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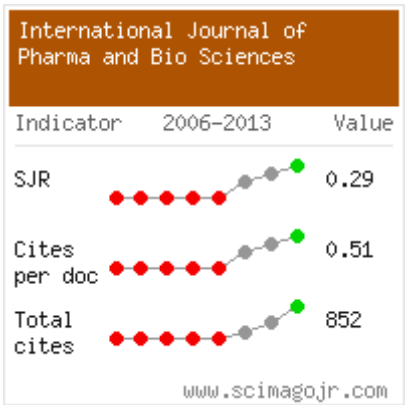

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ASSOCIATION OF NON-HDL CHOLESTEROL WITH RISK OF CARDIOVASCULAR DISEASE DEFINED BY TOTAL CHOLESTEROL/ HDL-CHOLESTEROL RATIO

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ABSTRACT

Non-HDL Cholesterol provides a single estimate of the cholesterol content in all proatherogenic lipoproteins. Total Cholesterol/ HDL-Cholesterol Ratio is a powerful predictor of cardiovascular disease (CVD). Therefore, this study was interested to find an association of non-HDL Cholesterol with risk of CVD defined by total Cholesterol/ HDL-Cholesterol Ratio. This study included 753 lipid profile data of adults collected for a period of 3 months. Lipid profile parameters were measured by enzymatic colorimetric method on a fasting venous sample. Non-HDL Cholesterol was calculated by subtracting the HDL Cholesterol from total cholesterol. Risk of CVD was defined by Total Cholesterol/ HDL-Cholesterol Ratio as ≥5. Sensitivity, specificity and cutoff of non-HDL Cholesterol for CVD was 70.9%, 71.5% and 137 mg/dl respectively. Non-HDL Cholesterol can be used as an economical and reliable parameter to assess the risk of CVD.

KEYWORDS: **Non-HDL Cholesterol, Total Cholesterol/ HDL-Cholesterol Ratio, cardiovascular disease**

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INTRODUCTION

Dyslipidemia is recognized as one of the major risk factors for cardiovascular diseases (CVD)[1]. Various lipid profile parameters and their indices are used to assess the risk of CVD. Non high density lipoprotein cholesterol (non-HDL-C) is currently gaining importance as National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP-III) has identified it as one of the parameters for assessment of CVD risk[2]. Non-HDL-C is calculated as the difference between total cholesterol (TC) and high density lipoprotein cholesterol (HDL-C) i.e. Non-HDL-C= TC- HDL-C. Non-HDL-C is a marker that integrates the atherogenic potentials carried by low density lipoprotein cholesterol (LDL-C), Lipoprotein (a), intermediate density lipoprotein cholesterol (IDL-C), very low density lipoprotein cholesterol (VLDL-C), chylomicron remnants and small dense LDL-C[3]. Since, HDL-C is least affected by food intake, non–HDL-C may be of use where patients have difficulty in providing a fasting blood sample for estimating lipid profile[4]. Total Cholesterol/ HDL-Cholesterol Ratio (TC/ HDL-C ratio) has a strong association with CVD in both males and females[5]. A ratio of ≥5 indicates a higher risk of CVD. In a prospective study, high baseline levels of TC/ HDL-C ratio was associated with significantly increased risk of future myocardial infarction[6]. Presently, calculation of non-HDL-C and interpretation of its values for risk assessment is not in practice. Considering its convenience of measurement and practical aspects, this study intended to find an association of non-HDL-C with risk of CVD defined by TC/ HDL-C ratio.

MATERIALS AND METHODS

This was an observational study conducted by the Department of Biochemistry, M. S. Ramaiah Medical College, Bangalore. The data of lipid profile parameters [TC, HDL-C, LDL-C and Triglycerides (TGL)] measured by enzymatic colorimetric method in a fasting venous sample on a fully automated Cobas® 6000 analyzer (Roche Diagnostics, Basel, Switzerland) was obtained from the M. S. Ramaiah Hospital Laboratory. Non-HDL-C was calculated as the difference between TC and HDL-C. Lipid profile data of 753 adults (≥18 yrs) was included and those of children and pregnant women were excluded in the context of primary hyperlipoproteinemia and hemodilution respectively. Institutional Ethical Committee Clearance was obtained to perform the study. Individuals with risk of CVD were identified by TC/ HDL-C ratio. Accordingly sensitivity, specificity and optimized cut-off value of non-HDL-C for CVD risk were calculated. Receiver operating characteristics curve (ROC) and area under curve (AUC) were also obtained to find its association with risk of CVD.

