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Original Article

Is evaluation of non-HDL-C better than calculated LDL-C in CAD patients? MMIMSR experiences

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ABSTRACT

Objective: The present study aimed to establish a better marker for the assessment of coronary artery disease (CAD).
Methods: One hundred patients of CAD (aged 20–60 years) of both sex and patients of hypertension with symptoms of CAD were selected for the study.50 age and sex matched healthy controls were chosen for the present study. Serum total cholesterol, triglycerides and HDL-C were estimated in Simens Dimensions RxL. LDL-C, VLDL-C were calculated by Friedwald Formula while non-HDL-C was calculated by subtracting HDL-C level from total cholesterol level. The comparison of non-HDL-C and friedwald calculated LDL-C was made in terms of independent'*t*' test, serum TG levels (TG $\leq$ 200 mg/dl and TG > 200 mg/dl) and area under receiver operating characteristic (AUROC) curve.
Results & conclusion: The non-HDL-C levels (mean ± S.D) were higher in both test and control groups to that of the levels of friedwald calculated LDL-C. The area under receiver operating characteristic (AUROC) curve was significantly higher for non-HDL-C than for friedwald calculated LDL-C. The predictive value of non-HDL-C and friedwald calculated LDL-C were also compared in group A (serum TG $\leq$ 200 mg/dl) and group B (serum TG > 200 mg/dl). Non-HDL-C levels showed a significant difference in both the groups while the results were non-significant to that of friedwald calculated LDL. Thus, non-HDL-C is much specific and sensitive parameter for assessment of CAD risk. Moreover, non-HDL-C levels can also be done in non-fasting state with accuracy, thereby, it is patient friendly parameter. Therefore, the authors strongly suggest the incorporation of non-HDL-C in routine lipid profile panel.

1. Introduction

Cardiovascular disease is the foremost cause of mortality and morbidity across the globe. According to the WHO data of the year 2019, 17.9 million people die owing to cardiovascular disease (CVD) each year[1]. Dyslipidemia has been clearly identified as most important atherosclerotic risk factor eventually leading to the progression of cardiovascular disease[2]. The World Health Organization had also reported that dyslipidemia is significantly associated with more than half of global cases of ischemic heart disease[3].

The traditional approach to the management of dyslipidemia focuses mainly on Low density lipoprotein cholesterol (LDL-C) which is frequently considered as a primary target of lipid lowering therapy for cardiovascular diseases. LDL-C on the routine lipid panel is mostly calculated by friedwald equation considering it as a cost-effective valuable tool and primary laboratory method over many decades. Despite its extensive use in predicting cardiovascular risk, it has become a sub-optimal marker for a plethora of reasons. Firstly, LDL-C concentration reflects only the amount of cholesterol present in LDL particles. Secondly, in hypertriglyceridemia (TG > 200 mg/dl), this equation gives inaccurate results as already reported by Japan Atherosclerotic Society (JAS) 2012 guidelines, and several other studies conducted recently[4–7]. Surprisingly, even in healthy individuals LDL-C has been giving erroneous results with range of 13.3–13.5%[8]. Besides these limitations, the estimation of LDL-C requires fasting sample which results in delay in reporting thereby, causing inconvenience for both patients and clinicians.

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Therefore, latest diagnosis of the lipid related disorders should be based on such a parameter which is unaffected by these limitations. Several recent epidemiologic studies have documented that non-HDL-C is more strongly associated with coronary artery disease risk than calculated LDL-C[9–13]. Moreover American and European Cardiological Societies, International Atherosclerosis Society, Expert Dyslipidemia Panel and the National Lipid Association have strongly recommended non-HDL-C in routine lipid profile panel whose value can be simply calculated at no additional cost by subtracting HDL level from Total Cholesterol level and it further helps in quantifying total atherogenic burden by measuring aggregate amount of cholesterol[14].

Unfortunately, non-HDL-C has been neglected so far despite its efficacy in comparison to LDL-C in CAD risk reduction. Although Lipid Association of India has recommended non-HDL-C as a co-primary target but still several premier institutions and hospitals have not acknowledged its incorporation in routine lipid profile panel[15]. The present study was aimed to assess the usage of non-HDL-C evaluation in the primary prevention of cardiovascular disease risk.

