Calculated Low Density Lipoprotein-Cholesterol: Friedewald's Formula versus Other Modified Formulas

Calculated LDL - Cholesterol

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***Abstract*- The accurate and precise estimation of LDL-cholesterol is of utmost importance in the patients of coronary heart disease. Friedewald's formula is the most commonly used method for the measurement of LDL-cholesterol in routine clinical laboratories. This formula has certain limitations and to overcome these limitations, several modifications in this classical formula have been suggested and validated against the directly measured LDL-cholesterol values. In this article the utility of these modified formulas has been discussed.**

Keywords- Friedewald's Formula; LDL– Cholesterol; Modified Formulas

I. INTRODUCTION

LDL-cholesterol (LDLc) is considered as a major risk factor in the development of coronary heart disease [1, 2] and as the primary basis for diagnosis, treatment and risk classification of patients with hyperlipidemia [3, 4]. Therefore, the accurate and precise estimation of LDLc is of utmost importance in the patients of coronary heart disease.

The reference method for serum LDLc is β-quantitation procedure (BQ) [5] which involves ultracentrifugation technique. This procedure is time consuming, expensive and requires large volume of serum. Moreover, the technique is not suitable for routine purpose and is not available in routine laboratories. The two commonly used methods used in clinical laboratories for quantification of LDLc are (i) by calculation using Friedewald's formula which incorporates the value of total cholesterol, triglyceride and HDL-cholesterol, and (ii) by direct homogeneous assays for LDLc measurement. In this article the utility of calculated LDLc using the landmark Friedewald's formula and other modified formulas is discussed.

II. FRIEDEWALD'S FORMULA

Friedewald et al. [6] in 1972 first described a formula for LDLc calculation using serum total cholesterol (TC), HDL-Cholesterol (HDLc) and triglycerides (TG) values. This formula became a landmark for LDLc estimation as an alternative to ultra centrifugation technique. This formula is:

LDLc = TC – HDLc - TG/5

(mg/dl)

In this formula TG/5 gives a measure of VLDL-cholesterol (VLDLc) because VLDL carries most of the circulating TG. Hence VLDLc can be estimated reasonably well from measured serum TG (TG/5 for mg/dl and TG/2.2 for mmol/L). This is the method of choice for routine quantification of LDLc by most clinical laboratories due to its simplicity, reliability and cost effectiveness. However, this formula has some limitations such as: (i) presence of chylomicrons and TG concentration >400 mg/dl results in under-estimation of LDLc. A greater difference in the Friedewald estimated LDLc versus directly measured LDLc occurred at lower LDLc and higher TG levels [7] and this equation gives overestimation of LDLc in sera having low TG and high TC levels [8, 9]. (ii) in Type III HLP or dysbetalipoproteinemia. this formula gave over estimation of LDLc as compared to BQ [10, 11], (iii) the calculation is not recommended for type II diabetics, nephrotic syndrome and chronic alcoholic patients due to increased TG levels and lipoprotein alterations [12-14], (iv) each component's (TC, HDLc and TG) analytical error is added, hence it is difficult to achieve the recommended [15] total analytical error (not exceeding $\pm$12% with $\leq$4% imprecision and $\leq$4% inaccuracy or bias), (v) this formula can be applied in fasting serum specimen only.

To overcome these limitations, several modifications in this formula have been suggested in Table 1.

