

CORRELATION BETWEEN HDL-CHOLESTEROL LEVEL AND ANGIOGRAPHIC SEVERITY OF CORONARY ARTERY DISEASE AND IT'S COMPARISON IN PATIENTS WITH AND WITHOUT TYPE 2 DIABETES MELLITUS

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ABSTRACT

BACKGROUND

There has been enough evidence that HDL cholesterol plays a major role in reverse cholesterol transport and thereby reduces coronary artery atherosclerotic plaque burden and quantitatively low HDL cholesterol increases coronary artery plaque burden. Recent evidence suggests that in diabetic patients, there is functional impairment in HDL cholesterol which increases the risk of coronary artery disease.

So, the present study is conducted in order to compare the severity between diabetic and non-diabetic group of patients with coronary artery disease and to correlate with HDL-C values.

The objectives of the study were to study the correlation between quantitative HDL cholesterol level and angiographic severity of coronary artery disease and to compare these findings between diabetic and non-diabetic group of patients.

MATERIALS AND METHODS

90 Patients with acute ST segment elevation myocardial infarction diagnosed on ECG findings and admitted in ICCU of KIMS Hospital, of which 45 patients had diabetes mellitus.

Based on angiographic findings, coronary artery disease severity was calculated using revised BCIS-1 Jeopardy score, and the data obtained was analysed by different statistical methods.

RESULTS

Out of 90 patients in the study, Mean HDL-C in patients with and without T2DM was 44 mg/dl and 43 mg/dl respectively (p value 0.47). In non-diabetic patients HDL-C was negatively correlated to BCIS1 Jeopardy score ($r=0.65$, $p<0.001$). In patients with T2DM there was a positive correlation between HDL-C and BCIS1 Jeopardy score ($r=0.38$, $p=0.01$).

CONCLUSION

From this study we can conclude that HDL-C though is thought to be protective cholesterol, appears to be appropriate in patients without T2DM. In patients with poorly controlled T2DM, HDL C levels does not show protective role in our study. This could be attributed to the functional impairment of HDL-C in patients with poorly controlled diabetes mellitus.

KEYWORDS

ST Elevation MI; Type 2 Diabetes Mellitus; HDL-Cholesterol.

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BACKGROUND

Coronary artery disease (CAD) is a major cause of death as well as an economic burden to both developed and developing countries. The prevalence of CAD in urban areas of India is between 2.5%-12.6% and in rural areas, it is between 1.4%-4.6% and about 0.2% to 24% of CAD patients are having Diabetes Mellitus (DM).¹

Several trials which included treatment to increase HDL-C, showed no significant reduction in the prevalence of CAD.

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Thus, an absolute HDL-C level might not directly reflect the severity of CAD in diabetic patients. Factors such as endothelial dysfunction, accelerated atherosclerosis, functional impairment of HDL-C can explain the increased disease severity in patients with Diabetes Mellitus. Evidence shows diminished transfer to HDL-C of unesterified cholesterol and of cholesterol-esters in patients with type 2 Diabetes Mellitus.²

Several studies have showed the significant inverse relation between HDL-C level in blood and the risk of Coronary artery disease, further the association between CAD and metabolic syndrome is strong and consistent. The major role of HDL-C is reverse cholesterol transport and thus reducing the atherosclerotic burden in the coronary artery. Reverse cholesterol transport involves the uptake of cellular cholesterol from extra hepatic sources and transport by large HDL particles and its uptake by the liver, mediated by

hepatic receptors. 80% of HDL originates from the liver and 20% from the intestine.

Further HDL-C is also known for its in vitro anti-inflammatory action and its role in endothelial functioning.

Cholesterol efflux capacity of HDL correlates inversely with coronary endothelial dysfunction. In contrast, several studies have brought into light that in addition to the absolute blood HDL-C levels the true functioning capability of the particle, playing role in reverse cholesterol transport. This led to the critical analysis of functional dysfunction of HDL-C and role of endothelium.

MATERIALS AND METHODS

Source of Data

Patients with acute ST segment elevation myocardial infarction diagnosed on ECG findings and admitted in ICCU of KIMS Hospital, Hubli, and undergoing coronary angiography.

Methods of Collection of Data

The study will be conducted on 2 groups of patients.