2. Methods

This is a case–control study conducted in department of Biochemistry in collaboration with department of Cardiology in MM Superspeciality Hospital, Mullana, Ambala. Patients of CAD (aged 20–60 years) who presented for the first time in cardiology OPD were included in the study and the patients of hypertension with symptoms of CAD were also included in the study. One hundred consecutive patients were taken for the study. Patients of Acute M.I, Diabetes mellitus, Kidney disorders, Liver diseases as well as patients on follow up/on extensive medical treatment and on lipid lowering drugs were excluded from the present study. Fifty age and sex matched healthy individuals were selected as controls. The study was duly approved by institutional ethical committee and informed consent was taken from all participants of the study.

Detailed history of the patients was recorded. 3 ml blood was collected in plain vial and serum was separated using standard protocol. After the collection of blood sample, serum total cholesterol (TC), triglycerides (TG), High Density Lipoprotein-Cholesterol (HDL-C) were estimated by Simens Dimensions RxL in the clinical biochemistry lab, Department of biochemistry, MMIMSR. LDL and VLDL were calculated by Friedwald Formula and non-HDL-C was calculated by subtracting the HDL level from Total Cholesterol level i.e. TC–HDL-C. Quality control was maintained throughout this study.

2.1. Statistical analysis

The significance between the groups was determined using independent student'*t*' test. Significance is considered only at $p < 0.05$. To compare the predictive values of non-HDL-C and friedwald calculated LDL-C, ROC analysis was done. The area under ROC (AUROC) is considered a global performance indicator for a prognostic factor[16]. Greater area under curve of the ROC curve indicates better marker of the study. Further, both the parameters were also compared in terms of serum triglyceride levels (TG $\leq$ 200 mg/dl and TG > 200 mg/dl). All the statistical analysis was done using SPSS 20 version.

3. Results

Among the 150 individuals who had participated in the study, males outnumbered females. The maximum number of the patients were of age group 40–50 years. The blood pressure of less than 120/80 mm/Hg was considered normal.

Serum TC, TG, HDL, LDL, VLDL and non-HDL were measured for all the subjects. The results (mean ± S.D) of friedwald calculated LDL-C and non-HDL-C are illustrated in Fig. 1.

To compare the predictive values of non-HDL-C and friedwald calculated LDL-C with respect to serum triglycerides levels, patients were divided into 2 groups; Group A (serum TG $\leq$ 200 mg/dl) and Group B (serum TG > 200 mg/dl). On comparison non-HDL-C levels showed a significant difference in both the groups while the results were non-significant for friedwald calculated LDL-C (Table 1).

To compare the predictive values of non-HDL-C and friedwald calculated LDL-C, ROC curve analysis was done and on comparison area under Receiver Operating Characteristic curve (AUROC) for non-HDL-C was found to be significantly higher (0.835 at 95% Confidence Interval; 0.771, 0.898) than for friedwald calculated LDL (0.667 at 95% Confidence Interval; 0.582, 0.752) (Fig. 2).

4. Discussion and conclusion

Low-density lipoprotein cholesterol (LDL-C) has been recommended as the primary treatment target on lipid management in coronary artery disease as reported earlier. Despite of having so many advantages over friedwald calculated LDL-C; incorporation of non-HDL-C in routine lipid panel has been neglected so far. In view of this, the present study was done to study the usefulness of non-HDL-C in CAD risk assessment at MMIMSR, Ambala.

There are growing evidences which also suggest the role of non-HDL-C in predicting the CAD risk[9–12]. Studies conducted by Seki R et al.[17], Bhavan Kumar et al.[7], Aggarwal J et al.[5] and Lawrence Baruch et al.[18] compared the LDL-C (both direct and calculated) and non-HDL-C levels to confirm the predictive value of both the parameters in assessment of CAD. Seki R et al and Aggarwal J et al. compared non-HDL-C and LDL in terms of ROC analysis, pearson correlation and independent '*t*' test while Bhavan Kumar et al. and Lawrence Baruch et al. compared non-HDL-C and LDL in terms of student '*t*' test, ANOVA and Fisher's z-transformation. Interestingly, non-HDL-C was found to be more significantly associated with CAD than friedwald calculated LDL-C as well as direct LDL.

