

Non HDL Cholesterol as a Better Predictor of Coronary Heart Disease Risk in Obesity

K. Tamilmani¹, V. Yogeswari², K. Menaka Shanthi³, K.R. Minu Meenakshi Devi*

¹Associate Professor, Department of Biochemistry, Govt. Villupuram Medical College, Villupuram

²Associate Professor, Department of Biochemistry, Govt. Vellore Medical College, Vellore

³Associate Professor, Department of Biochemistry, Govt ESIC Medical College, Coimbatore

*Associate Professor, Department of Biochemistry, Govt. Coimbatore Medical College, Coimbatore

Received: 30-12-2022 / Revised: 12-01-2023 / Accepted: 10-02-2023

Corresponding author: Dr. K.R. Minu Meenakshi Devi

Conflict of interest: Nil

Abstract

Background: Elevated triglyceride (TG), low density lipoprotein(LDL-C) and lower high-density lipoprotein cholesterol (HDL-C) levels found in metabolic syndrome, type 2 diabetes and Obesity are commonly associated with coronary heart disease (CHD). Non-HDL-C (total cholesterol minus HDL-C) provides a measure of the overall cholesterol content of atherogenic lipoproteins, and hence predicts the potential risk conferred by elevated levels of atherogenic TG-rich remnants. **Aim:** This study aims to assess whether there is an increase in risk of CHD in obese individuals with elevation of non HDL cholesterol and its correlation with LDL cholesterol.

Settings and Design: This is an observational case control study with 307 participants.

Materials and Methods: 158 cases of CHD and 149 controls were recruited for this study. 3mL of venous plasma was collected and analysed for lipid profile, glucose. Non-HDL cholesterol was calculated from cholesterol and HDL values. Obesity was identified by calculation of BMI.

Statistical Analysis: The analysis of the results was done using unpaired 't' test, Pearson correlation.

Results: Non HDL cholesterol is increased significantly in CHD patients with obesity than controls.

Conclusion: Non HDL cholesterol is a better predictor of CHD and is comparable to LDL cholesterol in obese individuals.

Keywords: Atherosclerosis, Coronary Heart Disease, Non HDL Cholesterol, Obesity.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Elevated triglyceride (TG) and low density lipoprotein(LDL-C) and lower high-density lipoprotein cholesterol (HDL-C) levels, are the

hallmarks of the atherogenic lipid profile found mostly in metabolic syndrome, type 2 diabetes and Obesity and are commonly

associated with coronary heart disease (CHD). With mild to moderate elevation of TG (150-500 mg/dl), very-low-density lipoprotein (VLDL) accumulates and so do high levels of atherogenic TG-rich, cholesterol-enriched remnant particles. Indeed, in hypertriglyceridemia, the quantity and quality of all apo B-containing lipoproteins are abnormal. Non-HDL-C (total cholesterol minus HDL-C) is an easily calculated parameter that provides the cholesterol content of all atherogenic lipoproteins, and thus indicates the potential risk conferred by elevated levels of atherogenic TG-rich remnants. This is additional to the risk associated with low-density lipoprotein cholesterol (LDL-C).

Non-HDL-C level has been found to be a strong predictor of future cardiovascular risk among patients whether or not they exhibit symptoms of vascular disease, and is recently recommended as a secondary treatment target (after LDL-C) in patients with elevated TG by the National Cholesterol Education Program Adult Treatment Panel III [1-5]. Hence in this study we attempt to establish the risk of CHD associated with Elevated Non HDL Cholesterol.

Aim

1. To assess whether there is increased risk of CHD in Obese individuals with elevation of non HDL cholesterol
2. Comparison of Non HDL cholesterol with LDL cholesterol for Atherosclerotic risk

Materials and Methods

The present study was done in Stanley Medical College between November 2011 to November 2012. It was carried out in two groups, apparently healthy controls and patients with angiographically confirmed diagnosis of Coronary Heart Disease. The study was approved by the Institutional Ethical Committee.

Study population

Tamilmani *et al.*

The study sample comprised of 158 CHD patients chosen from the Department of Cardiology, Stanley Medical College and Hospital. The diagnosis of CHD was established by ECG, cardiac markers and angiography. 149 Controls were recruited from Master Health Check up clinic during their visit to this hospital. Healthy, age-matched people, without a family history of CHD were selected to serve as the control group. Subjects with diabetes, hypertension, hypothyroidism, autoimmune diseases were excluded from the control group.

Sample collection

3ml of peripheral venous blood was drawn under sterile conditions with disposable syringes from all the cases and controls of the study. The blood was transferred to a plain tube and allowed to stand for 20 minutes. After clot retraction the plain tube was centrifuged at 3000 revolutions for ten minutes to separate the serum.

