 2- Diabetes, Group-3 Diabetes with CAD

Table 3: Distribution of study participants by hypertension status

P value	Group 3		Group 2		Group 1		Hypertension
	%	n	%	n	%	N	
0.002	40.0	8	45.0	9	0	0	Yes
	60.0	12	55.0	11	100.0	20	No
		20		**20**		**20**	**Total**

Group 1-Controls, Group 2- Diabetes, Group-3 Diabetes with CAD

Table 4: Distribution of study participants by alcohol status

P value	Group 3		Group 2		Group 1		Alcohol
	%	n	%	n	%	N	
0.032	25.0	5	30.0	6	0	0	Yes
	75.0	15	70.0	14	100.0	20	No
		20		**20**		**20**	**Total**

Group 1-Controls, Group 2- Diabetes, Group-3 Diabetes with CAD

Table 5: Distribution of study participants by smoking status

P value	Group 3		Group 2		Group 1		Smoking
	%	n	%	n	%	N	
0.006	40.0	8	35.0	7	0	0	Yes
	60.0	12	65.0	13	100.0	20	No
		20		**20**		**20**	**Total**

Group 1-Controls, Group 2- Diabetes, Group-3 Diabetes with CAD

Table 6: Random blood sugar level of study participants in different groups

P Value	SD	Mean	Random blood sugar level
<0.001	19.3	98.2	Controls
	74.5	263.8	Diabetes
	57.2	228.7	Diabetes with Coronary artery disease

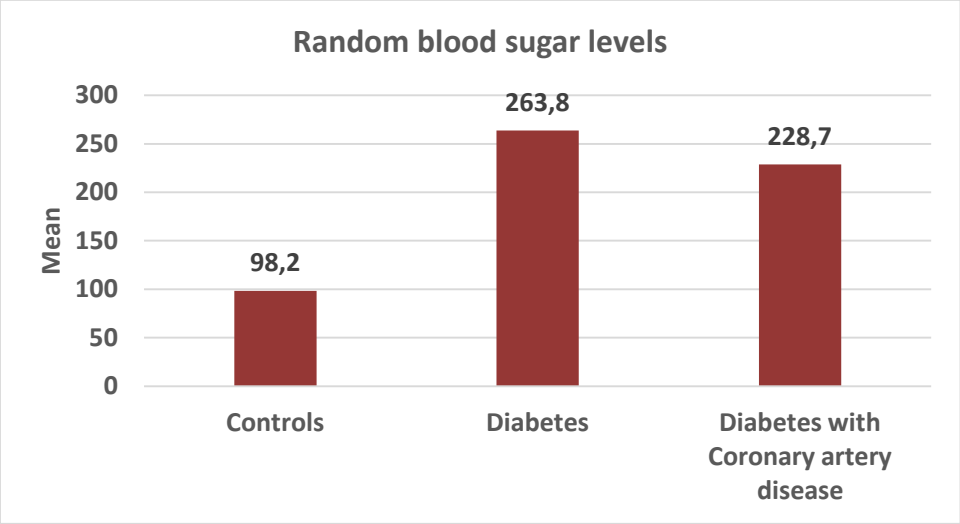


Table 7: BMI level of study participants in different groups

P Value	SD	Mean	BMI
0.002	1.2	22.6	Controls
	2.4	25.0	Diabetes
	2.4	23.7	Diabetes with Coronary artery disease

