

Evaluation of non-HDL cholesterol as a cardiovascular risk marker in type II diabetic patients

Deepa M.^{1*}, Priyadarshini K. S.², H. V. Shetty³, Usha S. M. R.⁴, Mamatha V.⁵

^{1,5}III year Post Graduate and Tutor, ³HOD and Professor, ^{2,4}Professor, Department of Biochemistry, Rajarajeswari Medical College and Hospital, Bangalore, Karnataka, INDIA.

Email: doctor.deepa@gmail.com

Abstract

Objectives: Type 2 diabetes mellitus patients have higher risk of experiencing cardio vascular disease (CVD) events than normal healthy population. Diabetic dyslipidemia is the major contributor of CVD events. It commonly manifests with elevated triglycerides and low levels of HDL cholesterol with predominance of small dense LDL particles amidst relatively normal LDL-C cholesterol levels. In diabetics Non HDL Cholesterol is strong predictor of CVD than LDL-C or TG as it provides a single index of all the apo B containing atherogenic lipoproteins. The current study aims to evaluate the significance of Non-HDL cholesterol over LDL cholesterol levels in patients with Type 2 diabetes mellitus and assess its role as a cardiovascular risk marker. **Methodology:** Hundred and four Type 2 Diabetes mellitus patients between 30-70 years attending medicine OPD at RRMCH were included in the study group. Serum samples were analysed for Total Cholesterol (TC), HDL-C and LDL-C using ERBA EM 360, autoanalyser. Non HDL-C was calculated by subtracting HDL-C from TC (Non HDL-C=TC-HDL-C). **Results:** The mean \pm SD of serum LDL-C in study group was 112.92 ± 29.59 mg/dl and the mean \pm SD of serum Non HDL-C level was 146.40 ± 40.95 mg/dl. We further divided the study group into two sub groups. One subgroup with serum LDL-C values <100 mg/dl and the other with serum LDL-C values >100 mg/dl. 34 patients (33%) had LDL-C values <100 mg/dl with mean \pm SD of 83.97 ± 12.05 mg/dl and Non HDL-C with mean \pm SD of 109.78 ± 14.95 mg/dl. 70 patients (67%) had LDL-C values >100 mg/dl with mean \pm SD of 126.98 ± 24.99 mg/dl and Non HDL-C with mean \pm SD of 164.19 ± 37.63 mg/dl. 67% of type 2 diabetic patients had elevated Non HDL-c levels compared to LDL-C levels. **Conclusions:** Non HDL-C is a significant index of dyslipidemia among patients with type 2 Diabetes mellitus compared to LDL-C. Advantages of Non HDL-C over LDL-C being cost effective, easily measured, independent of fasting state and hypertriglyceridemia which accompanies type 2 Diabetics. We conclude from our study that Non HDL cholesterol should be included in the lipid panel tests and treating Non-HDL cholesterol will reduce the cardiovascular disease mortality associated with type 2 diabetes mellitus.

Keywords: Atherogenic lipoproteins, CVD, LDL-C Non-HDL-C, Type 2 DM.

*Address for Correspondence:

Dr Deepa. M, III year Post Graduate and Tutor, Department of Biochemistry, Rajarajeswari Medical College and Hospital, Bangalore-560071, Karnataka, INDIA.

Email: doctor.deepa@gmail.com

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INTRODUCTION

Patients with type 2 diabetes have high rates of cardiovascular disease (CVD), much of which may be preventable with appropriate treatment of lipid abnormalities. Diabetic dyslipidemia most commonly manifests as elevated triglycerides and low levels of HDL cholesterol, with a predominance of small, dense LDL particles amidst relatively normal LDL cholesterol levels. In diabetic patients, Non-HDL cholesterol may be a stronger predictor of CVD than LDL cholesterol or triglycerides because it correlates highly with atherogenic lipoproteins. Target goals for LDL and Non-HDL cholesterol in patients with diabetes are < 100 and < 130