Group a: Patients of acute STEMI with type 2 DM.

Group b: Patients of acute STEMI without type 2 DM.

Sample Size

A total of 90 cases of STEMI were included in the study of which 45 were Diabetic patients during the period extending between December 2015 to December 2016. Sample size is calculated to be 90, using the software nMaster taking into consideration the correlation coefficient as 0.28 between severity of CAD and HDL Cholesterol level from previous study, 80% power and 95% confidence interval.

Exclusion Criteria

1. Patients admitted with unstable angina or non-STEMI.
2. Patients on statin therapy.
3. Patients with previous history of PTCA or CABG.
4. Patients with previous history of acute coronary syndrome.
5. Patients not willing for CAG.

Patients admitted with above inclusion criteria were divided into two groups based on HbA1c values into diabetic and non-diabetic group, HbA1c value of >6.5% was classified into diabetic group.

Each patient was evaluated with History, clinical examination, and lab investigations.

Which included?

- Electrocardiogram.
- 2D-ECHO.
- Coronary angiography.
- HbA1c
- Lipid profile.

Renal function test which includes Serum urea and Serum creatinine.

Based on angiographic findings, coronary artery disease severity is calculated using revised BCIS-1 Jeopardy score.

Statistical Analysis

Appropriate statistical tests of significance were applied and correlation between variables was evaluated and the results were obtained which is being presented further.

RESULTS

Characteristics	With DM N (%)	Without DM N (%)	X ² value	p value
Age Group (Years)			1.969	0.37
30-49	8 (42.1)	11 (57.9)		
50-59	17 (60.7)	11 (39.3)		
≥ 60	20 (46.5)	23 (53.5)		

Table 1. Age Distribution in Patients With and Without Diabetes Mellitus

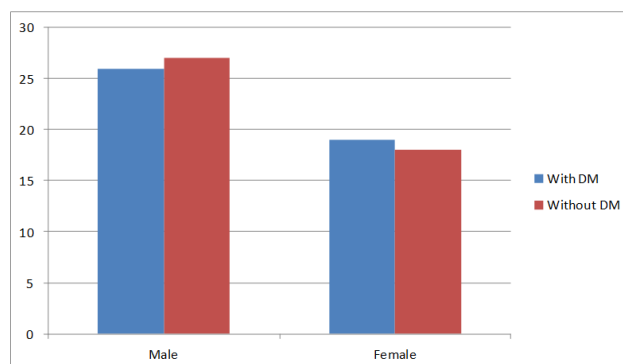


Chart 1. Sex Distribution in Patients With and Without Diabetes Mellitus

It was observed that there was no significant difference either in age distribution or sex distribution between two study groups and the groups were comparable.

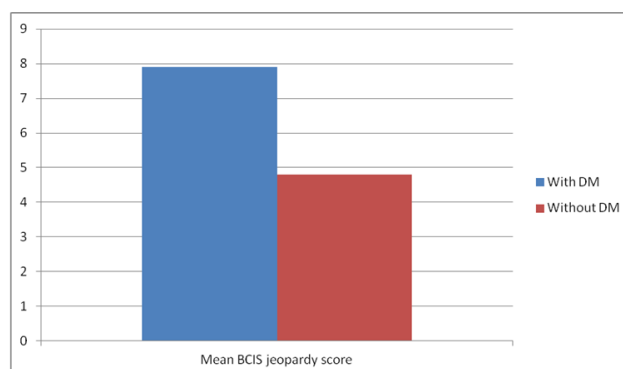


Chart 2. Graph Showing Mean BCIS Jeopardy Score in Patients with and Without Diabetes Mellitus

It was found that the mean BCIS Jeopardy score was high in patients with Diabetes mellitus which was statistically significant (p<0.001). This indicates that patients with diabetes had more severe coronary artery disease with a higher atherosclerotic burden.

Sl. No.	Characteristics	Mean (SD)		p Value
		With DM	Without DM	
1	HDL mg/dl	44 (7.7)	43 (7.6)	0.47

Table 2. Showing Mean HDL-C Level in Both Group of Patients

It was observed in the study that there was no statistically significant difference in the mean HDL Cholesterol level between the two study groups even though patients with T2DM had higher mean HDL-C levels.

