

COMPARISON OF DIRECT AND INDIRECT LDL CHOLESTEROL LEVELS CALCULATIONS (FRIEDEWALD & CHEN) IN PATIENTS AT PROF. DR. I.G.N.G. NGOERAH GENERAL HOSPITAL DENPASAR

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ABSTRACT

Elevated LDL cholesterol (LDL-C) levels are one of the risk factors for coronary heart disease. Accuracy in measuring LDL-C levels helps determine the evaluation and therapy. Measurement of LDL-C levels is directly or indirectly. The gold standard is beta/β quantification. Examination of LDL-C using the Friedewald Formula is the most commonly used method but gives less precise results at levels of triglyceride more than 400 mg/dL. Therefore, many formulas have appeared, and the Chen Formula is one of them. This study aimed to compare the mean difference of LDL cholesterol levels calculated by the Friedewald and Chen Formula against LDL direct (homogeneous enzymatic colorimetric assay). This study was an analytical observational with a cross-sectional design conducted at Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar. The sample used was 95 patients who performed lipid profile examinations in April-June 2023 through consecutive sampling techniques and analyzed with SPSS version 25. Based on the independent t-test of LDL direct with Friedewald and Chen Formulas, the p-values were 0.205 and 0.206 (p>0.05), and there was no significant difference between the direct and indirect methods. Friedewald and Chen Formulas gave results in good agreement at triglyceride < 400 mg/dL. Both formulas can be used as needed. However, the direct method is recommended because the results are more accurate even if the triglyceride > 400 mg/dl. Future researchers are advised to continue research for comparing using other formulas.

Keywords: Friedewald Formula., Chen Formula., LDL Cholesterol.

INTRODUCTION

Cardiovascular disease is the leading cause of mortality and morbidity worldwide.¹ Low-density lipoprotein cholesterol (LDL-C) is the largest cholesterol transporter in the blood and proatherogenic, causing atherosclerotic plaque and narrowing of blood flow.² LDL-C level is the marker of atherosclerosis.³ Elevated LDL-C level is one of the risk factors for coronary heart disease.⁴ According to the NCEP guideline, LDL-C levels < 100 mg/dL are optimal, while the range of 160-189 mg/dL is considered high. A decrease in LDL cholesterol concentration can reduce the risk of coronary heart disease.^{5,6} Therefore, in knowing the risk stratification, evaluation, and treatment, accuracy in measuring LDL cholesterol levels is needed.⁷ The gold standard measurement of LDL cholesterol levels is beta/β quantification.⁸ Still, this examination as a routine examination is not recommended because of higher cost, special equipment requirements, and time-consuming.⁹

The homogenous assay method is one of the direct examinations of LDL-C levels without requiring separation between free and bound labels and can provide accurate results but needs expensive reagents.¹⁰ This method can

used even if the specimen sample is not fasting or the triglyceride > 400 mg/dL.¹¹ Measurement of LDL-C with the Friedewald formula is still often used because it costs less than the direct method.¹² The Friedewald method with the following equation: $LDL-C = TC - HDL-C - (TG/5)$.¹³ Friedewald formula needs other parameters in the calculation, such as total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) levels. Patients with triglycerides of more than 400 mg/dl and or not fasting before the examination will give inaccurate results in this calculation.^{14,15} In recent years, formulas have been developed for measuring LDL-C to provide better results as the Chen, Anandaraja, Vujovic, de Cordova, Puavilai, and Dansethakul formulas.¹⁶

The Chen formula was introduced in 2010 with the following equation: $LDL-C = Non-HDL-C \times 90\% - TG \times 10\%$.¹¹ A study by Rim et al. showed the smallest difference in measurement in the Chen formula compared to the Anandaraja, Friedewald, and de Cordova formulas. Based on Bland & Altman Plot analysis, The Chen formula calculation best matches the direct LDL-C examination.¹⁷

The increasing number of formulas encourages researchers to conduct research in comparing the

measurement of LDL cholesterol levels indirectly using the Friedewald formula and the Chen formula to the direct measurement using the homogenous assay methods in patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital to see if there is a significant difference between the direct measurement and calculation using the Friedewald and Chen formulas.

MATERIALS AND METHODS

This study is an analytical observational with a cross-sectional study design to compare LDL cholesterol levels directly and indirectly in patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital. This study was performed at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar in July 2023. The target population was patients who had a lipid profile examination in Bali. The affordable population was patients with a lipid profile examination at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar in April-June 2023.

Sampling using a non-probability method with consecutive technique with inclusion criteria were females and males aged > 18 years who performed a complete lipid profile examination (TC, TG, HDL, LDL-direct) and TG > 400 mg/dL is exclusion criteria. The data used were secondary data obtained from medical records. This research has received ethical clearance from the Research Ethics Commission of the Faculty of Medicine, Udayana University. The ethical clearance number was 409/UN14.2.2.VII.14/LT/2023.

The sample size was determined using the comparative analytic observational research sample formula and the minimum sample size of 95 samples. The data were processed using SPSS software version 25. The data will be analyzed with an Independent t-test for normal distribution or Mann-Whitney for non-normal distribution with a level of significance of p<0,05.