mg/dl, respectively. Failure to consider the importance of Non-HDL cholesterol in type 2 diabetes may result in under treatment of patients with diabetes.¹ Patients with type II diabetes have 2 - 4 times higher risk of experiencing cardiovascular disease (CVD) than adults without diabetes and their relative risk of dying from CVD is about twice as high, much of which may be preventable with appropriate treatment of dyslipidemia. The elevated CVD risk affecting patients with Type II diabetes may be attributed to a combined dyslipidemia characterized by elevated triglycerides, elevated triglyceride rich remnant lipoproteins (TGRLP), elevated apolipoprotein (apo) B and low levels of HDL cholesterol, with a predominance of small, dense LDL particles amidst relatively normal LDL Cholesterol levels. More recent data suggests that measurement of Non-HDL Cholesterol level (Calculated as Total Cholesterol minus HDL Cholesterol) could be more representative of all atherogenic, apolipoprotein (apo) B containing lipoproteins –LDL, VLDL, IDL and Lipoprotein (a). Although apolipoprotein B can be accessed directly, measurement of Non-HDL Cholesterol is more practical, reliable and inexpensive and can be considered as a surrogate marker for apolipoprotein B in routine clinical practice.¹ 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 is the sum of cholesterol accumulated in all lipoproteins, except HDL, such as: chylomicrons, VLDL and their remnants, IDL, LDL and Lp (a). The concentration of Non-HDL-C is calculated using a simple equation: Non-HDL-C (mg/dL) = TC –HDL-C.² Unlike LDL cholesterol, which can be incorrectly calculated in the presence of postprandial hypertriglyceridemia, Non-HDL cholesterol is reliable when measured in the non-fasting state.¹ As Non-HDL cholesterol measures the apo B-containing lipoproteins, it can serve as an additional tool to assess cardiovascular risk in people whose risk is not accurately identified by LDL cholesterol alone. This is especially important in patients with diabetes, in whom LDL levels may not be significantly elevated. Moreover, Non-HDL cholesterol is particularly atherogenic in the presence of the hypertriglyceridemia that usually accompanies diabetes.¹ Non-HDL-C was introduced as another means to refine risk estimation beyond LDL-C from Friedewald's formula in the presence of raised triglycerides (TG) levels (≥ 200 mg/dl), since associated changes in VLDL TG/VLDL-C ratio may lead to LDL-C under calculation. As it actually estimates the level of all apoB-carrying lipoproteins, Non-HDL-C may represent a simple and inexpensive surrogate to apoB measurement, especially in selected patients groups, such as

hypertriglyceridemic patients and/or patients with diabetes. Non-HDL-C may be more appropriate in higher-risk patients or in the setting of elevated triglycerides levels or cardio metabolic states.³ Liu *et al.* compared the diagnostic value of Non-HDL-C as a prognostic factor of acute coronary events and myocardial infarction among healthy subjects and diabetics.⁴ 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. Significantly higher concentrations of Non-HDL-C and higher relative risk of coronary events among patients with diabetes were observed and the risk in particular grade levels of Non-HDL-C was 1.5 to over 2.5 times higher in Diabetics than in healthy subjects. Ruminska *et al.* evaluated the usefulness of Non-HDL-C in the lipid disorders in children and adolescents with simple obesity. Patients with elevated Non-HDL-C (> 123 mg /dL) had significantly higher values of waist circumference and Serum TC, LDL-C, TG, TC: HDL-C, TG:HDL-C and lower HDL-C.⁵ Study done by S Zabeen *et al.*, found Non-Hdl cholesterol to be useful in assessing the risk of atherosclerosis in type 2 DM and hence to be included in the lipid profile for assessing and guiding treatment.⁶ The effect of serum lipids on the process of coronary arteries calcification (CAC), regarded as an early marker of subclinical atherosclerosis was described in recent study by Orakzai *et al.*⁷ Of all lipid parameters, only the Non-HDL-C showed a significant association with the process of atherogenesis. The Bogalusa Heart Study proved a relationship between the value of Non-HDL-C in childhood and risk of cardiovascular disease in adulthood.⁸ A strong association between Non-HDL-C, denoted at the age of 5-17 years and the intima-media thickness (IMT) in carotid artery in adults was documented. Kawamoto *et al.* observed excessive IMT value and CHD risk with the increasing Non-HDL-C values in patients over 65 years old.⁹

MATERIAL AND METHODS

The present study was undertaken to evaluate NON-HDL-Cholesterol as a cardiovascular risk marker in type 2 diabetic patients and to assess the significance of NON-HDL-Cholesterol over LDL-Cholesterol levels in type 2 diabetic patients. Study subjects were patients diagnosed with Type 2 diabetes mellitus. Study conducted at Medicine OPD at Raja Rajeswari Medical College and Hospital, Bangalore between January 2013 - June 2013

Inclusion Criteria

Cases

104 known Type-2 Diabetic patients, between 30-70 years belonging to both the sexes were included in the

study.

Exclusion Criteria

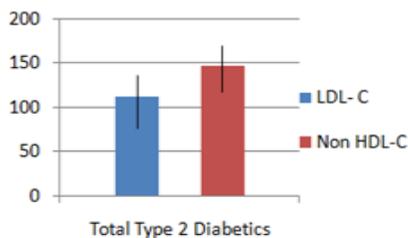
Patients with Thyroid disorders, Pregnancy, History of Alcohol intake and Drugs causing dyslipidemia. Patients satisfying the inclusive criteria were enrolled in the study, after obtaining written informed consent. Study was undertaken with due approval from the institutional ethical committee, RRMCH, Bangalore. There were no financial liabilities on the study subjects. 12 hours fasting venous blood was collected from antecubital vein under aseptic precautions. 2 ml blood was allowed to clot in Clot Activator tubes and serum was separated by centrifugation. The estimation was carried out in a fully automated chemistry analyser ERBA EM 360 for: Total cholesterol (TC) and HDL-C and Non HDL-C = (Total cholesterol-HDL-C) Blood glucose by glucose-oxidase - Peroxidase method., Total Cholesterol by CHOD-PAP method, HDL direct by Immunoinhibition method., LDL direct by Immunoinhibition method. Triglyceride by GPO-ADPS method. and NON HDL-C=TOTAL CHOLESTEROL-HDL-C.