Sl. No.	Correlated Variables	r Value	Direction	p Value
1.	BCIS score vs HDL	0.65	Negative	<0.001*

Table 3. Correlation between Coronary BCIS Score and HDL-C Level in Patients Without Diabetes Mellitus

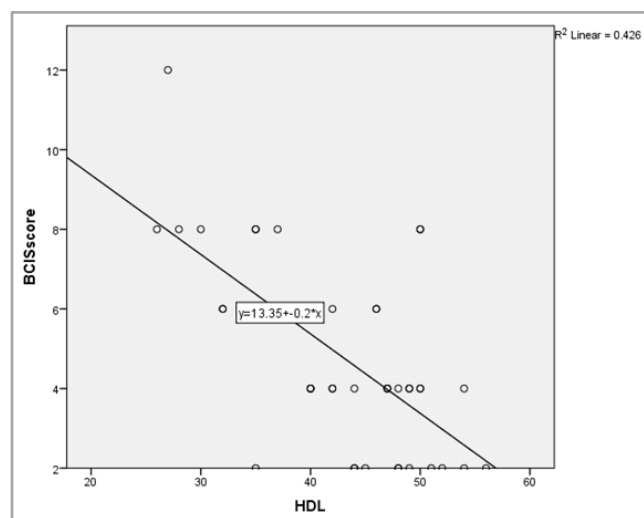


Chart 3. Scatter Plot showing Correlation between Coronary BCIS Score and HDL-C Level in Patients without Diabetes Mellitus

There was a convincing, statistically significant negative correlation between HDL cholesterol level and BCIS score in patients without diabetes which reflects the protective role of HDL cholesterol.

Sl. No.	Correlated variables	r value	Direction	p Value
1.	BCIS score vs. RBS	0.10	Positive	0.48

Table 4. Correlation between Angiographic Severity and HDL Cholesterol among Diabetes Patients

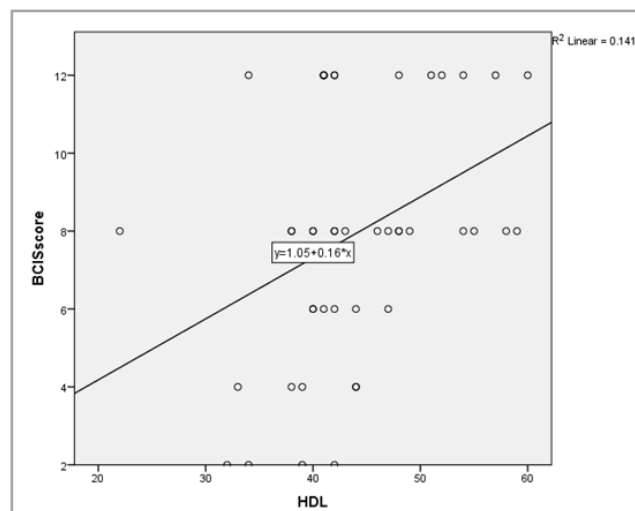


Chart 4. Scatter Plot showing Correlation between BCIS Score and HDL Cholesterol in Patients with T2DM

Unlike the significant negative correlation as seen in non-diabetics, in patients with T2DM, the correlation was positive. In other words, the protective role of HDL cholesterol is not seen in patients with T2DM even though they had higher mean HDL-C level when compared to non-diabetics.

DISCUSSION

From the time of inscription of the concept that HDL cholesterol is protective cholesterol helping in reverse cholesterol transport and thus reducing the risk of coronary disease, several studies have been conducted showing statistically significant negative correlation between HDL cholesterol levels and coronary artery disease severity. However, we also have come across studies stating that reduced HDL cholesterol just signifies an increased risk of CAD but does not indicate a proportional rise in risk with respect to HDL-C level. Even follow up studies with repeated CAG have shown convincingly that the extent of coronary occlusion progression is significantly high with lower HDL-C particle.