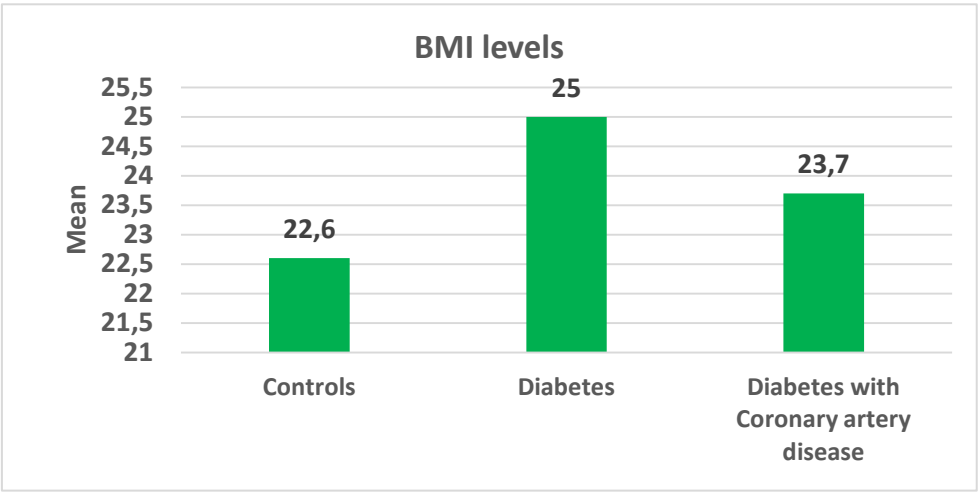


Table 8: GFR level of study participants in different groups

P Value	SD	Mean	GFR
<0.001	10.8	100.8	Controls
	18.6	83.8	Diabetes
	21.4	77.9	Diabetes with Coronary artery disease

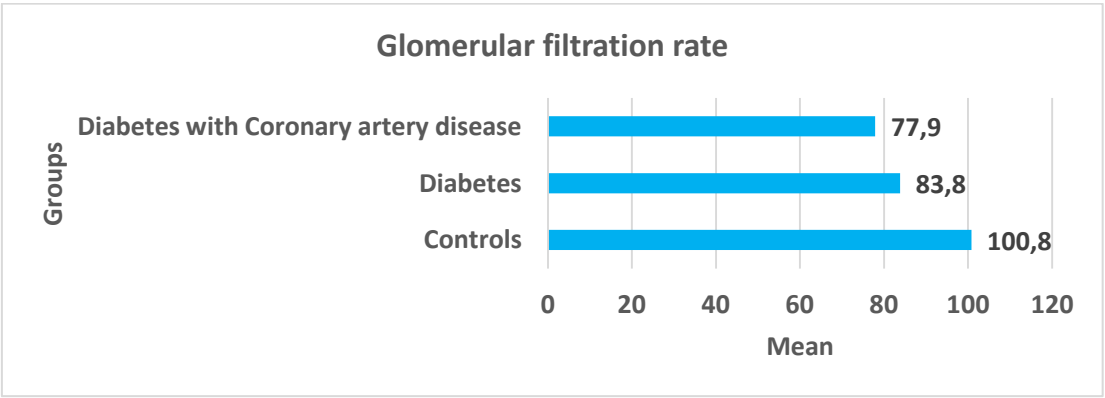


Table 9: Non- HDL level of study participants in different groups

P Value	SD	Mean	Non HDL
0.04	25.9	126.1	Controls
	37.2	157.0	Diabetes
	47.2	141.9	Diabetes with Coronary artery disease