RESULTS AND DISCUSSION

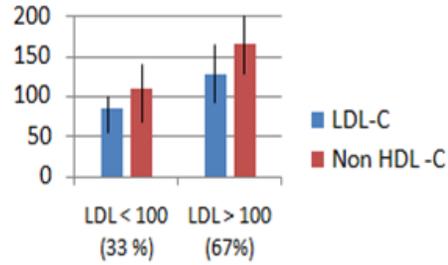
The data collected was tabulated and analyzed using descriptive statistics. The results were compared using student t test.

Table 1: NCEP ATP III Goals for LDL Cholesterol and Non-HDL Cholesterol in High-Risk Patients

Risk Category	Primary Target: LDL Cholesterol	Secondary Target: Non-HDL Cholesterol
CHD or CHD risk equivalents, including diabetes	< 100 mg/dl	< 130 mg/dl
Multiple(2+)Risk Factors	<130mg/dl	<160mg/dl
0-1 Risk Factors	<160mg/dl	<190mg/dl



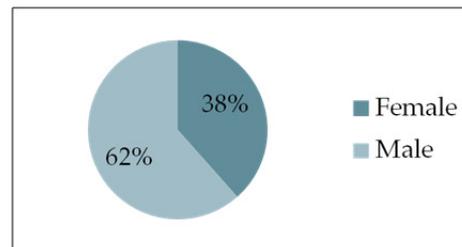
Graph 1: IDL-c and non HDL-c in study group



Graph 2: IDL-c and non-HDL-c in sub groups

Table 2: Bar diagram representing the IDL-c and non-HDL-c in the study group

STUDY GROUP	LDL	NON HDL-C
TYPE 2 DIABETICS	112.92 ± 29.59	146.40 ± 40.95
LDL < 100 (33%)	83.97 ± 12.05	109.78 ± 14.95
LDL > 100 (67%)	126.98 ± 24.99	164.19 ± 37.63



Graph 3: Sex ratio in the study subjects

The mean ± SD of serum LDL-C in study group was 112.92 ± 29.59 mg/dl and the mean ± SD of serum Non HDL-C level was 146.40 ± 40.95 mg/dl. We further divided the study group into two sub groups. One subgroup with serum LDL-C values <100 mg/dl and the other with serum LDL-C values >100 mg/dl. 34 patients (33%) had LDL-C values <100 mg/dl with mean ±SD of 83.97±12.05 mg/dl and Non HDL-C with mean ± SD of 109.78 ± 14.95mg/dl. 70 patients (67%) had LDL-C values >100mg/dl with mean ± SD of 126.98 ± 24.99 mg/dl and Non HDL-C with mean ± SD of 164.19± 37.63 mg/dl. 67% of type 2 diabetic patients had elevated Non HDL-C levels compared to LDL-C levels. Males were predominant in the study group with 62% and females with 38%. Our study correlated with similar studies done by Anne L. Peters (2008): concluded that Non-HDL cholesterol to be an important CVD risk predictor and therapeutic target in patients with diabetic dyslipidemia. Glenn A. Hirsh *et al* (2002): Concluded that measurement of non HDL-C rather that LDL-C would be a better target for therapy, especially in persons with hyper triglyceridemia levels > 200mg/dl. S. Zabeen *et al* (2012): Concluded that Non HDL-C can be useful in accessing the risk of atherosclerosis in Type-2 DM and therefore it should be included in lipid profile for accessing the risk and guiding treatment. VeraBittner (2007): Concluded

Non HDL-C to be a strong predictor of CVD risk and labs should be increased to report this as part of every lipid profile.

CONCLUSION

Non HDL-C is a significant index of dyslipidemia and hence a useful cardiovascular risk marker among patients with Type 2 Diabetes Mellitus compared to LDL-C. Advantages of Non HDL-C over LDL-C are: Cost effectiveness, easily measured, Independent of fasting state and hypertriglyceridemia which accompanies Type2 Diabetics. Non HDL cholesterol is useful in assessing the risk of atherosclerosis in type 2 DM, and hence it should be included in the lipid profile for effective approach in guiding treatment. We conclude from our study that Non HDL cholesterol should be included in the lipid panel tests and it is a stronger predictor of CVD than LDL Cholesterol or Triglycerides, since it correlates with the atherogenic Lipoproteins and hence a useful CVD risk marker.

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