

# Role of Non High Density Lipoprotein Cholesterol (Non HDL-C) in Predicting Coronary Artery Disease

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## ABSTRACT

**Background:** Low density lipoprotein cholesterol (LDL-C), for many years has been a good and established marker for coronary artery disease (CAD). But many people with normal LDL-C are found to be suffering from CAD. This indicates that along with LDL-C, triglycerides and other cholesterols except HDL-C should be considered while predicting CAD. Thus, nowadays non HDL-C is gaining more importance as predictor of CAD. This study aims at establishing the role of non HDL-C in predicting CAD. **Methods:** This is a prospective cross sectional study and comprised a total of 100 subjects which includes equal number of study group and control. Study group includes patients diagnosed with CAD based on ECG, ECHO report and other biomarkers. Control group consisted of subjects without CAD who attended master health check-up in RMMCH with no history of CAD. Their lipid profile parameters were analyzed using ERBA CHEM 5+V<sub>2</sub> (Semi Auto Analyzer) and statistical analysis was done. **Results:** Out of 50 CAD patients in study group, 28 were male and 22 were female and majority of CAD diagnosed patients were in the age group of 56-75 years. There were statistically significant differences in LDL-C ( $p=0.039$ ) and non-HDL-C ( $p=0.027$ ) levels when study and control groups were compared. **Conclusion:** Our study concludes that non HDL-C having a better predictive value than LDL-C for atherosclerosis, especially in patients with TGL levels > 150 mg/dl.

**Key words:** Coronary Artery Disease (CAD), High density lipoprotein, Low density lipoprotein, Triglycerides, Cholesterol.

## INTRODUCTION

Coronary Artery Disease (CAD) causes more deaths and disability and incurs greater economic costs than any other illness in the developed countries.<sup>1</sup> CAD causes significant mortality and morbidity even in developing countries, like India. Various risk factors have been illustrated as the predisposing factors such as smoking, alcohol, obesity, hypertension, diabetes mellitus, and dyslipidemia. Atherosclerosis is the main cause of CAD, which is a chronic inflammatory disease of arteries. Atherosclerotic plaque formation and pathological remodeling of vascular walls consequently lead to impaired tissue perfusion and ischemia.

Low density lipoprotein cholesterol (LDL-C) is constantly regarded as a key factor for

atherosclerosis and a primary target of lipid lowering therapy for cardiovascular diseases.<sup>2</sup> Recently, it has been found that non HDL cholesterol has a distinct advantage over LDL cholesterol in predicting coronary artery disease.

### Non HDL-C as a risk factor for cardiovascular disease

Non HDL-C is the sum of cholesterol accumulated in all lipoproteins except HDL, such as chylomicrons, VLDL, and their remnants IDL (Intermediate Density Lipoproteins), LDL (Low Density Lipoproteins), LP (Lipoprotein).<sup>3</sup> It was found that increased level of non HDL-C by 1 mg/dl increases the risk of death due to cardiovascular disease by 5% and seems to be a better predictive indicator than the

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traditional lipid risk factors.<sup>4</sup> Our study aims to identify non High Density Lipoprotein Cholesterol (non-HDL-C) as a risk predictor for atherosclerosis in rural population.

## MATERIALS AND METHODS

This is a cross sectional prospective study carried out over 3 months period among the patients of coronary artery disease who are admitted in Rajah Muthiah Medical College and Hospital (RMMCH), Annamalai Nagar, Tamil Nadu, where the patients were recruited based on inclusion and exclusion criteria. Patients diagnosed with coronary artery disease aged more than 35 years of either sex with a history of acute chest pain based on reports of ECG, ECHO cardiogram and cardiac enzymes were included. Patients with less than 35 years of age, already in therapy with statins, other lipid lowering agents, chronic kidney disease, chronic liver disease and thyroid patients were excluded. The study group (n=50) consists of patients diagnosed with CAD and control group (n=50) consists of patients who attended master health check-up in RMMCH. In study group, patients who are diagnosed with CAD were not on statins due to cost factor or discontinuation. This exclusion criteria also limits our sample size. The control subjects were such chosen that they did not have any CAD. Convenient sampling was used to recruit all eligible patients and a validated data collection form was used to collect data from the patients. The data collection form provides the information regarding the patient's demographic profile, socioeconomic status, personal habits, disease risk factor histories and cholesterol levels were recorded. CAD was diagnosed based on clinical history, ECG changes, ECHO cardiogram and biochemical parameters. Lipid profile levels like Total Cholesterol (TC), Triglycerides (TGL), Low Density Lipoprotein Cholesterol (LDL-C) and High Density Lipoprotein Cholesterol (HDL-C) were performed in biochemistry laboratory of RMMCH, Annamalinagar, from ERBA CHEM 5+V<sub>2</sub> (SEMI AUTO ANALYSER). Non HDL-C was calculated by using the formula

$$\text{Non HDL-C (mg/dl)} = \text{TC} - \text{HDL-C}$$

Non HDL-C was considered normal if below 130 mg/dl.<sup>5</sup> National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) (NCEP-ATP III) (as shown in Table 1) guidelines was used to define hypercholesterolemia as Total Cholesterol (TC) > 200 mg/dl, LDL-C as >100 mg/dl.

