

## Is Non - High-Density Lipoprotein Cholesterol (Non HDL-C) A Better Predictor Of Future Risk Of Cardiovascular Mortality?

Kader Sahib A<sup>1</sup>, Chenniappan M<sup>2</sup> and Rajajeyakumar M<sup>3\*</sup>

<sup>1</sup>Apollo Hospitals, Trichy-620010, Tamilnadu, India

<sup>2</sup>Ramakrishna Nursing Home, Trichy & Dr.M.G.R Medical University, Tamilnadu, India

<sup>3</sup>Department of Physiology, Chennai Medical College Hospital and Research Centre (SRM Group), Irungalur, Trichy-621105, Tamilnadu, India

### Introduction

Non-HDL-C is a secondary lipid treatment target, after achieving LDL-C goal. Non-HDL-C is a calculation of total cholesterol minus high-density lipoprotein cholesterol (HDL-C)  $\text{Non HDL} = \text{TC} - \text{HDL-C}$  or  $\text{Non HDL} = \text{VLDL} + \text{IDL} + \text{LDL}$ . Non-HDL-C comprises the cholesterol carried by all potentially atherogenic particles, including LDL, intermediate-density lipoproteins, very low-density lipoproteins (VLDL), chylomicron, and lipoprotein (a). Epidemiological studies support non-HDL-C as a stronger predictor of ASCVD morbidity and mortality than LDL-C. Non-HDL-C changes and levels during treatment of dyslipidemia are more strongly associated with reduced risk for atherosclerotic coronary heart disease (CHD) than changes in LDL-C or on-treatment levels of LDL-C. In view of this, non-HDL-C, which is a measure of lipids associated with all apoB-containing particles, was proposed as an alternative method for CVD risk score classification [1]. Non-HDL cholesterol has been recommended from 2001 as a secondary target by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) for patients with triglycerides greater than 200 mg/dl. In addition, nonHDL cholesterol has a superior diagnostic value compared to LDL as a measure of vascular risk event [2].

### Possible Explanations for the Superiority of Non-HDL-C over LDL-C for Predicting ASCVD Event Risk Include

1. Apo B like LDL, some triglyceride-rich lipoprotein remnants enter the arterial wall and thus contribute to the initiation and progression of atherosclerosis.
2. Apo B Non-HDL-C correlates more closely than LDL-C with Apo B and thus more closely correlates with the total burden of atherogenic particles.
3. Apo B Elevated levels of triglycerides and VLDL-C reflect hepatic production of particles with greater atherogenic potential, such as those having poor interactivity with hepatic receptors, resulting in longer residence time in the circulation.

### Residual Risk for ASCVD after Statin Therapy

The risk of ASCVD to a patient after statin therapy and the desired LDL goal is called the residual risk. This residual risk is primarily due to high non HDL-C levels. After achieving LDL goal, elevated non HDL-c levels can be either due to increased TGL or reduced HDL. In diabetes, the typical dyslipidemia triad is characterized by increased TGL, reduced HDL and increased small dense LDL. In India, because of the increased prevalence of diabetes mellitus compared to western population where all the guidelines are published, non HDL-c will help us to identify and treat "at risk" individuals even more completely.

### Risk of CHD in Indian Population

Various studies have demonstrated that the risk of CHD is higher in

Indian population as compared to other ethnicities. It is estimated that Indians have a CHD risk that is 3 to 4 times that of white Americans, 6 times that of the Chinese and 20 times that of the Japanese. Indians also have a very high rate of DALYs. India is one of the few countries that have 20 to 29 DALYs lost per 1000 population due to CHD. Another disturbing tendency in Indian population is the propensity of CHD towards younger population. It has been demonstrated that CHD incidence in young in India is 12 to 13% as compared to 5% in the western countries and up to 40% of the CHD patients in the urban population as compared to the rural population [3].

### Moving Beyond LDL

1. Characteristic lipid abnormalities, such as high triglycerides and low HDL, Lp (a) with normal LDL values, are common in association with insulin resistance in South Asians.
2. Hence, European / American recommendations on the use of statins as first-line agents may not be entirely applicable to all populations.

Normal total cholesterol and normal LDL may not offer protection in Indian population.

### Conclusion and Recommendation

- 1) Non-HDL-c reduction should be the secondary goal of therapy after achieving target LDL.
- 2) Non HDL-c is a better predictor of cardiovascular risk.
- 3) Increased non HDL-c even after bringing LDL to goal is primarily due to increased TGL.
- 4) In diabetics and Indian dyslipidemia, the scenario of normal LDL levels and raised TGL levels are common.
- 5) Statin therapy which primarily targets LDL may not offer complete protection since the residual risk (due to increased non HDL-C) persists even after LDL target is reached.
- 6) Fibrates are the preferred agent to treat increased triglycerides.

**\*Corresponding author:** Rajajeyakumar M, Assistant Professor, Department of Physiology, Chennai Medical College Hospital and Research Centre (SRM Group), Irungalur, Trichy-621105, Tamilnadu, India, Tel: 09751382650; E-mail: [rajakumar60@gmail.com](mailto:rajakumar60@gmail.com)

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They should be either combined with statins or given alone as and when warranted.

- 7) Apo-B which is a carrier protein for all atherogenic lipid particles. Apo-B levels may be a good marker of atherogenic dyslipidemia; but its use is limited due to the cost of testing.
- 8) Non-HDL-C is more accurate predictor of CV risk than LDL-C in disease in which elevated TG is present (metabolic syndrome and diabetes) which are commonly seen among Indians. Once LDL-C goal is achieved with lifestyle with drugs, the next target for therapy is non-HDL-C, which primarily aims at correcting serum triglyceride levels [4].
- 9) The clinical importance of moderate and high-intensity statin therapy, and the use of nonstatin treatment could improve reduction of the adverse outcomes [5].

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