Research Article

# Comparison of the values of low density lipoprotein by the direct and indirect methods (friedewald equation)

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## Abstract

**Background:** LDL-c is routinely estimated in clinical practice to guide treatment for hypercholesterolemia by Friedewald formula. It is also measured by direct homogenous assays in critical cases when accuracy is needed. **Objective:** To determine if, and to what extent LDL level is underestimated when it is calculated by the Friedwald formula compared with the LDL measured by a direct method. **Methodology:** About 1140 lipid profile reports wherein LDL was measured directly in fasting state and TG< 400 mg/dl were taken for the study. The data was divided based on the TG levels into four groups, A - <99mg/dl, B-100-199 mg/dl, C-200-299 mg/dl and D- < 400 mg/dl. LDL was calculated using Friedewald's formula and was compared with homogenous enzymatic method derived direct LDL in all the groups. Data was statistically analysed to arrive at results. **Results:** A positive correlation was noted between the two methods of measured LDL in all the groups. In subjects with TG <100 there was no variation between c-LDL and d-LDL. Difference of 10-15mg was found in subjects with TG <300.Difference between c-LDL and d-LDL s increased with increase in TG level, 20-25mg when TG btw 300-400. **Conclusion:** The c- LDL tends to underestimate d- LDL as TG increases especially with TG>300.

**Key words:** LDL, hypercholesterolemia, Friedewald's formula,homogenous assay.

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## INTRODUCTION

The Low Density Lipoproteins (LDL) is a heterogeneous population of spherical particles, with hydrophobic oily cores consisting of cholesteryl ester and triglycerides (TG). These particles are coated with a native surfactant of phospholipids, free cholesterol and apolipoproteins. On an average, LDL carries two thirds of the total cholesterol (TC) in serum. Each LDL particle contains one molecule of Apo lipoprotein B-100(apo B- 100), which is the main protein component of LDL, and the other minor apolipoproteins are Apo E and Apo C II[1] Many studies have demonstrated a strong positive correlation between low-density lipoprotein cholesterol (LDL-C) concentrations in serum and the incidence of coronary heart disease (CHD) .[4,5]The association between total cholesterol (TC) and risk of developing CHD has been well established by studies such as the Framingham Heart Study. Most of the cholesterol in circulation is carried by LDL, which has been shown to be primarily responsible for the association with CHD risk .Pathological studies have shown that increased LDL-C concentrations correlate highly with the extent of atherosclerotic lesions.[6] A reduction of LDL-C decreases the risk and ameliorates the symptoms of CHD by causing a regression in the lesions.[7,8]

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## OBJECTIVE OF THE STUDY

To determine if, and to what extent LDL level is underestimated when it is calculated by the Friedwald formula compared with the LDL measured by a direct method.

## METHODOLOGY

This is a record based study done at Rajarajeswari Medical College and Hospital, Bengaluru. About 1140 lipid profile reports wherein LDL was measured directly in fasting state and TG< 400 mg/dl were taken for the study. The data was divided based on the TG levels into four groups, A - <99mg/dl, B-100-199 mg/dl, C-200-299 mg/dl and D- 300-400 mg/dl. LDL was calculated using Friedewald's formula and was compared with homogenous enzymatic method derived direct LDL in all the groups. Homogenous assay from Wako chemicals using Diasys reagents done in Piramal BS 300 fully autoanalyser. Our lab has a tie up with BIORAD EQAS and our external quality EQAS score is < 2 SD. Data was statistically analysed to arrive at results.

## RESULTS

Present record based study consisted of 1140 lipid profile reports. A positive correlation was noted between the two methods of measured LDL in all the groups. In about 70 subjects with TG< 100mg/dl there was no variation between c-LDL and d-LDL. Negligible variation was seen in 645 subjects with TG between 100- 200mg/dl. Difference of 10-15mg was found in 288 subjects with TG between 200- 300mg/dl.Difference between c-LDL and d-LDL increased with increase in TG level in 133 subjects, 20-25mg when TG between 300-400mg/dl. Statistical Analysis was done by Pearson's correlation and Student's paired't' test. The same is depicted in table 1 and Fig 1.