The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) report suggests non

HDL-C should be a secondary target of lipid lowering therapy among persons with triglyceride levels >200 mg/dl.<sup>6</sup>

As per American Health Association (AHA) scientific statement on triglycerides and cardiovascular disease, TGL<100 mg/dl were considered optimum and TGL levels<150 mg/dl was considered as within normal limits and did not require any hypertriglyceridemia and therapeutic intervention.<sup>7</sup>

Statistical analysis results were presented as mean ± Standard deviation (SD) and with 95% confidence intervals. The independent Student't' test was used to compare the means of various blood parameters between the study and control groups. Significant levels were considered at p<0.05. Statistical analysis was performed by using SPSS 14 version.

## RESULTS

In a total of 100 subjects participating in the study, males constituted about 61% of total sample population compared with females constituting 39% (as shown in Figure 1).

The age range of the total population was 35-85 years. Patients were further classified into 5 age groups out of which majority of CAD patients were found at the age of 56-75 years, followed by 46-55 years and other age groups (depicted in Table 2).

On comparison of risk factors like diabetes, hypertension, smoking and alcohol consumption in study group, it was found that majority of patients are non-diabetics, non-hypertensive, smokers and equal amount of alcoholic and non-alcoholics (as shown in Table 3). In our study the role played by diabetes mellitus and hypertension as risk factors for CAD was found to be less, contrary to the present trends. This could be due to small sample size and limited study group. However, other risk factors non HDL-C could be playing a greater role in causation of CAD. This study to be confirmed by larger studies.

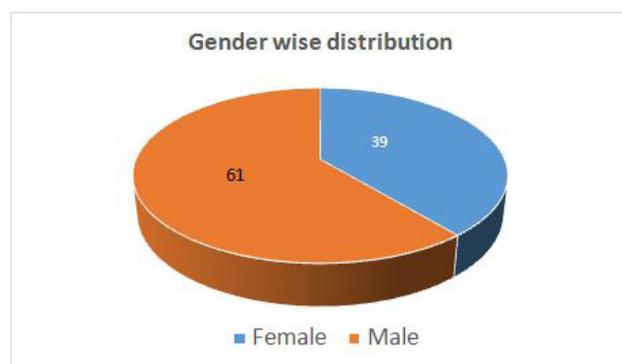


Figure 1: Gender Wise Distribution

**Table 1: Therapeutic targets for low density lipoprotein cholesterol (LDL-C) and non-high density lipoprotein cholesterol (non HDL-C) as recommended by the National Cholesterol Education Program Adult Treatment Panel III**

Risk level	LDL cholesterol Goal	Non HDL Cholesterol Goal
<b>CHD and CHD risk equivalents*</b>	<100mg/dl	<130 mg/dl
<b>Multiple (2+) risk factors (10-year CHD risk ≤20%)</b>	<130 mg/dl	<160 mg/dl
<b>0-1 risk factor</b>	<160 mg/dl	<190 mg/dl

CHD = coronary heart disease; \*CHD risk equivalents include persons with CHD, those with peripheral vascular disease or symptomatic carotid artery disease, patients with diabetes, and patients with multiple risk factors for CHD who have a 10 year risk of hard CHD end points of >20%.

**Table 2: Age Wise Distribution**

Age (in yrs.)	STUDY GROUP (with CAD)	CONTROL	PERCENTAGE (%)
36-45	4	16	20
46-55	10	18	30
56-65	14	11	23
66-75	14	2	16
76-85	8	3	11
<b>TOTAL</b>	<b>50</b>	<b>50</b>	-

**Table 3: Risk Factor Distribution**

RISK FACTOR	STUDY GROUP (50) (with CAD)	CONTROL (50)	PERCENTAGE (%)
<b>Diabetic</b>	15	5	20
<b>Non-diabetic</b>	35	45	80
<b>Hypertensive</b>	8	03	11
<b>Non-hypertensive</b>	42	47	89
<b>Smoker</b>	26	14	40
<b>Non-smoker</b>	24	36	60
<b>Alcoholic</b>	25	12	37
<b>Non-alcoholic</b>	25	38	63

**Table 4: Lipid Parameters**

	Levels (mg/dl)	Study Group (with CAD)	Control
<b>LDL – C</b>	≤100	32	25
	101-130	9	13
	131-160	6	10
	>160	3	2
<b>Non - HDL - C</b>	<130	14	19
	131-160	8	13
	161-190	12	11
	>190	16	7
<b>TGL</b>	<150	26	29
	>150	24	21