TABLE 1 SUMMARY OF FRIEDEWALD'S AND OTHER MODIFIED FORMULAS FOR CALCULATION OF LDLC

DOI: 10.5963/LSMR0402002

Formula	Reference	Advantages	Disadvantages/Limitations
LDLc=TC-HDLc-TG/5	Friedewalde et al. [6]	Extensive experience, used in many clinical studies, well established clinical significance, convenient and inexpensive	Not valid in samples having TG >400 mg/dl, over estimation in sera with low TG and high TC, not recommended in diabetics, alcoholics and nephrotic syndrome, not applicable in non-fasting specimens.
LDLc=3/4 (TC-HDLc)	Cordova and Cordova [16]	Can be used in non-fasting specimen, validated in large number (10664) of Brazilian individuals with wide range of TC, HDLc and TG levels	Did not performe better than Friedewald's formula in healthy south African population, to be validated in other populations also.
LDLc=nonHDLcX90%-TGX10%	Chen et al. [18]	Validated in 2180 Chinese subjects, correlated well with directly measured LDLc even when TG> 400mg/dl	To be validated in other populations.
LDLc=TC-TG/6.85-HDLc	Vujovic et al. [19]	Validated in 1043 Serbian patients, better than Friedewald's and Anandaraja's formulas.	To be validated in other populations, not validated in specimens with TG>400mg/dl.
LDLc=TC-TG/5-HDLc+(15.3XTG:TC-12.4)	Saiedulla et al. [21]	Validated in Bangladesi population with TG up to 1000mg/dl, better correlated with directly measured LDLc in high TG specimens	To be validated in other populations and to be used with caution in high risk individuals.
LDLc=TC/1.19+TG/1.9-HDLc/1.1	Ahmadi et al. [9]	Validated in Iranian population, worked well with low TG specimens	Validated in too less subjects (115) and only in sample with TG up to 300 mg/dl only.
LDLc=0.9TC-0.9TG/5-28	Anandaraja et al. [23]	HDLc value not needed (economical), validated in 1008 Indian subjects, also validated in Brazilian and Greek population, low total error due to omission of HDLc.	Not worked better than Friedewald's equation in another Indian study [24]
LDLc=TC-HDLc-TG/6	Puavikai et al. [27]	Validated in 1079 fasting samples, better than Friedewald's formula when TG was > 200 mg/dl (200-499)	To be validated in other populations. Authors suggested to do direct LDLc in patients with hypertriglyceridemia in the treatment of LDLc in high risk cardiovascular disease.
LDLc=0.41TC-0.32TG+1.70ApoB-0.27	Planella et al. [29]	HDLc not required, LDLc estimate was more close to the value estimated by ultracentrifugation method as compared to Friedewald's formula, can be used in specimen with high TG value.	To be validated in other populations, costly due to incorporation of Apo B.
LDLc=0.358TC+0.776Apo B-0.149TG	Wagner et al. [32]	Exhibited a lower bias against LDLc by BQ as compared to Friedewald's formula.	Validated in only 64 diabetic patients, to be Validated in other populations, costly due to Apo B.
LDLc=0.94TC-0.94HDLc-0.19TG	Hattori et al. [33]	Better correlated with Ultracentrifugation data from 2179 Japanese subject.	To be validated in other populations.

A. Cordova and Cordova [16]

These authors have suggested most recently a new formula based on a large Brazilian database containing directly measured lipid values from 10664 fasted individuals comprising of healthy, hyperlipidemic, diabetics and other metabolic conditions with every possible range and combination of TG, TC, HDLc and LDLc.

LDLc = 3/4 (TC - HDLc)

This formula out performed several other LDLc formulas including the classical Friedewald's formula over a wide range of TC, HDLc and TG values in Brazilian population. This formula could be suitable for non-fasting specimens also as it incorporates only TC and HDLc and these two parameters are not much affected by non-fasting conditions. However, the authors have suggested validating this formula in other populations. Onyenekwu et al. [17] found that Friedewald formula showed better agreement with direct LDLc than the Cordova formula in healthy South African population.

B. Chen et al. [18]

LDLc = non HDLc x 90% - TG x 10%

DOI: 10.5963/LSMR0402002

(mg/dl)

This formula was validated in 2180 cases from Chinese population. Chen et al. found that LDLc calculated by both Friedewald's and this modified formula correlated well with directly measured LDLc when TG was < 400 mg/dl but when TG was > 400 mg/dl the modified formula correlated better with directly measured LDLc. This modified formula had a stable LDLc/non-HDLc ratio and the interference caused by hypertriglyceridemia might be significantly diminished.