Lipid profile (total cholesterol, HDL cholesterol, Triglycerides) was estimated in Beckmann AU480 Fully automated biochemistry analyser

Lipid profile was done by the following methods:

Total cholesterol – CHO-PAP Method.

Triglycerides – GPO-PAP Method.

HDL - Direct Method .

LDL was calculated by Friedwald formula.

Non-HDL cholesterol was calculated by the formula,

Non HDL cholesterol = Total Cholesterol – HDL Cholesterol

Blood Sugar was done by GOD-POD Method.

Obesity was identified by calculation of BMI by the formula,

$$\frac{\text{Body weight in kg}}{\text{Height in m}^2}$$

$$\text{Height in m}^2$$

BMI >30 is considered as Obesity

Ethics: The study was approved by the Institutional Ethical Committee

Age and lipid profile levels between CHD patients and control subjects were compared using student 't' test. Odd's ratio and confidence interval was used to find the association between lipid profile and Atherosclerotic risk. Pearson Correlation coefficient was used to compare the non HDL-C and LDL cholesterol levels.

Statistics: The statistical analysis was done using SPSS software version 20.

Results

158 CHD subjects and 149 Control subjects were evaluated for the association of non HDL cholesterol vs LDL cholesterol for atherosclerotic risk.

Table 1: Characteristics of study and control groups

	Study subjects	Controls
Mean Age in years (Range)	52.92 (37-72)	52.95(20-75)
Sex (M/F)	123/35	112/37
Smoking	80	50
Alcohol	75	47
Diabetes	29	0
Hypertension	109	0
Total Cholesterol(mg/dl)	207.85 ± 47.52	178.30 ± 41.38
Triglycerides(mg/dl)	186.13 ± 99.31	148.07 ± 50.25
LDL(mg/dl)	128.98 ± 42.19	117.29 ± 38.20
HDL(mg/dl)	41.54 ± 9.07	45.52 ± 9.21
Non-HDL Cholesterol(mg/dL)	166.3 ± 47.41	132.8 ± 40.59
BMI	26.51 ± 4.36	23.65 ± 4.26
Obesity(BMI >30)	46	11

Table.1 shows the characteristics of study and control groups. The mean age, sex, number of smokers, alcoholics, diabetics, hypertensives, and Obesity among study and control groups. Total cholesterol, TGL, HDL, LDL, BMI values were given as mean ± SD.

Table 2: Age and Lipid Profile distribution in CHD subjects and controls

		Mean ± SD	T	p
Age	Patients	52.92 ± 10.24	0.029	0.97
	Controls	52.95 ± 7.45		
T.Cholesterol	Patients	207.85± 47.52	5.8	0.0001*
	Controls	178.3 ± 41.38		
TGL	Patients	186.13± 99.31	4.2	0.0001*
	Controls	148.07± 50.25		
HDL	Patients	41.54 ± 9.07	3.81	0.0002*
	Controls	45.52 ± 9.21		
LDL	Patients	128.98± 42.19	2.54	0.01*
	Controls	117.29 ± 38.2		
Non-HDL Cholesterol	Patients	166.3 ± 47.41	6.64	0.01*
	Controls	132.8 ± 40.59		

* p < 0.05 is considered significant.

Table 2 shows the mean age and lipid profile distribution between study and control groups. There was no significant difference with respect to age in study subjects and controls, but the Cholesterol, TGL, HDL, LDL and non HDL cholesterol values differ significantly between the two groups. Thus it was considered that increase in cholesterol, TGL, LDL, non HDL cholesterol and decrease in HDL were risk factors for the disease, $p < 0.05$.

Table 3: Association of Risk Factors and incidence of CHD

Risk Factors	OR	CI	p
Smoking	2.03	1.28 - 3.22	0.00*
Alcohol	1.96	1.23 – 3.12	0.00*
Obesity	5.15	2.55 – 10.41	0.00*

* $p < 0.05$ -considered significant

Table 3 shows the relationship of risk factors with CHD. There was statistically significant difference in risk factor status between the two groups, $p < 0.05$. Alcohol OR-1.96(95% CI 1. 23-3.12) and Smoking OR-2.03(95% CI 1.28-3.22) were associated with a two fold increase in CHD incidence. Obesity OR-5.15(95% CI 2.55-10.41) was associated with five fold increase in the incidence of the disease.