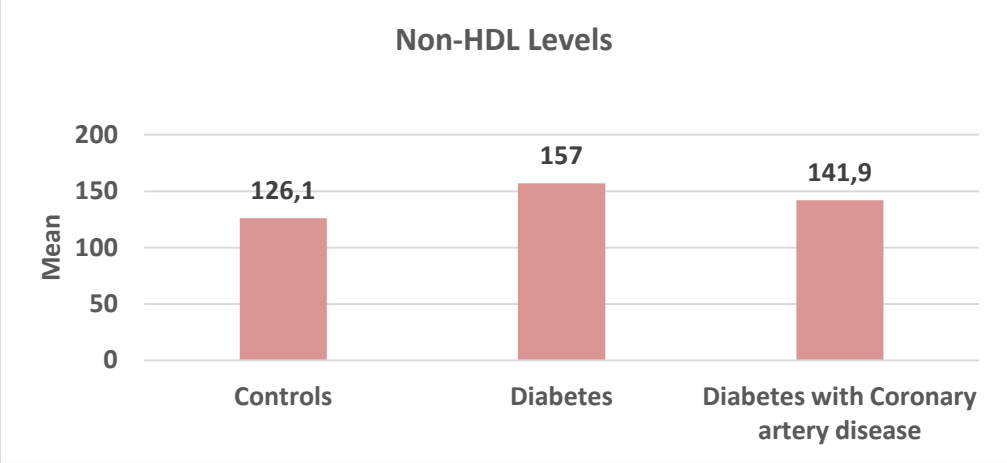


Table 10: TC/HDL ratio of study participants in different groups

P Value	SD	Mean	TC/HDL
<0.001	0.6	4.0	Controls
	1.1	5.4	Diabetes
	1.1	5.1	Diabetes with Coronary artery disease

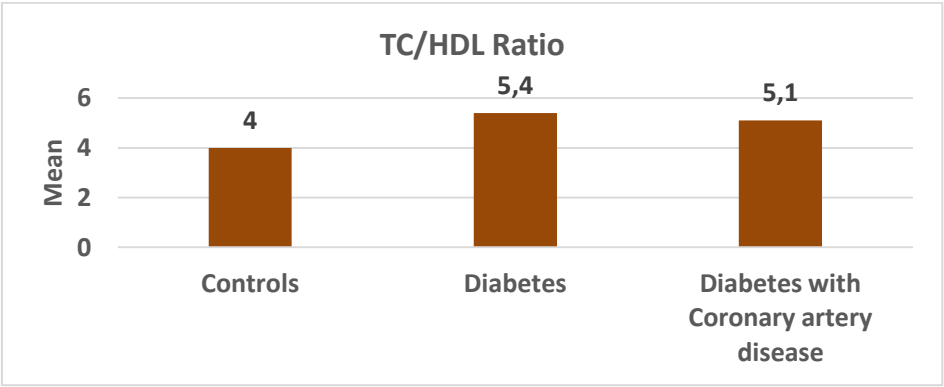


Table 11: LDL/HDL level of study participants in different groups

P Value	SD	Mean	LDL/HDL
0.01	0.6	2.5	Controls
	0.8	3.3	Diabetes
	0.8	3.1	Diabetes with Coronary artery disease

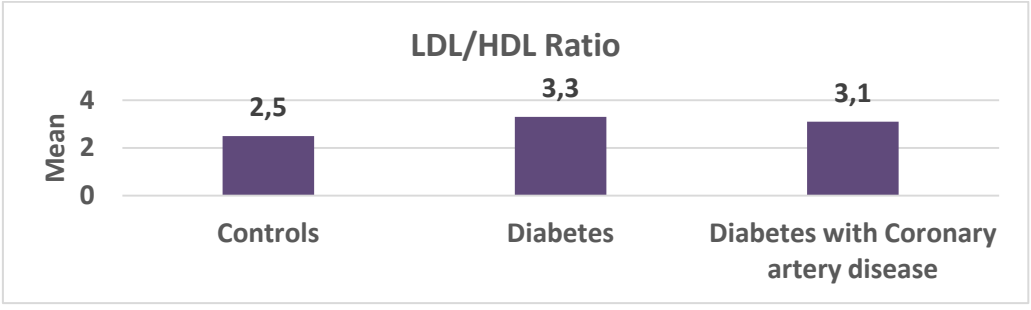


Table 12: Lipoprotein lipase level of study participants in different groups

P Value	SD	Mean	LPL
<0.001	2.1	46.2	Controls
	3.7	27.5	Diabetes
	3.3	17.5	Diabetes with Coronary artery disease