C. Vujovic et al. [19]

LDLc = TC – TG/6.85 – HDLc

(mg/dl)

Vujovic et al. validated this new formula for LDLc calculation in 1043 patients form Serbian population with TG < 400 mg/dl. LDLc values by this formula were compared with directly measured LDLc, Anandaraja's formula and Friedewald's formula. The values of LDLc by direct measurement were found to be highest followed by the modified formula LDLc, Anandaraja's LDLc and Friedewald's LDLc. The modified formula of Vujovic et al. was better correlated with direct LDLc as compared to Anandaraja's and Friedewald's LDLc in these Serbian patients. However, most recently Anwar et al. [20] found that both Friedewald's and Vujovic modified formula did not have a uniform performance as compared to direct homogeneous assay for LDLc estimation at different TG levels in 300 healthy Pakistani subjects.

D. Saiedullah et al. [21]

These authors suggested a simple modification of Friedewald's formula to calculate LDLc up to serum TG concentration of 1000 mg/dl. The modification was based on the absolute differences between direct LDL-cholesterol and LDL-cholesterol calculated by Friedewald formula and the linear regression equation of the absolute difference with serum triglyceride to total cholesterol ratio. The modified equation was:

LDLc = TC - TG/5 - HDLc + (15.3 X TG: TC – 12.4)

(mg/dl)

Parvin et al. [22] further validated this formula in 309 sera (fasting) from Bangladeshi population having TG up to 1000 mg/dl and TG/TC < 4 and found that LDLc calculated by this modified formula and by the original Friedewald's formula correlated strongly and significantly with measured LDLc within and above the valid TG range of Friedewald's formula. However, LDLc by Friedewald's formula was significantly lower than the measured value of LDLc in both TG <400 mg/dl and >400 mg/dl sera but no difference was observed between LDLc by modified formula and the measured LDLc. Hence, this formula can be used to calculate LDLc in Bangladesh population even in sera having TG>400 mg/dl. However, the authors have suggested that this formula should be used with caution in case of high risk individuals.

E. Ahmadi et al. [9]

Ahmadi et al. proposed a new formula for LDLc calculation:

LDLc = TC/1.19 + TG/1.9 – HDLc/1.1

(mg/dl)

LDLc = TC/1.19 + TG/0.81 – HDLc/1.1 – 0.98

(mmol/L)

This formula was validated in two groups of 115 Iranian subjects each, one with TG<100 mg/dl (Group A) and the other with TG 150 -300 mg/dl (Group B) and compared the LDLc calculated by the new formula with directly measured LDLc and Friedewald's LDLc. Statistical analysis showed that when TG was <100 mg/dl the Friedewald's calculated LDLc was significantly overestimated whereas when TG was 150-350 mg/dl no significant difference between calculated and measured LDLc was observed. However, the modified formula compensated this overestimation caused by low triglycerides. Therefore, to correct the positive effect (overestimation) of low TG this modified formula may be used. However, Onyenekwu et al. [17] found that Friedewald formula performed better than this formula at very low TG levels in healthy South African population.

F. Anandaraja et al. [23]

LDLc = 0.9TC -0.9 TG/5 -28

DOI: 10.5963/LSMR0402002

(mg/dl)

In this formula only TC and TG were used. However, they have not included sera having TG > 350mg/dl. The new formula appeared to be more accurate than Friedewald's formula in Indian population. However, Shalini et al. [24] reported that Friedewald's formula was better in agreement with measured LDLc (Direct homogeneous method) than Anandaraja's formula in Indian subjects. Interestingly, this new formula was found to be working well in Brazilian [25] and Greek population [26]. But most recently Cordovea and Cordova [16] found that their formula (LDLc = ¾ (TC – HDLc) out performed Anandaraja's formula in Brazilian population.