In the present study, the non-HDL-C and friedwald calculated LDL were also compared with respect to serum triglyceride levels (TG $\leq$ 200 mg/dl and TG > 200 mg/dl). Non-HDL-C was found to be significantly associated while results were non-significant for friedwald calculated LDL-C (Table 1). This is a major landmark change in strategy which we normally follow. This study demonstrated the superiority of non-HDL-C over friedwald

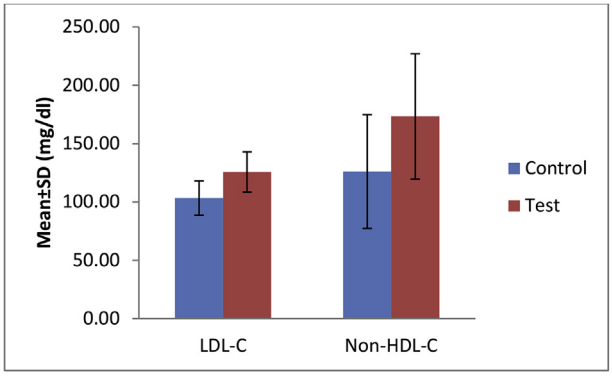

Fig. 1. Friedwald calculated LDL-C and non-HDL-C levels in control and test group.

Table 1
Comparison of calculated LDL and Non-HDL-C in group A (serum triglycerides ≤ 200 mg/dl) and group B (serum triglycerides > 200 mg/dl).

Parameter	Group	*N*	Mean ± S.D	t-value	*p*-value
LDL-C (mg/dl)	A (≤200)	42	115.15 ± 43.29	0.562	0.575
	B (>200)	58	121.00 ± 56.45		
non-HDL-C (mg/dl)	A (≤200)	43	157.81 ± 39.74	2.569	0.012*
	B (>200)	57	184.92 ± 59.95		

*The data presented as mean ± S.D. *N* denotes number of subjects. The significance was determined by independent student '*t*' test using SPSS 20 version. $P < 0.05$ was considered statistically significant.

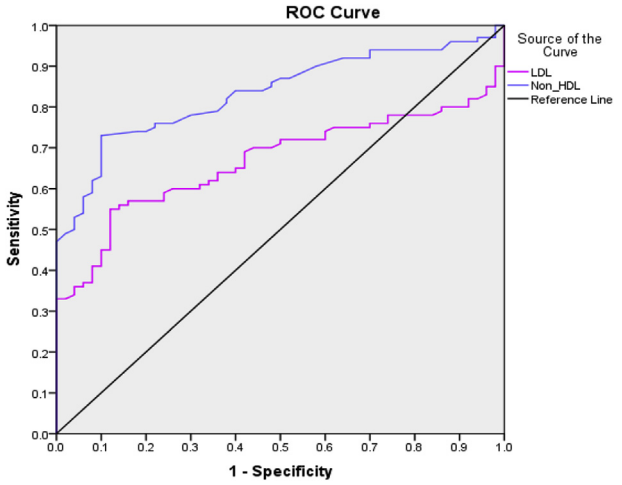

Fig. 2. Receiver Operating Characteristic curve for friedwald calculated LDL-C and non-HDL-C.

calculated LDL-C in patients of CAD having elevated TG level and hence, clinicians on follow up of this group should target non-HDL-C instead of LDL-C. These results are in accordance with recent studies[4–7], including The Lipid Research Clinics Program follow-up study[6] leading to the conclusion that non-HDL-C offers competitive performance compared to friedwald calculated LDL-C.

Non-HDL-C level can be estimated via non-fasting sample thus, making it more patient friendly and fastens the clinical decision as well. Moreover, 2018 guidelines have also highlighted the utility of non-fasting sample in clinical decision making[19] thereby, allowing the non-HDL-C as primary therapeutic target. It would certainly benefit the patients as well as entire healthcare system. Henceforth, the authors strongly suggest the incorporation of non-HDL-C in routine lipid profile panel for the better diagnosis and treatment of coronary artery disease risk.

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Conflicts of interest

All authors have none to declare.

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