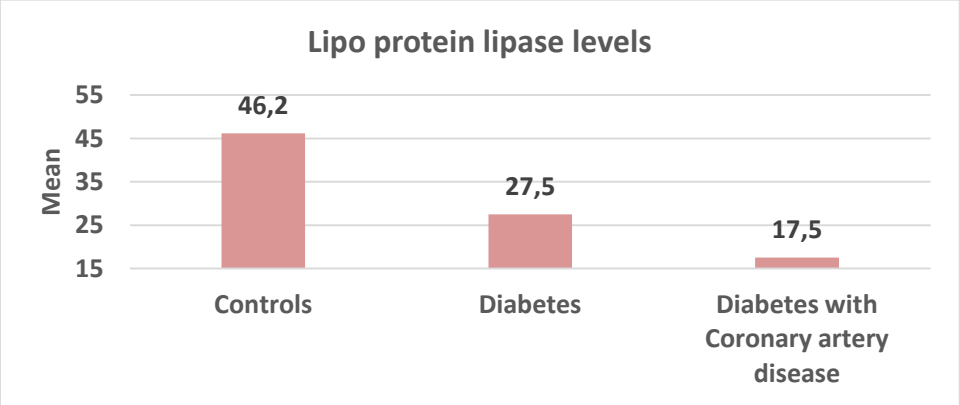


Table 13: Correlation of LPL with other parameters

P value	Correlation coefficient (r)	Parameter 2	Parameter 1
0.14	-0.19	Non-HDL	LPL
0.001	-0.43	TC/ HDL	LPL
0.007	-0.34	LDL/HDL	LPL
0.03	-0.27	TG/HDL	LPL

Discussion

Lipoprotein lipase levels are reduced in patients with diabetes mellitus. Patients with diabetes are at increased risk of developing coronary artery disease due to increased risk of atherosclerosis. The crucial role of LPL in lipid metabolism is illustrated by genetic LPL deficiency a rare disorder characterized by severe hypertriglyceridemia and low HDL cholesterol (HDL-C) levels.[5]

In this study we observed a male preponderance of 60% due to associated comorbidities of smoking and diabetes mellitus. The control group had no risk factors in terms of diabetes, systemic hypertension, smoking or alcohol usage. While the diabetic and CAD groups included individuals with the above mentioned risk factors. There were no significant differences in coronary risk factors such as hypertension, diabetes mellitus, smoking and body mass index as seen in a study done by takashi in Japanese population.[6]