G. Puavikai et al. [27]

LDLc = TC – HDLc – TG/6

(mg/dl)

This modified formula was validated in 1079 samples (fasting) and the values of LDLc were compared with direct LDLc and Friedewald's LDLc. The comparative values by these three methods were:

Direct LDLc > Modified formula LDLc > Friedewald's formula LDLc

The modified formula gave better correlation with direct LDLc when TG was > 200 mg/dl (200-499). Puavikai et al. [28] further validated this formula in sera having TG < 300mg/dl but regard less of time from last food intake. The modified formula had 83.8% accuracy when compound to directly measured LDLc ± 10mg and this equation was more accurate than the Friedewald's equation with OR of 2.63. The authors offer that to save the cost this new modified formula should be used to calculate LDLc. Then direct LDLc measurement could be reserved for patients with hypertriglyceridemia in the treatment of LDLc in high risk cardiovascular disease.

H. Planella et al. [29]

Proposed a formula which incorporated ApoB but excluded HDLc. Using this formula the estimated LDLc was more close to that estimated by ultracentrifugation method as compared to Friedewald's formula in patients with dyslipidemia. Others also found that this formula provides better estimate of LDLc in hypertriglyceridemic samples [30, 31]. However, inclusion of ApoB means higher cost of the test.

LDLc = 0.41TC - 0.32TG + 1.70ApoB-0.27

(mmol/L)

I. Wagner et al. [32]

Wagner et al. also suggested a formula incorporating ApoB and found that it exhibited a lower bias against LDLc by BQ as compared to bias by Friedewald's formula against BQ in Type II diabetic patients.

LDLc = 0.358TC + 0.776ApoB - 0.149TG

(mg/dl)

J. Hattori et al. [33]

LDLc = 0.94TC - 0.94HDLc - 0.19TG

(mg/dl)

This formula was validated using ultracentrifugation data from 2179 subjects and was found to give better estimate of the corrected LDLc.

Another less studied formula incorporates ApoA:

K. Wallduis et al. [34]

LDLc = 18.53 + 0.99TC – 0.1TG – 0.61ApoA - 1

(mg/dl)

Thus we can see that now so many modifications of original Friedewald's formula are available and these modified formulas do provide some improvements in overcoming the limitations of Friedewald's equation. However, most of these modified formulas

DOI: 10.5963/LSMR0402002

were validated against direct homogeneous assays for LDLc estimation and not compared with accurate reference method. Most of the modified formulas correlated well with directly measured LDLc when serum TG was < 400 mg/dl. These direct methods do have some advantages over calculated LDLc such as:

(i) total imprecision is better than calculated LDLc;
(ii) non-fasting samples can be assayed for LDLc;
(iii) the interference by TG is considerably decreased.

Despite these advantages the direct methods are not the perfect ones because (i) the composition of lipoproteins influences the ability of direct methods to specifically measure the cholesterol contents of one lipoprotein class in presence of other types of lipoproteins [35], (ii) only 5 of 8 direct method for LDLc measurement met NCEP total error goals for non diseased individuals but all the 8 method failed in diseased individuals [35], (iii) In most cases directly measured LDLc values are overestimated which would result in more drug usage, thus exposing patient to more potential adverse effects and at a much greater cost with little evidence of benefit [36]. On the other hand some direct method give underestimation of LDLc [37, 38], thereby misclassify many individual into a lower NCEP category and thereby these individuals may miss drug intervention for prevention of cardiovascular event, (iv) the LDLc estimation by direct method is costly (almost equal to the combined cost of TC, HDLc and TG).

III. CONCLUSION

1. Friedewald's formula still has an upper hand over the modified equations especially when TG is < 200mg/dl because Friedewald's formula has the advantage of extensive experience, used in many clinical studies, well established clinical significance, convenient and inexpensive when TC, HDLc and TG are measured [39]. Some modified formulas have shown better performance in sera with high TG concentration but these are to be validated in different populations and compared with reference method.

