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COMPARISON AND CORRELATION BETWEEN LOW DENSITY LIPOPROTEIN LEVELS ESTIMATED BY DIRECT METHOD VERSUS INDIRECT METHOD USING FRIEDWALD FORMULA IN PATIENTS PRESENTED TO OUR TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: One of the major risk factors for the development of coronary heart disease is high low-density lipoprotein (LDL) cholesterol. Reduction in LDL cholesterol levels decreases the risk of development of coronary heart disease. The optimum LDL levels in a normal healthy individual have to be maintained at a concentration of <100 mg/dL.

Objectives: the present study aimed to estimate, compare and correlate LDL concentration measured at different levels of TG levels by direct and indirect method in patients attending our tertiary care hospital.

Methodology: We included a total of 200 patients who have been referred to clinical biochemistry laboratory for lipid profile, out of 200 subjects 124 were males 76 were females. We divided the total subjects into three groups depending on the levels of triglycerides. Lipid profile parameters [total cholesterol, Tag, LDL, HDL, VLDL] were estimated in a fully automated biochemistry analyser as per the manufactures instructions. LDL was also calculated by Friedwalds formula: LDL = Total cholesterol-HDL-TG/5 (VLDL cholesterol). Student t test was used for the comparison of LDL concentration by direct and indirect method and Pearson's Correlation coefficient was used to check the correlation.

Results: In the present study, we found strong correlation between direct method and Friedewald formula calculated LDL levels in subjects having triglyceride concentration less than 400 mg/dL. We found no statistical significant differences in LDL levels in Group I, II and III respectively and also we found strong positive correlation existed between the two methods for the determination of LDL levels.

Conclusion: Friedewalds Formula can be used to estimate LDL cholesterol, and direct LDL should be employed only in those cases wherein Friedewalds formula cannot be used like non-fasting samples, patients with TGs more than 400 mg/dl, disorders related to lipoproteins (Type III hyperlipoproteinemia) and secondary hyperlipoproteinemias.

Keywords: Cholesterol, Friedwald Formula And Direct Method, Low Density Lipoproteins, Triglycerides,

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INTRODUCTION

LDL is low density lipoproteins, which is composed of outer layer of phospholipids, apolipoproteins, free cholesterol and inner layer of triglycerides and cholesterol esters, it transports cholesterol from the liver to peripheral tissues.[1] It is known as bad cholesterol as its deposition in tissues and blood vessels accounts for major

cardiovascular consequences. It is implicated in the pathogenesis of atherosclerosis further atherosclerosis related complications on long term.[2] One of the major risk factors for the development of coronary heart disease is high low-density lipoprotein (LDL) cholesterol.[3] Reduction in LDL cholesterol levels decreases the risk of development of coronary heart disease.[4] The optimum LDL levels to be maintained at a concentration of <100 mg/dL in a normal healthy individuals.[5]

Low-density lipoprotein (LDL)-cholesterol, as estimated by the Friedewald formula (FF) in routine patient care, is a central focus of clinical practice guidelines throughout the world.[5,6] LDL can be calculated by FF (total cholesterol (TC) minus high-density lipoprotein (HDL)-cholesterol minus triglycerides (TGs)/5 in mg/dl) or measured directly in the laboratory. The FF is not valid for patients with TGs >400 and in patients for type 3 dyslipoproteinemia. A number of studies have studied the impact of TG on the FF. These studies suggest LDL may be underestimated by the FF at low LDL levels and higher TG levels.[7]

In the present study, we estimated LDL concentrations at different levels of triglycerides by direct and indirect method (FF) and compared them to check the statistical significance and correlation.

The present study was performed to estimate, compare and correlate LDL concentration measured at different levels of TG levels by direct and indirect method in patients attending our tertiary care hospital.

MATERIALS AND METHODS

This was a comparative clinical trial performed on patients visited and referred for routine lab investigation by various outpatient departments from the Institute. The present study was carried out for a period of one year from 2020 to 2021 at Raipur Institute of Medical Sciences, Raipur.