RESULTS

1. Characteristics and Results of Lipid Profile Examination of Study Subjects

The type of data taken consists of characteristics of subjects and the results of lipid profile examinations. The characteristics of the subjects are presented in **Table 1**.

Table 1. Characteristics of the Subjects

	n (%)	Range	Mean ± SD
Age (years)		20 – 91	58 ± 13,57
Sex			
➤ Male	54 (57%)		
➤ Female	41 (43%)		

*The data are normal distribution. SD: Standard Deviation.

The mean of the subjects was 58 years old and the majority of the sample was male (n = 54; 57%). This study used lipid profile examination data consisting of TC, LDL-

Direct, HDL, and Triglycerides. In addition, the results of indirect LDL levels were obtained through calculations using two formulas, Friedewald and Chen.

Table 2. The lipid profile examination of the study subjects

Measurements (mg/dL)	Mean ± SD
Total Cholesterol	163,28 ± 59,41
HDL	35,59 ± 13,39
Triglycerides	129,65 ± 65,203
LDL	
- Direct	110,57 ± 49,99
- Indirect Friedewald formula	101,80 ± 44,831
Chen formula	102,05 ± 42,1

*The data are normal distribution. SD: Standard Deviation. LDL: Low Density Lipoprotein, HDL: High Density Lipoprotein.

The mean LDL-direct level was higher than the LDL cholesterol of Friedewald Formula and Chen Formula. The mean LDL-direct level was higher than the LDL-C indirect Friedewald Formula and Chen Formula. The level of the LDL-direct, LDL cholesterol Friedewald, and Chen Formulas were tested with Kolmogorov Smirnov, and the results p>0.05. That indicates the data have a normal distribution.

2. Mean Difference Test

a. Comparison of LDL cholesterol Direct and Indirect (Friedewald) methods

Table 3. Independent T-Test Results for Direct and Indirect LDL Cholesterol (Friedewald)

	t	Mean Difference	Sig. (2-tailed)
Direct-Friedewald	1.273	8.768	0,205

*Eligible for independent t-test. Significant if p<0.05.

Based on **Table 3**, the obtained p-value = 0,205 (p>0.05). Thus, it means that there is no significant difference in LDL cholesterol levels directly and indirect methods (Friedewald formula).

b. Comparison of LDL cholesterol Direct and Indirect (Chen) methods

Table 4. Independent T-Test Results for Direct and Indirect LDL Cholesterol (Chen)

	t	Mean Difference	Sig. (2-tailed)
Direct-Friedewald	1.270	8.516	0,206

*Eligible for independent t-test. Significant if p<0.05.

Based on **Table 4**, the obtained p-value = 0,206 ($p > 0.05$). Thus, it means no significant difference in LDL cholesterol levels, direct and indirect (Chen formula).

DISCUSSION

The results test of the Independent T-Test LDL-direct and Friedewald formula got a p-value of 0,205; it means no significant difference between the direct and indirect method, Friedewald formula. These results are the same as a previous study by Syahida Djasang, which showed that the LDL-direct and indirect Friedewald methods at $\alpha = 0.05$ (t hit $0.1915 < t \text{ tab } 1.734$) did not find any significant differences.¹⁸ The study conducted by Cahyawati Rahayu and Afisyah Agriyanti also had the same, which compared the results of the LDL homogeneous method with the results of LDL Friedewald obtained of 0.625 ($p > 0.05$).¹⁹ A similar study conducted by Donaliazarti and May Valzon also found no difference between LDL-Friedewald and LDL-direct, with $p = 0.402$ in the independent t-test, this is because the sample levels used in the study had normal TG levels or $TG < 400 \text{ mg/dL}$ and the samples used were fasting patient samples before the examination.²⁰

The results test of the independent t-test LDL-direct and Chen formula got a p-value of 0.206; it means no significant difference between the direct and indirect methods of Chen formula. The study conducted by Martins et al. in South Africa showed that the LDL levels of Chen and Friedewald showed a smaller difference than the Cordova formula. In the study of Rim et al., the least difference was found in the Chen formula compared to the Friedewald, de Cordova, and Anandaraja formulas.¹⁷ Based on the research of Dona Liazarti and May Valzon, the results showed that LDL Chen had the least mean difference with LDL Direct at TG levels $< 400 \text{ mg/dL}$.¹¹

The mean of LDL-direct is sometimes higher or lower than the indirect LDL-C levels, which causes the indirect method to be influenced by other parameters, such as TC, TG, and HDL. Therefore, a miscalculation of just one of the parameters will also give an incorrect result.²¹ The Friedewald and Chen formulas both gave good results for $TG < 400 \text{ mg/dL}$. Both formulas can be used as needed. However, the direct method is recommended for use because the results are more accurate even if $TG > 400 \text{ mg/dL}$.

CONCLUSIONS AND SUGGESTIONS

From the analysis results, There is no significant difference between LDL cholesterol levels of the homogeneous assay method with Friedewald formula in patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar and there is no significant difference between LDL cholesterol levels of the homogeneous assay method with the Chen formula in patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar. Especially at TG levels $< 400 \text{ mg/dL}$.

Future researchers are advised to continue research for comparing using other formulas.

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