2. Since LDLc is considered as the primary basis for diagnosis, treatment and risk classification of patients with hyperlipidemia one can argue that estimation of only LDLc by direct method is sufficient but since lipid lowering drugs not only reduce LDLc but also affect TG and HDLc levels, many physicians would like to know all the changes in these lipid parameters [39]. Moreover, NCEP (ATP III) recommendation included TC, TG and HDLc as well as LDLc in screening all adults does not favor replacing calculation with a direct LDLc measurement.

3. The different modified formulas have been validated in different population and each formula was found suitable for a particular population, hence it is imperative to validate all these formulas in various populations, both normal healthy and diseased, and then only the best formula can be chosen. Till then it would be better to calculate LDL by Friedewald's formula (to reduce the cost) up to TG concentration of < 200 mg/dl or preferably < 150 mg/dl and use direct homogeneous method for sera having TG > 150 mg/dl.

REFERENCES

[1] W. P. Castelli, R. J. Garrison, P. W. Wilson, R. D. Abbott, S. Kalousdian and W. B. Kamel, "Incidence of coronary heart disease and lipoprotein levels: the Framingham study," JAMA, vol. 256, pp. 2835-8, 1986.

[2] A. Y. Cheng and L. A. Letter, "Implementation of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines," Curr Opin Cardiol, vol. 21, pp. 400-4, 2006.

[3] Executive summary of the Third Report of the National Cholesterol Education Program (NCEP), Exper Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (2001), JAMA, vol. 285, pp. 2486-7, 2001.

[4] J. G. Keevil, W. W. Cullen, R. Gangnon, P. E. Mc Bride and J. H. Stein, "Implications of cardiac risk and low density lipoprotein cholesterol distributions in the United States for the diagnosis and treatment of dyslipidemia: data from National Health and Nutrition Examining Survey 1999 to 2002," Circulation, vol. 115, pp. 1363-70, 2007.

[5] T. Cole, C. Ferguson, D. Gibson and W. Nowatzke, "Optimization of quantification methods for high throughput applications," Clin Chem., vol. 047, pp. 712-21, 2001.

[6] W. T. Friedewald, R. I. Levy and D. S. Fredrickson, "Estimation of the concentration of low–density lipoprotein cholesterol in plasma, wthout use of preparative ultracentrifuge," Clin Chem., vol. 18, pp. 499-02, 1972.

[7] S. S. Martin, M. J. Blaha, M. B. Elshazly, E. A. Briton, P. P. Toth, et al., "Friedewald-estimated versus directly measured low density lipoprotein cholesterol and treatment implications," J Am Coll Cardiol., vol. 62, pp. 732-9, 2013.

[8] T. Y. Wang, M. Haddad and T. S. Wang, "Low triglycerides levels affect calculation of low density lipoprotein cholesterol value," Arch Pathol Lab Med., vol. 125, pp. 404-5, 2001.

[9] S. A. Ahmadi, M. A. Boroumand, K. G. Moghaddam, P. Tajik and S. A. Dibaj, "The impact of low serum triglycerides on low density lipoprotein cholesterol estimation," Arch Iranian Med., vol. 11, pp. 318-21, 2008.

DOI: 10.5963/LSMR0402002

[10] J. R. Mc Namara, J. S. Cohn, P. W. Wilson and E. J. Schaefer, "Calculated values for low-density lipoprotein cholesterol in the assessment of lipid abnormalities and coronary disease risk," Clin Chem., vol. 236, pp. 36-42, 1990.

[11] I. Jialal, S. Hirany, S. Devaraj and T. Sherwood, "Comparison of an immunoprecipitation method for direct measurement of LDL-cholesterol with –quantitation (ultracentrifugation)," Am J Clin Pathol., vol. 104, pp. 76-81, 1995.

