

Original Article

Unveiling the atherogenic lipoprotein particle: A case-control study

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Abstract

One of the leading causes of death and morbidity in the globe is cardiovascular disease (CAD). According to the WHO statistics from the year, 17.9 million individuals die worldwide every year from cardiovascular diseases. One of the simplest alternatives to computed LDL levels is to make use of non-HDL lipoprotein. Comparing non-HDL cholesterol to LDL cholesterol has shown that multiple research studies have demonstrated non-HDL cholesterol's superior ability to identify risks for CAD. In order to compare and contrast LDL and non-HDL cholesterol levels in individuals with CAD, the present investigation will compare and contrast these two measurements. Fifty healthy people between the ages of thirty and seventy-five were included in the study as controls, whereas 130 patients with CAD diagnoses were included as cases. The study was conducted among 180 patients who were diagnosed with cardiovascular disease. The positive relationship between non-HDL-cholesterol and LDL cholesterol levels is seen by the Pearson correlation. Using non-HDL cholesterol, an independent T-test yields a positive result of <0.001 . The study's conclusion is that non-HDL cholesterol yields results that are similar to Friedwald's well-established LDL-C. Non-HDL-C can be used as a marker for CAD deduction and also for diagnostic and therapeutic markers for CAD.

Keywords: troponin I, coronary artery diseases, non-high-density lipoprotein, low-density lipoprotein, total cholesterol.

Introduction

Among the most prevalent leading causes of death and morbidity worldwide is cardiovascular illness. Over seventeen million individuals die each year from cardiovascular disease (CVD), according to the World Health Organization's statistics from the year [1]. Coronary artery disease, the most common cause of death worldwide, is a primary cardiovascular disorder resulting in plaque formation and constriction of the coronary arteries.

Genetic, environmental, and lifestyle factors influence the condition [2]. A particular class of protein called troponin is present in cardiac muscles. The blood often does not contain troponin. Troponin is released into the circulation when the heart muscles are harmed.

Greater troponin levels get released into the circulation as the damage to the heart progresses. A recently published or persistent heart attack may be indicated by elevated blood troponin levels. A heart attack occurs whenever the blood supply to the heart is stopped. This obstruction may be life-threatening. However, prompt medical attention and diagnosis can save the life of patients [3]. The most significant coronary artery disease risk factor for developing coronary artery disease, according to research, is dyslipidemia [4].

Additionally, according to the World Health Organisation, more than half of all instances of ischemic cardiovascular disease worldwide are highly correlated with dyslipidemia cholesterol, which is regarded as the conventional indicator for treating dyslipidemia. It is frequently computed in the laboratory using the widely



used and simple Friedwalds solution. The rise of triglycerides in the blood and VLDL cholesterol levels, reduction of HDL cholesterol, and an increase in tiny dense LDL cholesterol particles are common characteristics of dyslipidemia. The American Diabetes Association (ADA) issued revised recommendations that specify the top priorities in the treatment of dyslipidemia among patients with diabetes based on epidemiological investigations linking dyslipidemia to heart disease, especially coronary artery disease (CHD), as well as preliminary findings from the major statin medication trials. However, it has several problems since it provides false findings by displaying the number of cholesterol levels in both elevated and LDL cholesterol levels on its own.

LDL cholesterol assessment needs a fasting condition, which is inconvenient for patients and physicians and is another downside. So, an entirely novel marker that does not have the aforementioned issues can be employed. One of the simplest substitutes for computed LDL levels is non-HDL cholesterol. When analyzed alongside LDL cholesterol, several studies have demonstrated that non-HDL cholesterol is more effective at identifying risk factors for cardiovascular disease [5–7]. The most recent diagnosis of lipids-related illnesses should be made based on a metric unaffected by these restrictions. Modern studies using epidemiology have shown that non-HDL cholesterol has a greater correlation to the risk of coronary artery disease than estimated LDL-C.

Therefore, this study aims to evaluate LDL cholesterol levels in individuals with coronary artery disease, also known as CAD, compared to non-HDL cholesterol levels. Sadly, notwithstanding non-HDL-C's effectiveness in lowering CAD risk compared to LDL-C, it has thus far been ignored. Despite the Lipid Organisation of India's recommendation that non-HDL-C be included as a coprimary objective, several prestigious institutes and health care centers have refused to include it in standard lipid profile panels [8]. The aim of this article is to find out the role of non-HDL cholesterol in the primary prevention of coronary artery disease.

Material and methods

This study was done on diagnosed coronary artery disease patients coming to Chettinad Hospital and Research Institute, Kelambakkam. Case-control study

This study was conducted only after getting approval from the institutional ethical committee. The total sample size is 180 patients. Among them, 130 pa-

tients with diagnosed CAD were taken as cases, and 50 healthy subjects were taken as control, with the age group between 30–70 years taken as control and participated in the study.

Inclusion criteria- Known cases of diagnosed CAD patients visiting Chettinad Academy and Research Institute who are interested in participating are included in the study. Exclusion criteria – Patients suffering from Acute M.I., Diabetes mellitus, Kidney disorders, and Liver diseases and patients on follow-up/extensive medical treatment and lipid-lowering drugs will be excluded from the present study.

