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Validation of the Modified Friedewald's Formula to Calculate Low-density Lipoprotein Cholesterol in Bangladeshi Population

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Summary:

Objective: A modification of Friedewald's formula was proposed to calculate LDL cholesterol in Bangladeshi population up to serum triglyceride concentration of 1000 mg/dL. The aim of this study was to validate the modification of Friedewald's formula in Bangladeshi population.

Methods: Serum total cholesterol, triglyceride, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol concentrations were measured in specimens obtained form 314 adult Bangladeshi subjects selected conveniently. LDL cholesterol concentrations were also calculated by modified Friedewald's formula and original Friedewald's formula. Results were expressed as mean ± SD and calculated LDL cholesterol was compared with measured LDL cholesterol by two-tailed paired t test and Pearson's correlation coefficient (r).

Results: The mean ± SD of measured LDL cholesterol was 138.3 ± 54.58 mg/dL. LDL cholesterol calculated by modified Friedewald's formula and original Friedewald's formula were 135.9 ± 59.26 mg/dL (P>0.05) and 123.5 ± 65.75 mg/dL (P<0.001) respectively. Compared to measured LDL cholesterol, calculated LDL cholesterol were 2.47 mg/dL and 17.20 mg/dL lower for modified formula and original formula respectively. The correlation coefficient (r) with measured LDL cholesterol was 0.8601 (P<0.0001) for LDL cholesterol calculated by the modified Friedewald's formula and 0.8565 (P<0.0001) for the LDL cholesterol calculated by the original Friedewald's formula.

Conclusion: The study validates the modified Friedewald's formula to calculate LDL cholesterol in Bangladeshi population.

Key words: Friedewald's formula, LDL cholesterol, Calculated LDL cholesterol

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Introduction:

The reference method for the measurement of serum low-density lipoprotein (LDL) cholesterol is the ß-quantification.[1] It is not readily available and also impractical in the routine laboratory. Direct methods have been developed and are recommended to measure LDL cholesterol alternatively. The direct methods are costly and require expensive automation. So the most convenient method of LDL cholesterol estimation is the Friedewald's formula that allows the calculation of LDL cholesterol from serum total cholesterol (TC), serum triglycerides (TG) and high-density lipoprotein (HDL) cholesterol [LDL cholesterol = TC – TG/5 – HDL cholesterol].[2] This formula is applicable up to serum TG concentration of 400 mg/dL and it is the most commonly used procedure in clinical practice worldwide as well as in Bangladesh. But this formula underestimates LDL cholesterol in different populations studied as well as in Bangladesh.[3,4,5,6] A recent study in our population proposed a modification of Friedewald's formula to calculate LDL cholesterol up to serum TG concentration of 1000 mg/dL.[7] The modification of Friedewald's formula was based on the absolute differences between direct LDL cholesterol and LDL cholesterol calculated by Friedewald's formula (ÄLDL

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cholesterol) and the linear regression equation of the absolute difference with serum triglyceride to total cholesterol ratio. The linear regression equation, ÄLDL cholesterol = (15.3×TG:TC – 12.4) mg/dL was added to the original Friedewald's formula to get the modified equation, LDL cholesterol = TC – TG/5 – HDL cholesterol + (15.3 ×TG:TC – 12.4) (when all concentrations are expressed in mg/dL). The aim of this study was to validate the modified formula for the calculation of LDL cholesterol.

Methods and materials:

The study was conducted in Armed Forces Institute of Pathology (AFIP), Bangladesh during the period of January to March, 2011. Serum total cholesterol (TC), serum triglyceride (TG), serum high-density lipoprotein (HDL) cholesterol and serum low-density lipoprotein (LDL) cholesterol were measured on 314 sera obtained from adult subjects of both sexes after 12 hours fast. Serum TG and TC were measured by enzymatic end-point method. HDL cholesterol and LDL cholesterol were measured by direct automated method using ABX Pentra 400 clinical chemistry analyzer (France). All kits, calibrators and quality controls were purchased from Horiba, France through local distributor.

Subjects with serum TG concentration > 1000 mg/dL and TG/TC > 4 were excluded. Subjects with serum TG d" 400 mg/dL were considered as group A and subjects with serum TG > 400 mg/dL were considered as group B.

Results were expressed as mean±SD and compared by two-tailed paired t test and Pearson's correlation coefficients of calculated LDL cholesterol with measured LDL cholesterol (using GraphPad Prism 5.04 for Windows and STATISTICA 8.0 for Windows).

Results:

Mean ± SD of age of the total study subjects was 48.28 ± 11.08 years, in which 65% subjects were males and 35% subjects were females. The mean ± SD of lipid parameters in group A, group B and in the total study subjects are presented in table I and comparison of calculated LDL cholesterol and measured LDL cholesterol is shown in table II. In the total study subjects, the mean ± SD of measured LDL cholesterol, LDL cholesterol calculated by modified Friedewald's formula and LDL cholesterol calculated by original Friedewald's formula were 138.3 ± 54.58 mg/dL, 135.9 ± 59.26 mg/dL and 123.5 ± 65.75 mg/dL respectively. The difference between measured LDL cholesterol and LDL cholesterol calculated by modified Friedewald's formula was not statistically significant (P>0.05, table II); but the difference between measured LDL cholesterol and LDL cholesterol calculated by original Friedewald's formula was statistically significant (P<0.0001, table II). Pearson's correlation coefficients of measured LDL cholesterol with LDL cholesterol calculated by modified Friedewald's formula and original Friedewald's formula were 0.8601 (P<0.0001) and 0.8565 (P<0.0001) respectively.