[12] J. Rubies-Prat, J. L. Reverter, M. Senti, Pedro-Bolet, I. Salinas, A. Lucas, et al., "Calculated low density lipoprotein cholesterol should not be used for management of lipoprotein abnormalities in patients with diabetes mellitus," Diabetes care, vol. 16, pp. 1081-6, 1993.

[13] M. Nauck, A. Kramer-Guth, W. Bartens, W. Marz, H. Wieland, C. Wanner, "Is the determination of LDL cholesterol according to Friedewald accurate in CAPD and HD patients?" Clin Nephro., vol. 46, pp. 319-25, 1996.

[14] C. Matas, M. Cabre, A. La Ville, E. Prats, J. Joven and P. R. Turner, "Limitations of the Friedewald formula for estimating low-density lipoprotein cholesterol in alcoholics with liver disease," Clin Chem., vol. 40, pp. 404-6, 1994.

[15] National Cholesterol Education Program, (1995) Recommendations on lipoprotein measurement, Working Group on Lipoprotein Measurement, NIH Publication No. 95-3044, Bethesda, MD: National Institute of Health, National Heart, Lung and Blood Institute.

[16] C. M. Cordova and M. M. Cordova, "A new accurate simple formula for LDL-cholesterol estimation based on directly measured lipids from alarg cohort," Ann Clin Biochem., vol. 50, pp. 13-9, 2013.

[17] C. P. Onyenekwo, M. Hoffmann, F. Smit, T. E. Matsha and R. T. Erasmus, "Comparison of LDL-cholesterol estimate using the Friedewald formula with a directly measured LDL-cholesterol in a healthy South African population," Ann Clin Biochem., Jan 21 2014. [Epub ahead of print].

[18] Y. Chen, X. Zhang and B. Pan, "A modified formula for calculating low density lipoprotein cholesterol values," Lipids Health Dis., vol. 9, pp. 52-7, 2010.

[19] A. Vujovic, J. Kotur-Stevuljevic, S. Spasic, N. Bujisic, J. Martinoric, N. Vujovic et al., "Evaluation of different formulas for LDLc calculation," Lipids Health Dis., vol. 9, pp. 27-35, 2010.

[20] M. Anwar, D. A. Khan and F. A. Khan, "Comparison of Friedewald formula and modified Friedewald formula with direct homogeneous assay for low density lipoprotein cholesterol estimation," J Coll Physicians Surg Pak., vol. 24, pp. 8-12, 2014.

[21] M. Saeidullah, M. Rahman and M. A. H. Khan, "A simple modification of Friedewald's formula to calculate low-density lipoprotein cholesterol up to serum triglycerides concentration of 1000 mg/dl," Bang J Med Biochem., vol. 2, pp. 62-5, 2009.

[22] M. Parvin, M. Saiedullah, M. Khan, M. R. Rehman and M. S. Islam, "Validation of the modified Friedewald's formula to calculate low-density lipoprotein cholesterol in bangladeshi population," J Bang Coll Phys Surg., vol. 30, pp. 141-4, 2012.

[23] S. Ananandaraja, R. Narang, R. Godeswar, R. Laksmy and K. K. Talwar, "Low density lipoprotein cholesterol estimation by a new formula in Indian population," Int J Cardiol., vol. 102, pp. 117-20, 2005.

[24] S. Gupta, M. Verma and K. Singh, "Does LDL-C estimation using Ananadaraja's formula give a better agreement with direct LDL-C estimation than the Friedewald's formula?" Ind J Clin Biochem., vol. 27, pp. 127-33, 2012.

[25] R. Gasko, "Low density lipoprotein cholesterol estimation by the Anandaraja's formula-confirmation," Lipids Health Dis., vol. 5, p. 18, 2006.

[26] I. F. Gazi and M. Elisaf, "LDL-cholesterol calculation formulas in patients with or without the metabolic syndrome," Int J Cardiol., vol. 119, pp. 414-15, 2007.