The detailed history of the patients will be recorded. 5 ml blood will be collected in red topped vacutainer and serum will be separated using standard protocol. After the collection of blood samples, serum total cholesterol (TC) Dimension clinical chemistry system, biochemical assay method CHOL method, triglycerides (TG) dimension clinical chemistry system, and biochemical assay method High-Density Lipoprotein-Cholesterol (HDL-C) dimension clinical chemistry system, biochemical assay method Automated HDL CHOLESTEROL method will be estimated by Siemens Dimensions RxL in the clinical biochemistry lab, Department of Biochemistry, CHRI. Friedwald's formula will calculate LDL and VLDL, and non-HDL-C will be calculated by subtracting the HDL level from the total cholesterol level. The collected data of the study subjects were analyzed with IBM SPSS (Statistical Package Social Service) version 29.

Statistical analysis

The significance between the groups was determined using the 't-test. Significance is considered only at $p < 0.05$. To compare the predictive values of Non-HDL-C, Friedwald calculated a global performance indicator for a prognostic factor. The collected data of study subjects were analyzed with IBM SPSS (Statistical Package Social Service) version 29.0.

Results and discussion

Investigations for Fried Wald's computed LDL-C were not statistically significant ($p = 0.060$); Non-HDL-C, despite this, had a high correlation ($p = 0.002$). This indicates the advantages of non-HDL-C over LDL-C measured according to Friedwald's method in CAD patients. Therefore, instead of focusing on LDL-C, doctors monitoring this population ought to concentrate on nonHDL-C.

Table 1: Descriptive statistics for study participants.

	Parameter	N	Mean	Std. Deviation
Case	TROP I	130	961.39	3419.454
	TC mg/dL	130	155.74	51.905
	TGL mg/dL	130	132.87	89.242
	HDL mg/dL	130	38.03	19.166
	LDL mg/dL	130	85.47	39.334
	VLDL mg/dL	130	25.28	15.741
	NON-HDL mg/dL	130	111.60	124.425
	Valid N (listwise)	130		
Control	TROP I	50	4.97	3419.454
	TC mg/dL	50	150.85	51.905
	TGL mg/dL	50	112.98	89.242
	HDL mg/dL	50	44.14	19.166
	LDL mg/dL	50	89.10	39.334
	VLDL mg/dL	50	22.56	15.741
	NON-HDL mg/dL	50	98.82	124.425
	Valid N (listwise)	50		

As reported earlier, low-density lipoprotein cholesterol (LDL-C) has been recommended as the primary treatment target for lipid management in coronary artery disease. Despite having so many advantages over Friedwald calculated LDL-C, incorporating non-HDL-C in routine lipid panels has yet to be addressed. Given this, the present study was done to study the usefulness of nonHDL-C in CAD risk. There are growing pieces of evidence suggesting the role of non-HDL-C in predicting CAD risk.

Table 1 shows the descriptive statistics for study participants, such as N=130 cases and N=50 control.

Table 2 shows the correlation analysis between TROP-I and lipid profile in CAD cases. TC, HDL-C, and LDL-C are non-significant. According to Kathariya *et al.* and Michael J. Blaha prove the same non-significance between these parameters. TGL, VLDL-C, and NON-HDL-C show statistically significant results; Erit Ingelsson also proves the same [9, 10]. According to Ronald, non-HDL-C (p=0.002) was found to be significantly associated, while results were non-significant for Fried Wald’s calculated LDL-C (p=0.060). M *et al.* and Matthijs Boekholdt also prove that the trop-I and TGL-C analysis correlates with coronary artery disease [11].

Table 2: Correlational analysis between TROP-I and lipid profile in CAD cases.

Lipid parameter	R-value	P-value
TC	0.107	0.152
TGL	0.159*	0.032
HDL	-0.095	0.204
LDL	0.127	0.060
VLDL	0.194*	0.009
NON-HDL	0.035*	0.002

Note: * – The data presented as correlation analysis between Trop-I & lipid profile in CAD cases, using IBM SPSS (Statistical Package Social Service) version 29.0. (P<0.05) was considered statistically significant.

Table 3: Independent sample T-test to determine the statistical difference between CAD cases and non-CAD controls.

Study parameters	Cad cases (Mean±SD)	Non-cad controls (Mean±SD)	P-value
TROP-I	961.39±3419.45	4.97±3419.45	<0.001*
TC	155.74±51.90	150.85±51.90	0.013*
TGL	132.87±89.24	112.98±89.24	0.037*
HDL	38.03±19.16	44.14±19.16	0.031*
LDL	85.47±39.33	89.10±39.33	0.072
VLDL	25.28±15.74	22.56±15.74	0.067
NON-HDL	111.60±124.42	98.82±124.42	<0.001*

Note: * – The data presented as Mean±S.D. N denotes the number of subjects. The significance was determined by an independent student's t-test using IBM SPSS (Statistical Package Social Service) version 29.0. (P<0.05) was considered statistically significant.