In group A, mean ± SD of age was 48.67 ± 11.59 years in which 67% subjects were males and 33% subjects were females. The mean±SD of measured LDL cholesterol, LDL cholesterol calculated by modified Friedewald's formula and LDL cholesterol calculated by original Friedewald's formula were 141.4 ± 54.78 mg/dL, 139.4 ± 58.11 mg/dL and 130.5 ± 63.02 mg/dL respectively. The difference between measured LDL cholesterol and LDL cholesterol calculated by modified

Table-I

Mean ± SD of lipid parameters

Parameters	Group A (n=233)	Group B (n=76)	Total subjects (n=309)
Total cholesterol (mg/dL)	222.1±65.2	237.9±71.8	226.0±67.1
Serum triglyceride (mg/dL)	289.2±51.3	518.6±103.1	345.6±119.8
Serum HDL cholesterol (mg/dL)	33.7±8.0	32.2±7.0	33.3±7.7
Measured LDL cholesterol (mg/dL)	141.4±54.8	128.8±53.2	138.3±54.6

Table II

Comparison of LDL cholesterol calculated by modified Friedewald's formula and original Friedewald's formula with measured LDL cholesterol

	Mean ± SD		
	TG: up to 1000 mg/dL (n=309)	Group A TGd"400mg/dL (n=233)	Group B TG>400 mg/dL (n=76)
Measured LDL cholesterol	138.3±54.58	141.4±54.78	128.8±53.20
LDL cholesterol by modified FF	135.9±59.26^{NS}	139.4±58.11^{NS}	125.0±61.79^{NS}
LDL cholesterol by original FF	123.5±65.75***	130.5±63.02***	102.0±69.71***
Correlation coefficient of mLDLC with measured LDL cholesterol	0.8601***	0.9044***	0.7242***
Correlation coefficient of fLDLC with measured LDL cholesterol	0.8565***	0.9014***	0.7348***
Difference between mLDLC and measured LDLC	-2.47±20.93^{NS}	-1.83±18.98^{NS}	-4.43±26.08^{NS}
Difference between fLDLC and measured LDLC	-17.20±31.71***	-11.21±23.54***	-35.58±44.29***

TG, Serum Triglyceride; FF, Friedewald's formula; mLDLC, LDL cholesterol calculated by modified Friedewald's formula; fLDLC, LDL cholesterol calculated by original Friedewald's formula; ***, P<0.0001; NS, Not statistically significant

Friedewald's formula was not statistically significant (P>0.05, table II); but LDL cholesterol calculated by original Friedewald's formula was significantly different from measured LDL cholesterol (P<0.0001, table II). Pearson's correlation coefficient (r) of measured LDL cholesterol with LDL cholesterol calculated by modified Friedewald's formula was 0.9044 (P<0.0001) and that of measured LDL cholesterol with LDL cholesterol calculated by original Friedewald's formula was 0.9014 (P<0.0001).

In group B, mean ± SD of age was 47.09 ± 12.47 years in which 62% subjects were males and 38% subjects were females. The mean ± SD of measured LDL cholesterol, LDL cholesterol calculated by modified Friedewald's formula and LDL cholesterol calculated by original Friedewald's formula were 128.8 ± 53.20 mg/dL, 125.0 ± 61.79 mg/dL and 102.0 ± 69.71 mg/dL respectively. The difference between measured LDL cholesterol and LDL cholesterol calculated by modified Friedewald's formula was not statistically significant (P>0.05, table II); but LDL cholesterol calculated by original Friedewald's formula was significantly different from measured LDL cholesterol (P<0.0001, table II). Pearson's correlation coefficient of measured LDL cholesterol with LDL cholesterol calculated by modified Friedewald's formula was 0.7242 (P<0.0001) and that of measured LDL cholesterol with LDL cholesterol calculated by original Friedewald's formula was 0.7348 (P<0.0001).

Discussion:

In this study, LDL cholesterol calculated by modified Friedewald's formula and original Friedewald's formula correlated strongly and significantly with the measured LDL cholesterol within and above the valid TG range of Friedewald's formula. LDL cholesterol calculated by original Friedewald's formula was significantly lower than measured LDL cholesterol in both groups (P<0.0001); but no significant difference was observed between measured LDL cholesterol and LDL cholesterol calculated by modified Friedewald's formula (P>0.05).

Our study findings conform to the findings of the recent study[7] done in our population, based on which modified Friedewald's formula to calculate LDL cholesterol up to serum TG concentration of 1000 mg/dL has been proposed.

Friedewald's formula was validated and modified in different populations. Study with large number of samples indicated that original Friedewald's formula can be used up to serum TG concentration of 800 mg/dL.[8] But in case of specimens with high serum TG, Friedewald's formula frequently underestimates LDL cholesterol and sometimes produces negative results. In these cases the results are not reportable. Since the correlation coefficient of LDL cholesterol calculated by original Friedewald's formula with measured LDL cholesterol is high and statistically significant, underestimation of LDL cholesterol can be subsided using the modified Friedewald's formula and can be used to calculate LDL cholesterol approximately when original Friedewald's formula is invalid. However, this calculation formula should be used with caution in case of high risk individuals.

Conclusion:

The present study is consistent with the previous study done in our population. So we also conclude that the modified Friedewald's formula can be used to calculate LDL cholesterol in Bangladeshi population.

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