We included 200 patients referred for fasting lipid profile testing from all clinical departments of our tertiary care hospital both males and females aged 18-60 years.

Patients with Triglyceride concentration >400 mg/dL, diabetes mellitus, advanced renal disease, liver failure, patients on lipid lowering therapy and patients <18 years were excluded from the study.

Lipid profile parameters [total cholesterol, Tag, LDL, HDL, VLDL] were estimated in a fully automated biochemistry analyser as per the manufactures instructions. LDL was also calculated by Friedwalds formula: LDL = Total cholesterol-HDL-TG/5 (VLDL cholesterol).

Statistical analysis:

Results were subjected for appropriate statistical analysis.

1) Student t test was used for the comparison of LDL concentration by direct and indirect method.
2) Pearson's Correlation coefficient was used to check the correlation.

RESULTS

We included a total of 200 patients who have been referred to clinical biochemistry laboratory for lipid profile, out of 200 subjects 124 were males 76 were females. We divided the total subjects into three groups depending on the levels of triglycerides as shown in table 1 and 2. In the present study we did not find any statistically significant differences between the two methods when the concentration of TG was <400 mg/dL [group I <200mg/dL, group II 201-300 mg/dL and group III 301-400 mg/dL] (table 3 & 4).

We found the strong positive correlation existed between direct method and FF calculated method for LDL (scatter plot 1, 2 & 3).

DISCUSSION

As per the National Cholesterol Education Program Adult Treatment Panel, the primary target for treatment of dyslipidaemia is LDL cholesterol, hence accurate measurement and reporting is utmost important. In our country mostly the labs are small sized or medium sized where the sample size varies from 100-500 per day, most of the laboratories are using FF calculated LDL for reporting LDL pertaining to the cost of Direct LDL kit method. It is very much important to ensure the reliability and accuracy of the reports generated. Hence we conducted the study to ensure the comparability and reliability, correlation between the two methods.

In the present study we did not find any statistically significant differences between the two methods when the concentration of TG was <400 mg/dL [group I <200mg/dL, group II 201-300 mg/dL and group III 301-400 mg/dL].

A study by Sahu *et al*[8] noted that the mean LDL calculated by FF was significantly higher than the direct LDL measurement at TG between 1 and 300 mg/dl. However, the study by Gupta *et al*[9] reported underestimation of LDL by FF at all levels of TG (ranging from 45 to 635 mg/dl). LDL was measured using direct homogenous assay (Daiichi Pure Chemicals Co. Ltd, Tokyo, Japan) in both the above studies. Anandaraja *et al*[10] noted that FF overestimated LDL in subjects with TG <350 mg/dl (LDL was measured using heparin precipitation method in their study).

Nauck *et al*[11] in their study observed, direct LDL method has no advantage when compared to calculated LDL method and recommended further validation for direct homogeneous methods. Mora *et al*[12] observed the nonassociation of direct LDL with Friedewalds LDL in nonfasting samples and they could not demonstrate any advantage of direct LDL in comparison to Friedewalds calculated LDL. They also stated using direct LDL may misclassify the patients into low-risk NCEP category because the results of direct LDL were 5–10 mg/dl lower when compared to Friedewalds calculated LDL. Gazi *et al*[13] observed Friedewalds calculated LDL was accurate for any value of TG below 400 mg/dl. In this study, we observed a similar finding since the LDL cholesterol calculated by Friedewalds formula correlated well with direct LDL at TGs below 400 mg/dl. Choi *et al*[14] observed that direct LDL values were 5% higher than calculated LDL and in diabetics, the difference was much higher. Sudha *et al*[15] observed Friedewalds calculated LDL method underestimated LDL levels in comparison to direct method and they concluded that direct LDL method is better than Friedewalds calculated LDL in diabetics. Lindsey *et al*[16] observed Friedewalds calculated LDL underestimated LDL levels by 20 mg/dl when compared to direct LDL method. Kaur et al[17] observed there was no significant difference between the LDL values measured by direct LDL method and Friedewalds calculated method in patients with metabolic syndrome.