This study demonstrated the superiority of non-HDL-C over Friedwald-calculated LDL-C in patients with CAD. Hence, clinicians following up on this group should target nonHDL-C instead of LDL-C.

Table 3 shows the independent sample T-test to determine the statistical difference between Coronary artery disease cases and non-coronary artery disease controls. There was a statistically significant difference in TC, TGL, HDL, and non-HDL with p=0.013, p=0.037, p=0.031, and p<0.001, respectively.

It is possible to detect non-HDL-C levels using a non-fasting specimen being examined, which is more kind to patients and expedites the clinical decision-making process. In light of this, the primary therapeutic goal might be non-HDL-C. It would be advantageous for the patients and the entire healthcare system. To improve the detection and treatment of coronary artery disease (CAD) risk, those conducting the study strongly propose integrating non-HDL-C in conventional high cholesterol levels and lipid panels proliferating.

Conclusion

Our study clearly shows that non-HDL and CAD significantly correlate with each other. It is regarded as a more accurate diagnostic for CAD versus LDL-C. When examined alongside Friedwald's computed LDL-C, non-HDL-C performs comparably. Non-fasting specimens can be used to assess non-HDL-C levels, which is more patient-friendly and speeds up clinical decision-making.

Consequently, the non-HDL-C can be used as the main treatment target. Both the patients and the entire system of healthcare would profit from it. As a result, the authors highly advise including non-HDL-C in standard cholesterol and lipid panels for improved assessment of coronary artery condition risk and therapy.

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Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The approval for this study was obtained from the Ethics Committee of the Chettinad Hospital and ReSearch Institute (approval ID: ID-II/0225/22).

Consent to participate

Written informed consent was obtained from all participants in this study.

References

1. Gupta R, Rao RS, Misra A, Sharma SK. Recent trends in the epidemiology of dyslipidemias in India. *Indian Heart J.* 2017 May 1;69(3):382–92.
2. Nayar S, Chokkalingam M, Reddy M, Age BB, 2015 undefined. Risk Factors for Coronary Artery Disease in a Semi-urban Area of Tamil Nadu. *chcmj. ac.in* [Internet]. [cited 2023 May 26]; Available from: http://www.chcmj.ac.in/journal/pdf/vol4_no1/Risk_Factors.pdf
3. Troponin Test: MedlinePlus Medical Test [Internet]. [cited 2023 May 21]. Available from: <https://medlineplus.gov/lab-tests/troponin-test/>
4. 2002 WHOTWHR, 2002 undefined. Quantifying selected major risks to health. *ci.nii.ac.jp* [Internet]. [cited 2023 May 22]; Available from: <https://ci.nii.ac.jp/naid/10013238390/>
5. Kastelein JJP, Van Der Steeg WA, Holme I, Gaffney M, Cater NB, Barter P, et al. Lipids, apolipoproteins, and their ratios about cardiovascular events with statin treatment. *Circulation.* 2008 Jun 10;117(23):3002–9.
6. Liu J, Sempos C, Donahue R, ... JDD, 2005 undefined. Joint distribution of non-HDL and LDL cholesterol and coronary heart disease risk prediction among individuals with and without diabetes. *Am Diabetes Assoc* [Internet]. 2014 [cited 2023 May 22]; Available from: <https://diabetesjournals.org/care/article-abstract/28/8/1916/23782>
7. Arsenault BJ, Rana JS, Stroes ESG, Després JP, Shah PK, Kastelein JJP, et al. Beyond Low-Density Lipoprotein Cholesterol. Respective Contributions of Non-High-Density Lipoprotein Cholesterol Levels, Triglycerides, and the Total Cholesterol/High-Density Lipoprotein Cholesterol Ratio to Coronary Heart Disease Risk in Apparently Healthy Men and Women. *J Am Coll Cardiol.* 2009 Dec 29;55(1):35–41.
8. Kathariya G, Aggarwal J, Garg P, Singh S, Manzoor S. Is the evaluation of non-HDL-C better than calculated LDL-C in CAD patients? MMIMSR experiences. *Indian Heart J* [Internet]. 2020 May 1 [cited 2023 May 21];72(3):189. Available from: [/pmc/articles/PMC7411097/](https://pubmed.ncbi.nlm.nih.gov/3411097/)
9. Kathariya G, Aggarwal J, Garg P, Singh S, Manzoor S. Is the evaluation of non-HDL-C better than calculated LDL-C in CAD patients? MMIMSR experiences. *Indian Heart J.* 2020 May 1;72(3):189–91.
10. Ingelsson E, Schaefer EJ, Contois JH, McNamara JR, Sullivan L, Keyes MJ, et al. Clinical utility of different lipid measures for prediction of coronary heart disease in men and women. *JAMA* [Internet]. 2007 Aug 15 [cited 2023 May 21];298(7):776–85. Available from: <https://pubmed.ncbi.nlm.nih.gov/17699011/>
11. Krauss RM, Siri PW. Metabolic abnormalities: triglyceride and low-density lipoprotein. *Endocrinol Metab Clin North Am.* 2004 Jun 1;33(2):405–15.