The intestine and liver synthesize apo A-I, the main protein of HDL. Nascent HDL particle so formed contains apo A-I, phospholipids, and some free cholesterol. These nascent HDL particles will mediate further cellular efflux of cholesterol. Nascent HDL particles capture membrane-associated cholesterol and promote the efflux of free cholesterol onto other HDL particles. While Acyl-CoA cholesterol acyl transferase (ACAT) converts cholesterol into cholesterol ester and helps in storage, ATP-binding cassette transporter (ABCA1) acts as cholesterol efflux pump and helps in reverse transport of cholesterol. Lecithin-cholesterol acyltransferase (LCAT), found on HDL converts free cholesterol into cholesteryl ester which is then sequestered into the core of HDL particle, eventually making the newly synthesized HDL spherical.

Reverse cholesterol transport also involves the uptake of cellular cholesterol from extra hepatic sources, such as lipid-laden macrophages, and its esterification by LCAT, transport by large HDL particles, and exchange for one

triglyceride molecule by Cholesteryl ester transfer protein (CETP). Finally, receptor mediated uptake of HDL-C occurs at the liver. Thus, reverse cholesterol transport is a complex, well-regulated mechanism.

It is also seen that long-standing uncontrolled Diabetes mellitus causes increased glycation of apoA1 and reduction in Paraoxonase. Paraoxonase is an enzyme associated with HDL cholesterol which has role in preventing the oxidation of lipoproteins, and in preventing atherosclerosis.³ Diabetes mellitus is often associated with dyslipidaemia, there is increased release of free fatty acid from insulin resistant cells.^{4,5} The excess free fatty acids are then converted to triglycerides in the liver, whose increased production in turn stimulates VLDL cholesterol (VLDL-C) and apolipoprotein B synthesis; the reduced activity of lipoprotein lipase in the insulin deficient state may also contribute to elevated triglyceride and VLDL-C levels.^{6,7} The consequence of these elevated lipid fractions is increased small dense LDL-C levels and decreased HDL-C⁸ which by itself poses an increased risk of atherosclerosis. Thus, presence of diabetes further magnifies the HDL dysfunction and results in far severe CAD in such patients. These patients in addition have a increased risk of carotid atherosclerosis and cerebrovascular accidents.⁹

In addition, factors such as obesity, high serum triglycerides,¹⁰ insulin resistance, endothelial dysfunction,^{11,12} glycation of paraoxonase¹³ and reduced function of angiopoietin-Like Protein,¹⁴ all contribute to different extent in HDL dysfunction and increased risk of CAD in Diabetes mellitus patients. A high intensity statin is known to reverse few of these dysfunctions and hence they play a significant role in Diabetes patients with CAD.¹⁵

The mean HDL-C was comparable between our study and other studies done in different countries.

In our study it was observed that there was a significant positive correlation between HDL-C level and the coronary artery disease severity in patients with type 2 DM. This was very opposite to what was found in patients without Diabetes. However, there are studies which do show lack of correlation between HDL-C and coronary artery disease severity and in different population.^{16,17,18,19,20,21} Also HDL-C has no role in promoting coronary collaterals.²²

Study	R value	P Value	
Our study	+0.38	0.01	Patients with T2DM
	-0.65	<0.001	Patients without T2DM
Dan Yang et al. ²³	-0.29	<0.05	
B. Yavuz et al. ²⁴	-0.159	0.001	

Table 5. Comparing the Correlation between Coronary Artery Disease Severity and HDL-C Level in Two Studies

From the study Dan Yang et al and Yavuz et al, we can see that the correlation between coronary artery disease severity and HDL-C level is in negative direction. This can be compared with our study in patients without T2DM.

However, the correlation is in a positive direction in patients with T2DM in our study. Many reasons could be contributing for this finding such as additional risk factors which include smoking, hypertension, life style and diet. However, one thing that cannot be ruled out for certain is the functional impairment of HDL-C in patients with T2DM. This probably reflects the higher degree of coronary artery disease even though patients have higher HDL-C in T2DM. Thus, an absolute value of HDL-C in T2DM patients might not be an ideal indicator for severity of coronary artery disease. However, most studies haven't compared between these angiographic severity scores and HDL-C levels separately in patients with and without T2DM. This could also be one of the reasons for the positive correlation noted in our study between HDL-C and BCIS score in patients with T2DM.

CONCLUSION

HDL-C though is thought to be a protective cholesterol in patients without T2DM. In patients with poorly controlled T2DM, HDL-C does not show any protective role in our study.

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