**Table 5: Statistical Analysis of Lipid Parameters**

	Patient group (with CAD)	Control group	P-value
Age (years)	61.12 ± 12.07	50.66 ± 11.13	<0.001*
Total cholesterol (mg/dl)	177.42 ± 47.14	186.10 ± 27.46	0.263
HDL-C (mg/dl)	43.50 ± 5.761	43.82 ± 4.42	0.831
LDL-C (mg/dl)	121.84 ± 43.52	104.56 ± 38.89	0.039*
Triglyceride (mg/dl)	151.56 ± 39.57	135.49 ± 31.58	0.24
Non-HDL-C (mg/dl)	148.41 ± 58.25	136.16 ± 45.89	0.027*

Though, LDL-C is constantly considered as key factor in cardiovascular disease, in our study group lipid parameter analysis (as shown in Table 4) shows that normal LDL-C levels (< 100 mg/dl) was seen in 32 out of 50 patients with CAD. But non HDL-C levels were raised (>130 mg/dl) in 36 out of 50 patients in study group. By traditional studies low LDL-C is associated with lower CAD incidences. But our study challenges this conditional theory, as 32 out of 50 patients in study group with CAD had LDL <100 mg/dl. Thus we suggest non HDL-C as better predictor for CAD than LDL-C.

Mean non HDL-C concentrations of study group and control patients were 148.41 ± 58.25 and 136.16 ± 45.89 respectively. Compared to study group and control, age ( $p < 0.001$ ), LDL-C ( $p = 0.039$ ) and non HDL-C ( $p = 0.027$ ) were found to be statistically significant whereas total cholesterol ( $p = 0.263$ ), HDL-C (0.831) and triglyceride ( $p = 0.24$ ) were found to be statistically non-significant (depicted in Table 5).

## DISCUSSION

A total number of 100 patients were included in the study consisting of both study group ( $n = 50$ ) and control ( $n = 50$ ). Out of 50 patients in study group, 28 were male and 22 were female, and majority of CAD diagnosed patients were in the age group of 56-75 years followed by other age groups.<sup>10</sup> Although diabetes, hypertension, smoking and alcohol consumption are risk factors for CAD, in our study smoking and alcohol consumption were the major and common risk factors than diabetes and hypertension.

It is a well-known fact that elevated levels of LDL-C remains a better predictor for coronary artery disease. However, our present study patients diagnosed with CAD had less number of LDL-C elevated patients and more number of non HDL-C elevated patients. On comparing these LDL-C and HDL-C levels in the study group, we found that non HDL-C is a better risk predictor than LDL-C in assessing CAD.

Few studies have proved the predictive value of non HDL-C and its superiority over LDL-C in causing

cardiovascular diseases.<sup>11-12</sup> A study by Arsenault *et al* encounters that non HDL-C could still predicts the CAD risk even at low LDL-C levels.<sup>13</sup> Another study postulates that non HDL-C was proposed to be a good predictor independent of LDL-C levels in initial CAD.<sup>14</sup>

A meta-analysis of relationship between non HDL-C reduction and CAD risk reported that non HDL-C is an important target of therapy for CAD prevention.<sup>15</sup> A recent epoch of data combines from 68 studies, non HDL-C was established as the best predictor among all cholesterol measures both for CAD events and strokes.<sup>16</sup> Our study affirms many observances as discussed above and states “non HDL-C is better indicator than LDL-C in predicting coronary artery disease”.

The number of patients obtained and study duration were limited. If the study was conducted for longer duration, more significant results in all outcomes may have been obtained. We could not evaluate the effect of age on non-HDL-C levels as we did not compare the results with a younger population.

## CONCLUSION

Our study concludes non HDL-C is having preferably better predictive value than LDL-C for atherosclerosis, especially in patients with TGL levels > 150 mg/dl. Non HDL-C levels should be taken into consideration while evaluating the risk of CAD and it should be included in every routine lipid profile panel as it incurs no additional cost. Non HDL-C is advantageous over LDL-C as it does not requires fasting blood samples. So far there is no specific drug to lower the non HDL cholesterol levels. However, there are few drugs which aid to decrease non HDL-C levels such as statins, fibrates, niacin and omega -3 rich fatty acid foods.

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## CONFLICTS OF INTEREST

The author has no conflict of interest.

## ABBREVIATION USED

AHA:	American Health Association
CAD:	Coronary artery disease
ECG:	Electrocardiogram
HDL:	High Density Lipoprotein

HDL-C:	High Density Lipoprotein Cholesterol
IDL:	Intermediate Density Lipoprotein
LDL:	Low Density Lipoprotein
LDL-C:	Low Density Lipoprotein cholesterol
LP:	Lipoprotein
NECP-ATP-III:	National Cholesterol Education Program Adult Treatment Panel III
RMMCH:	Rajah Muthiah Medical College and Hospital
SD:	Standard Deviation
TC:	Total Cholesterol
TGL:	Triglyceride
VLDL:	Very Low Density Lipoprotein

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