Table 4: Association of Non HDL cholesterol and Obesity in CHD risk among cases and controls

	Obese CHD patients (46)	Obese Controls (11)	p
Non-HDL cholesterol (>160mg/dL)- Elevated	23	1	0.02*
Non-HDL cholesterol (<160mg/dL)- Normal	23	10	

* $p < 0.05$ -considered significant

Table 4 shows the relationship of Non HDL cholesterol and Obesity among CHD patients and controls. There was statistically significant difference between the two groups, $p < 0.05$. The non HDL cholesterol level was higher in Obese individuals with CHD than Obese controls. Hence non HDL cholesterol may be a better predictor of CHD in Obese individuals

Figure 5: Comparison of Non HDL cholesterol between CHD patients and Controls

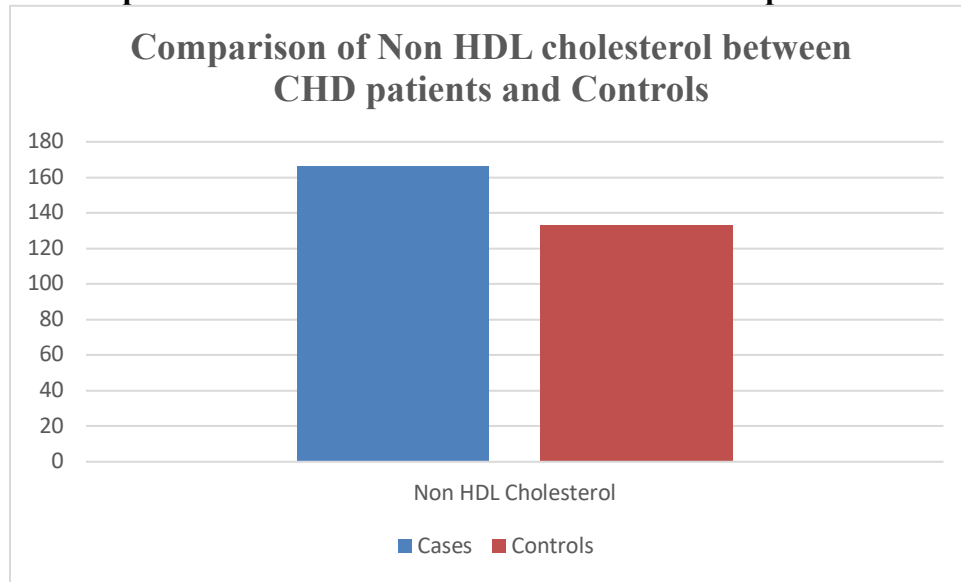


Table 6: Association of Non HDL cholesterol and Obesity in assessment of risk among CHD patients

	Obese CHD patients (46)	Non Obese CHD patients(112)	p
Non-HDL cholesterol (>160mg/dL)- Elevated	23	70	0.15
Non-HDL cholesterol (<160mg/dL)- Normal	23	42	

*p <0.05-considered significant

Table.6 shows the relationship of obesity and non HDL cholesterol among CHD patients. There was no statistically significant difference between the two groups, p>0.05. There was no difference in non HDL cholesterol levels between Obese and non Obese CHD patients. This shows that non HDL cholesterol predicts the CHD risk in individuals without Obesity also.

Table 7: Correlation of Non HDL cholesterol with Lipid profile and BMI in CHD patients

Variables		Non HDL cholesterol(mg/dL)
Cholesterol (mg/dl)	Pearson Correlation	0.975**
	Sig. (2-tailed)	0.000
	N	149
TGL (mg/dl)	Pearson Correlation	0.374**
	Sig. (2-tailed)	0.000
	N	149
VLDL (mg/dl)	Pearson Correlation	0.382**
	Sig. (2-tailed)	0.000
	N	149
HDL (mg/dl)	Pearson Correlation	-0.027
	Sig. (2-tailed)	0.745
	N	149

LDL (mg/dl)	Pearson Correlation	0.744**
	Sig. (2-tailed)	0.000
	N	149
BMI	Pearson Correlation	0.031*
	Sig. (2-tailed)	0.705
	N	149

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Table 7. Shows the Pearson correlation of Non HDL cholesterol with Total cholesterol, TGL, VLDL, HDL, LDL and BMI among CHD patients. The non HDL cholesterol shows stronger positive correlation with T. Cholesterol, LDL and BMI. There is strong negative correlation with HDL in CHD patients. This shows that non HDL is a good predictor of CHD risk in CHD patients with Obesity and is comparable to LDL in CHD patients.

Discussion

Atherosclerosis is associated with hypertriglyceridemia, high LDL-C, low HDL-C, changes in LDL, and accumulation of remnant lipoproteins [6-8].

Recently, non-High-Density Lipoprotein cholesterol (non-HDL-c) has been included as new target for the prevention of cardiovascular events. It reflects the full burden of the atherogenic lipoproteins and is crucial to prediction of CHD risk, [9] and shows close association with plaque progression [10,11]. In our study the total Cholesterol, Triglycerides, LDL cholesterol, and non HDL cholesterol are higher in CHD patients than in controls.