CONCLUSION

In the present study, we found strong correlation between direct method and Friedewald formula calculated LDL levels in subjects having triglyceride concentration less than 400 mg/dL. Friedewalds Formula can be used to estimate LDL cholesterol, and direct LDL should be employed only in those cases wherein Friedewalds formula cannot be used like nonfasting samples, patients with TGs more than 400 mg/dl, disorders related to lipoproteins (Type III hyperlipoproteinemia) and secondary hyperlipoproteinemias.

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TABLES AND FIGURES

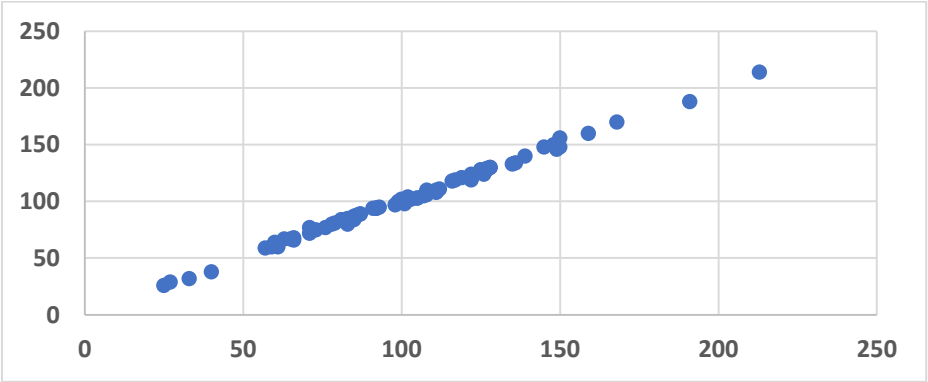
Table 1: Distribution of the study subjects according to the levels of Triglycerides	
Group I	<200 mg/dL
Group II	201-300 mg/dL
Group III	300-400 mg/dL

Table 2: Frequency Distribution of the study subjects according to the levels of Triglycerides	
	Number of subjects
Group I	148 (74%)
Group II	28 (14%)
Group III	24 (12%)

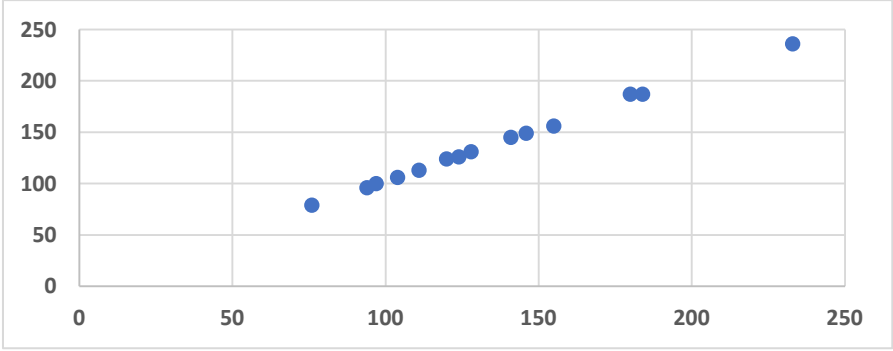
Table 3: Comparison of LDL between direct method and indirect method	
	Number of subjects (n=200)
Direct LDL	108.3±36.46
Indirect Friedewald Calculated LDL	106.7±37.83

Table 4: Comparison of LDL between direct method and indirect method at different levels of TG		
	Direct LDL	FF LDL
<200 mg/dL	102.8±.35.76	102.7±35.47
201-300 mg/dL	138.21±42.56	135.21±42.17
301-400 mg/dL	87.3±21.23	85±20.23

Scatter plot 1: shows the correlation between direct LDL and FF calculated LDL (TG <200 mg/dL) r = 0.98 [x-axis: Direct LDL, y-axis: FF calculated LDL]



Scatter plot 2: shows the correlation between direct LDL and FF calculated LDL (TG 201-300 mg/dL) r = 0.966



Scatter plot 3: shows the correlation between direct LDL and FF calculated LDL (TG 301-400 mg/dL) r = 0.947