**Table 1:** Data analysis of the study

| TG range (mg/dl) | n | R | Mean±SD D-LDL | Mean±SDC- LDL | p | cLDL – dLDL |
|---|---|---|---|---|---|---|
| < 99 | 70 | 0.99 | 36±17.6 | 36±14.1 | >1 | 1 |
| 100-199 | 645 | 0.97 | 67±31.8 | 60±28.4 | <0.01 | 7 |
| 200-299 | 288 | 0.98 | 116±33.9 | 98±19.9 | <0.001 | 19 |
| 300-399 | 133 | 0.96 | 195±49.4 | 204±94.6 | <0.0001 | 22 |

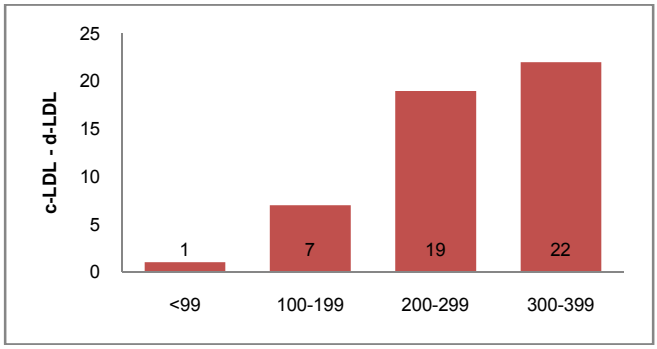


**Figure 1:** Difference btw c-LDL and d-LDL increases with high TG level

## LIMITATIONS OF THE STUDY

In patients with history of diabetes, hypertension, IHD where LDL level is important, as this was a record based study history could not be elicited.Small study population is taken.

## DISCUSSION

The LDL class comprises a heterogeneous and polydisperse population of particles with sizes between the large TG-enriched VLDL (density 1.006 kg/L) and the dense and small protein-rich HDL (density range, 1.063–1.21 kg/L). Classically, LDL particles are defined in terms of hydrated density as the fraction with density between 1.006 and 1.063 kg/L as obtained by preparative ultracentrifugation. diagnosis and management of adults with hypercholesterolemia are largely based on LDL-C concentration. The serum LDL-C concentrations used to classify adults for high risk of heart disease are: Desirable <130 mg/dl, Borderline high-risk 130-159 mg/dl, High risk >160 mg/dl (2). The goal for subjects with two or more risk factor like diabetes, family history, hypertension, cigarette smoking, low High Density Lipoprotein Cholesterol (HDL-C) is to achieve LDL-C of 100 mg/dl. [10] Therefore accurate and precise measurements of patients' LDL-C concentrations are necessary to appropriately identify individuals with hypercholesterolemia and to monitor the response to diet and drug treatments.[11] Therapy is targeted on lowering LDL-C values below a target value, which depends on the number of other risk factors [low HDL-cholesterol

(HDLC), cigarette smoking, hypertension, family history of CHD, and male gender present. In 1972, Friedewald *et al.* [12] published a report describing a formula to estimate LDL-C as an alternative to tedious ultracentrifugation. The calculation was actually proposed for use in epidemiologic studies, but was later adopted and became the method of choice by routine clinical laboratories, in part for economic reasons. Studies have shown that reliability of the LDL-C estimations decreases considerably with increasing TG.

## CONCLUSION

The c- LDL tends to underestimate d- LDL as TG increases especially with TG>300. For values of TG<200 LDL can be estimated by calculation.When accuracy is important in patients with h/o diabetes, hypertension and IHD it is better to measure LDL directly. Friedewald estimation only approximates LDL, the homogenous assay of LDL-c measurement is more specific and is less susceptible to interference from high TG levels, the assay kits are costly.

Hence c- LDL is a cost effective tool to measure LDL when accuracy is not crucial.

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