[27] W. Puavillai and D. Laorugpongse, "Is calculated LDLc by using the new modified Friedewald equation better than the standard Frieldewald equation," J Med Assoc Thai., vol. 87, pp. 589-93, 2004.

[28] W. Puavillai, D. Laorugpongse, C. Deerochanawong, R. N. Muthapongthavoru and R. N. Srilert, "The accuracy in using modified Friedewald equation to calculate LDL from nonfasting triglycerides: A pilot study," J Med Assoc Thai., vol. 92, pp. 182-7, 2009.

[29] T. Planella, M. Cortes, C. Martinez-Bur, F. Gonzalez-Sastre and J. Ordonez-Llanos, "Calculation of LDL-cholesterol by using apolipoprotein B for classification of nonchylomicronemic dyslipemia," Clin Chem., vol. 43, pp. 808-15, 1997.

[30] E. Bairaktari, K. Hatzidimou, C. Tzallas, M. Vini, A. Katsaraki, A. Tselepis, M. Elisaf and O. Tsolas, "Estimation of LDL cholesterol based on Friedewald formula and apoB levels," Clin Biochem., vol. 33, pp. 549-55, 2000.

[31] E. Bairaktari, M. Elisaf, C. Tzallas, S. A. Karabina, A. D. Tselepis, K. C. Siamopoulas and O. Tsolas, "Evaluation of five methods for determining low-density lipoprotein cholesterol (LDLc) in hemodialysis patients," Clin Biochem., vol. 34, pp. 593-602, 2001.

[32] A. M. Wagner, E. Zapico, R. Boner, A. Parez and J. Ordonez-Llanos, "The effect of VLDL particles on the accuracy of a direct LDL-cholesterol method in type 2 diabetic patients," Clin Biochem., vol. 36, pp. 177-83, 2003.

[33] Y. Hattori, M. Suzuki, M. Tsushima, M. Yoshida, Y. Tokunaga et al., "Development of approximate formula for LDL-cholesterol, LDL-apo B and LDL-chol/LDL -apo B as indices of hyperapobetalipoproteinemia and small dense LDL," Atherosclerosis, vol. 138, pp. 289-99, 1998.

[34] G. Walldius, I. Jungner, I. Holme, A. A. Aastveit, W. Kolar and E. Steiner, "High apolipoprotein B, low apolipoprotein A-I, and improvement in the prediction of fatal myocardial infarction (AMORIS study): a prospective study," Lancet, vol. 358, pp. 2026-33, 2001.

[35] W. G. Miller, G. L. Myers, I. Sakurabayashi, L. M. Bachmann, S. P. Caudil, A. Dziekonski et al., "Seven direct methods for measuring HDL and LDL cholesterol compared with ultracentrifugation reference measurement procedures," Clin Chem., vol. 56, pp. 977-86, 2010.

[36] M. Agrawal, H. J. Spencer and F. H. Faas, "Method of LDL cholesterol measurement influences classification of LDL cholesterol treatment goals:clinical research study," J Clin Investig Med., vol. 58, pp. 945-9, 2010.

DOI: 10.5963/LSMR0402002

[37] S. Sahu, R. Chawla and B. Uppal, "Comparison of two methods of estimation of low density lipoprotein cholesterol, the direct versus Friedewald estimation," Ind J Clin Biochem., vol. 20, pp. 54-61, 2005.

[38] S. Mora, N. Rifai, J. E. Buring and P. M. Ridker, "Comparision of LDL cholesterol concentration by Friedewald calculation and direct measurement in relation to cardiovascular events in 27,331 women," Clin Chem., vol. 55, pp. 888-94, 2009.

[39] M. Nauck, G. R. Warnick and N. Rifai, "Methods for measurement of LDL-cholesterol: a critical assessment of direct measurement by homogeneous assays versus calculation," Clin Chem., vol. 48, pp. 236-354, 2002.

DOI: 10.5963/LSMR0402002