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Importance of non HDL cholesterol –An update

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INTRODUCTION

Low-density lipoprotein cholesterol (LDL-C) is currently the primary treatment target for dyslipidemia management[1]. However; it has been shown that the risk for future coronary artery disease (CAD) events remains high in patients who have attained the guideline-recommended LDL-C goals. Many patients with cardio metabolic risk or diabetes have relatively normal levels of LDL-C but increased numbers of small dense LDL particles and other atherogenic lipoproteins[2]. LDL C concentration reflects only the amount of cholesterol contained in LDL particles but does not provide information about their number and structure. In addition, it does not include the participation of other lipoprotein fractions (Lipoprotein (a), VLDL) that are essential in the development of atherosclerosis[3]. Some of this residual risk may be a reflection of various other co morbid conditions that CAD patients have (diabetes mellitus, hypertension, physical inactivity, and smoking) and of their genetic predisposition to recurrent events[4].

There is need for a marker beyond LDL-C which can reflect the risk for recurrent cardiac events in patients. Non high density cholesterol (Non HDL-C) seems to be the answer.

Non HDL-C and risk of CAD

Modern laboratory diagnosis of lipid disorders and cardiovascular risk should be based on the use of indicators which present full impact of all plasma lipid components involved in atherogenesis. Non-HDL-C represents the cholesterol content present in all the atherogenic lipoproteins, such as: LDL-C, Very low-density lipoprotein cholesterol (VLDL-C), intermediate-density lipoprotein cholesterol (IDL-C), and lipoprotein (a)[4].

The concentration of non-HDL-C is calculated using a simple equation:

Non HDL C (mg/dL) = (Total Cholesterol) – (HDL C)

According to the Adult Treatment Panel III (ATP III) proposal, in individuals with hypertriglyceridemia (>200mg/dL), non-HDL cholesterol levels are a secondary goal of therapy after targeting LDL cholesterol levels. The treatment goal for non-HDL-C is 30 mg/dL above the LDL-C treatment target[1].

TABLE 1 : LDL-C and non-HDL-C goals in three CHD risk groups by NCEPATPIII[1]

Risk category	LDL-C(mg/dL)	Non-HDL-C
CHD and CHD risk equivalent (10-years CHD death risk >20%)	<100	<130
Multiple (≥ 2) risk factors (10-years CHD death risk <20%)	<130	<160
0-1 risk factor	<160	<190

Many studies have demonstrated that non-HDL cholesterol is a better predictor of CAD risk than is LDL cholesterol[5–7], and this may be especially true of statin-treated patients[8]. 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 traditional lipid risk factors[6]. Significantly, non HDL-C levels correlate with the subclinical atherosclerosis visible by imaging methods. According to Orakzai et al, of all the lipid parameters, only the non-HDL-C showed a significant association with the process of atherogenesis observed as coronary artery calcification[9].

The impact of elevated triglycerides levels in the calculation of LDL-C with the Friedewald formula suggests that non-HDL-C is beneficial in determining the risk of atherosclerosis and CAD in patients with hypertriglyceridemia[10]. Non HDL-C reflects the risk of both hypertriglyceridemia and LDL-C[11]. It might be an important estimate for diseases such as diabetes and obesity, in which excessive triglyceride values increase the concentration of small dense-LDL and decrease HDL-C.

It is important to note, though, that in a 2008 consensus statement by the American College of Cardiology Foundation and the American Diabetes Association, no triglyceride cut off level was defined for calculating non-HDL-C. The consensus panel concluded that routine calculation and use of non-HDL cholesterol constitute a better index than LDL cholesterol for identifying high-risk patients[2]. That does not mean, however, that LDL cholesterol should not be measured and used to guide therapy. On the other hand, the calculation of non-HDL cholesterol should be provided on all laboratory reports and should also be used to ascertain risk in patients with low to moderate LDL cholesterol levels (i.e., LDL cholesterol < 130 mg/dl). Apo B seems to be a sensitive index of residual CVD risk when LDL cholesterol or non- HDL cholesterol are 130 mg/dl or 160 mg/dl, respectively[2].

The role of non-HDL-C in predicting and reducing CAD risk in patients treated pharmacologically due to dyslipidemia is also noteworthy. In a meta-analysis of lipid-lowering therapies, a 1:1 correlation between the 1% non-HDL-C lowering and coronary heart disease risk reduction by lipid-modifying drugs was observed[12]. But this potential of non HDL-C to reduce the risk of cardiovascular events is not being utilized in clinical practice. The rate of target level attainment for non HDL-C remains poor as reported by Virmani et al. In their study, the goal attainment of LDL-C <100 mg/dL was seen in 80% of CAD patients, but the combined goal attainment for LDL-C (<100 mg/dL) and non-HDL-C (<130 mg/dL) remained low, at 51%[13]. Under stringent criteria for LDL-C (<70 mg/dL) and on-HDL-C (<100 mg/dL), this goal attainment fell to 13%. Another multinational study has reported the rate of non HDL-C goal attainment as 63% in all the risk categories of patients. In the high risk group, only 52% of patients successfully attained their targets for non HDL-C[14]. The reasons for this lower goal attainment include deficiencies in healthcare providers' awareness regarding non-HDL-C definition, calculation and treatment goals[15]. It has been suggested that direct reporting of non-HDL-C on standard lipid-panel results would improve goal attainment for non-HDL-C[16].

Advantages of incorporation of non HDL-C cholesterol in lipid panel can be enumerated as follows:

1 It measures the cholesterol content of all the atherogenic lipoproteins and thus superior to LDL-C for risk determination.
2 It can be calculated easily from the measured total cholesterol & HDL-C values without any additional expenses.
3 The established cut points for patients of different risk categories are already available.
4 There is no need of a fasting sample
5 Elevated non HDL-C with optimal LDL-C levels is a common occurrence in the setting of vascular disease, diabetes mellitus, the metabolic syndrome and renal insufficiency[10]. Non HDL-C represents the residual risk of cardiovascular events in these patients.
6 Reporting of non HDL-C along with other lipid profile parameters will definitely improve clinician and patient attitude for managing it in a better way.

Management of non HDL-C

The management of non-HDL cholesterol should always begin with lifestyle therapy because of the robust reductions in TG levels that may be achieved when combining dietary modification with an exercise regimen[17]. Foods that are high in omega-3 fatty acids may also be useful for TG lowering. In addition to lifestyle therapy, successful reduction of elevated non-HDL cholesterol may ultimately consist of combination therapy. This would include the use of a statin to serve as the foundation for LDL cholesterol lowering followed by a

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second therapy to bring non-HDL cholesterol to within the target range. The three categories of pharmaceuticals that would fall into this group include omega-3 fatty acid preparations, fibrates, and niacin[18].

CONCLUSION

Non HDL-C represents all the atherogenic particle of cholesterol and its treatment is grounded in a more holistic principle of dyslipidemia management. Currently it is the secondary treatment target according to NCEP ATP III guidelines and is not a part of lipid panel reporting in majority of laboratories. The consensus report of American college of cardiology foundation and American diabetes association has recommended its reporting as a routine part of lipid panel recently. There is need for better guideline and treatment goal dissemination to emphasize the role of this inexpensive and useful parameter in evaluation and management of cardiovascular disease risk.

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