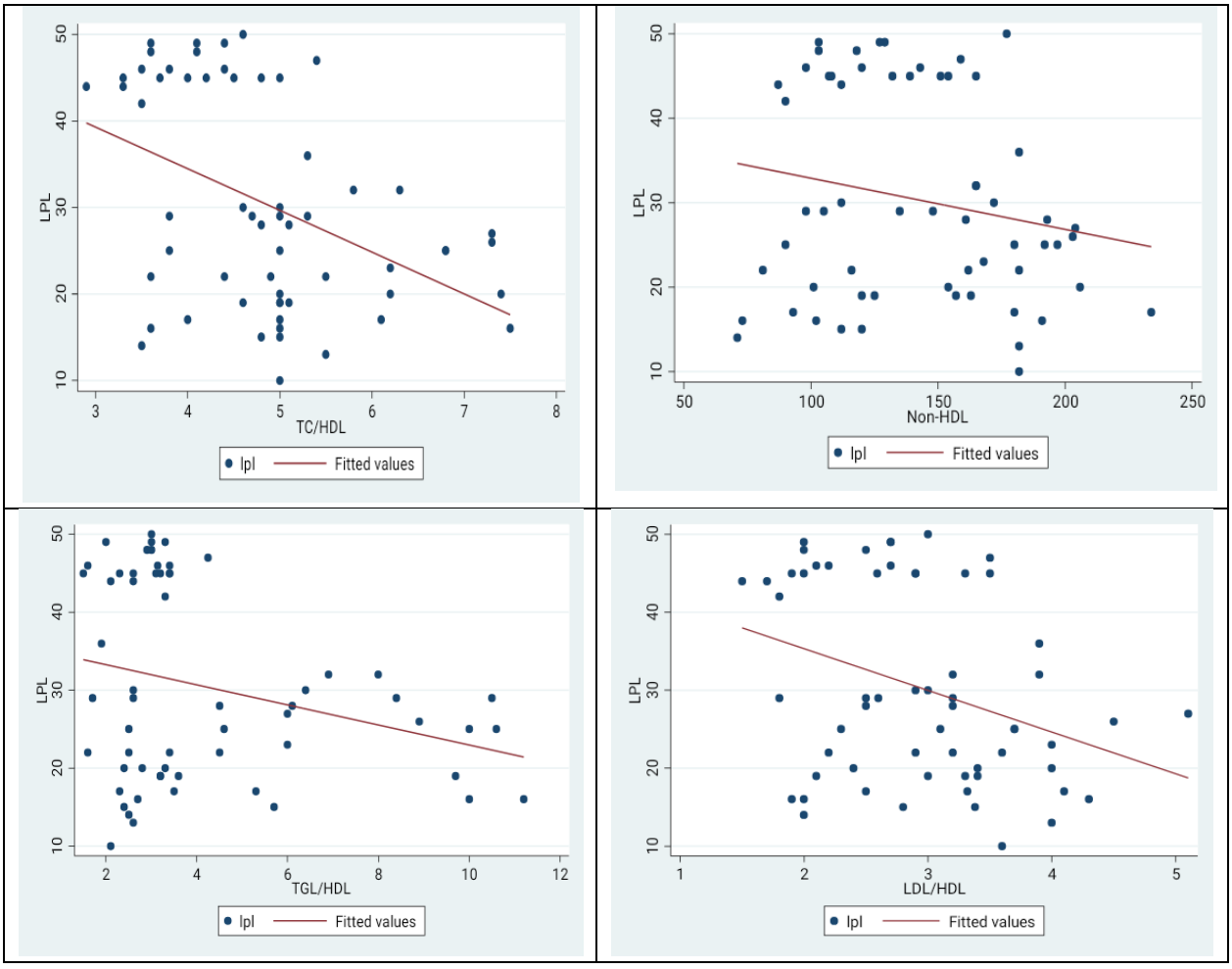
We also wanted to know the renal function in the three groups by calculating the estimated glomerular filtration rate between the three groups. The control population had a mean e-GFR of 100.8 while patients with diabetes had a mean e-GFR of 83.8 and diabetic with coronary artery disease population had a e-GFR of 77.9 with a p value of <0.001 which is statistically significant. This finding is similar to other studies where diabetes and coronary artery disease in combination has shown to reduce the renal function.[7,8]

In agreement with previous studies, we observed that coronary artery disease is strongly associated with diabetes HDL-C, TGL, TC and LDL-C levels.[9,10] However there were no significant differences of lipid profile while comparing them between the three groups. In this study, we also compared the non-HDL levels, TC/HDL, LDL/HDL ratios between the three groups and it was statistically significant with a p value <0.001.

In addition to finding the ratios of non-HDL, TC/HDL, LDL/HDL, TG/HDL we co-related these variables with lipoprotein lipase levels among the three groups and there were no significant correlation seen.[11,12] However this study shows the inverse relation of lipoprotein

lipase levels in patients with diabetes and coronary artery disease. The mean lipoprotein lipase levels in controls were 46.2 and in diabetic group it was reduced to 27.5 and it was further reduced to17.5 in diabetics with coronary artery disease group, thus establishing the inverse correlation of lipoprotein lipase

Co-relation scatter plot



Limitations

Less statistical power due to small study population. All patients with dyslipidemia irrespective of statin therapy were taken in the study which could have impacted the fasting lipid profile.

Conclusion

In patients with diabtetes and coronary artery disease lipoprotein lipase levels were significantly reduced and high levels of lipoprotein lipase could be atheroprotective thus explaining the possible role of lipoprotein lipase in the process of atherosclerosis in diabetes and CAD population.

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