Non-HDL-c comprises the cholesterol carried by all potentially atherogenic particles, including LDL-c, intermediate density lipoproteins, very low-density lipoproteins, and remnant lipoproteins. Several meta-analyses found that non-HDL-c correlated more closely with cardiovascular risk than LDL-c, both at baseline and during therapy [12,13].

In overweight or obese subjects, the cardiovascular risk is high. In these individuals the levels of triglycerides and remnant cholesterol, not LDL-C, predicts cardiovascular

outcome independent of other risk factors [1]. Hence non HDL cholesterol which includes all the Triglyceride rich lipoproteins is a better than LDL cholesterol. Non-HDL cholesterol levels includes all of the apoB containing lipoproteins in one number and are useful in assessing risk in the setting of hypertriglyceridemia.[2] In our study also Non HDL cholesterol level is higher in Obese individuals with CHD than Obese controls.

Non-HDL-c is considered a valuable predictor of premature atherosclerosis and coronary events such as myocardial infarction and cardiovascular mortality [9]. It represents the sum of all lipoproteins with atherogenic properties and so, in other words, non-HDL-c indicates all the atherogenic remnants [3-6]. In this study there is positive correlation of Non HDL cholesterol with LDL and BMI in CHD subjects and negative correlation with HDL.

Conclusion

Non HDL cholesterol is a better predictor of Coronary Heart Disease and correlates well with LDL cholesterol in assessment of atherosclerotic risk in susceptible individuals with risk factors like Obesity, Hypertension, Smoking and Alcoholics.

References

1. Remnant Cholesterol, Not LDL Cholesterol, Is Associated With Incident Cardiovascular Disease: Olga Castañer, Xavier Pintó, *et al.*
2. The Role of Lipids and Lipoproteins in Atherosclerosis MacRae F Linton¹, Patricia G Yancey² *et al.*, In: Endotext [Internet]. South Dartmouth (MA): MD Text.com, Inc.; 2000.
3. Puri R, Nissen SE, Shao M, *et al.* Non-HDL cholesterol and triglycerides: Implications for coronary atheroma progression and clinical events. *Arterioscler Thromb Vasc Biol.* 2016; 36(11):2220–2228.
4. Faludi AA, Izar MCO, Saraiva JFK, *et al.* Atualização da Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose - 2017. *Arq Bras Cardiol.* 2017; 109(2) Suppl 1:1–76.
5. Fruchart JC, Davignon J, Hermans MP, *et al.* Residual macrovascular risk in 2013: what have we learned? *Cardiovasc Diabetol.* 2014;13(1):26.
6. Wang D, Wang L, Wang Z, Chen S, Ni Y, Jiang D. Higher non-HDL-cholesterol to HDL-cholesterol ratio linked with increased nonalcoholic steato hepatitis. *Lipids Health Dis.* 2018;17(1):67.
7. Barbalho S, Tofano RJ, Bechara MD, Quesada K, Coqueiro DP, Mendes CG. Castelli Index and estimative of LDL-c particle size may still help in the clinical practice? *J Cardiovasc Dis Res.* 2016; 7(2):86–89.
8. Alibasic E, Ramic E, Bajraktarevic A, Ljuca F, Batic-Mujanovic O, Zildzic M. Atherogenic dyslipidemia and residual vascular risk in practice of family doctor. *Med Arh.* 2015;69(5):339–341.
9. Costa IFAF, Medeiros CCM, Costa FADF, *et al.* Adolescentes: comportamento e risco cardiovascular. *J Vasc Bras.* 2017; 16(3): 205–213.
10. Puri R, Nissen SE, Shao M, *et al.* Non-HDL cholesterol and triglycerides: Implications for coronary atheroma progression and clinical events. *Arterioscler Thromb Vasc Biol.* 2016; 36(11):2220–2228.
11. Zeb I, Budoff M. Coronary Artery calcium screening: does it perform better than other cardiovascular risk stratification tools? *Int J Mol Sci.* 2015;16(3):6606–6620.
12. Faludi AA, Izar MCO, Saraiva JFK, *et al.* Atualização da Diretriz Brasileira de Dislipidemias e Prevenção da Aterosclerose - 2017. *Arq Bras Cardiol.* 2017;109(2) Suppl 1:1–76.
13. Jacobson TA, Ito MK, Maki KC, *et al.* National lipid association recommendations for patient-centered management of dyslipidemia: part 1- full report. *J Clin Lipidol.* 2015;9(2):129–169.