RESULTS

A total of 753 subjects were included in the study aged between 18-93 yrs, of which 460 (61%) were males and 293 (39%) were females. Among males, 189 (41.0% of total males) and among females, 100 (34.1% of total females) were identified as having an increased risk of CVD when defined by TC/ HDL-C ratio i.e. a ratio ≥5. The study showed sensitivity and specificity of Non-HDL-C as 70.9% and 71.5% respectively with the optimized cut-off value of 137 mg/dl. Odds ratio (OR) was found to be of 6.08. On ROC analysis (figure I), non-HDL-C had AUC of 0.78. Other results obtained are shown as Tables I-III. Table I compares the Mean ± SD of age and lipid profile parameters including non-HDL-C between male patients with and without risk of CVD. Age of the patients with risk of CVD was significantly ($p<0.05$) higher than the patients without risk. The table also shows that there is significant ($p<0.01$) difference in all the lipid profile parameters except triglycerides between patients with and without risk of CVD. Table II shows a similar comparison in females. There is no significant difference in the age between patients with and without risk of CVD. The table shows that there is significant ($p<0.01$) difference in all the lipid profile parameters between patients with and without CVD risk. In Table III, using Pearson's correlation, non-HDL-C was found to have a significant positive correlation with TC ($r = 0.95$, $p<0.01$), TGL ($r = 0.47$, $p<0.01$), LDL-C ($r = 0.88$, $p<0.01$) and TC/ HDL-C ratio ($r = 0.29$, $p<0.01$).

Table I

Comparison of parameters between MALE patients with and without risk of CVD defined by TC/ HDL-C ratio

PARAMETERS	TC/ HDL-C RATIO ≥ 5 (with CVD risk)	TC/HDL-C RATIO <5 (without CVD risk)	p VALUE*
AGE	49.7 ± 13.7	53.3 ± 16.4	<0.05
TC	186.3 ± 51.1	159 ± 40.4	<0.01
TGL	222.7 ± 151	122.2 ± 63.1	0.98
HDL-C	29.1 ± 11.1	44.3 ± 12.5	<0.01
LDL-C	116.1 ± 48	97.6 ± 34.8	<0.01
NON-HDL-C	**157.2 ± 42.8**	**114.7 ± 34.6**	**<0.01**

student's't' test, p- value <0.05 is significant, p- value <0.01 is highly significant.

Table II
Comparison of parameters between FEMALE patients with and without risk of CVD defined by TC/ HDL-C ratio

PARAMETERS	TC/HDL-C RATIO ≥ 5 (with CVD risk)	TC/HDL-C RATIO <5 (without CVD risk)	p VALUE*
AGE	52.2 ± 12.7	50.8 ± 14.8	0.44
TC	199.1 ± 47.7	173 ± 38.2	<0.01
TGL	207.9 ± 99	118.6 ± 54.3	<0.01
HDL-C	31.7 ± 10.8	49.7 ± 12.4	<0.01
LDL-C	130 ± 44.4	106.3 ± 33.4	<0.01
NON-HDL-C	**167.4 ± 40.2**	**123.2 ± 34.2**	**<0.01**

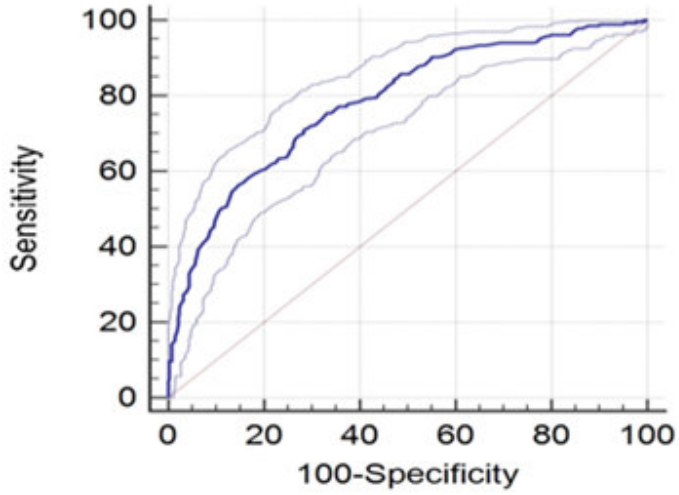
student's't' test, p- value <0.05 is significant, p- value <0.01 is highly significant.

Table III
Pearson's correlation between the various lipid profile parameters

	TC	**TGL**	**HDL-C**	**LDL-C**	**Non-HDL-C**	**TC:HDL-C**
TC	-	r = 0.35 p = <0.01	r = 0.36 p =<0.01	r = 0.91 p = <0.01	r = 0.95 p = <0.01	r = 0.07 p= 0.05
TGL	r = 0.35 p = <0.01	-	r = -0.27 p = <0.01	r = 0.13 p = 0.01	r = 0.47 p = <0.01	r = 0.36 p = <0.01
HDL-C	r = 0.36 p = <0.01	r = - 0.27 p = <0.01	-	r = 0.30 p = <0.01	r = 0.04 P = 0.27	r = -0.63 p = <0.01
LDL-C	r = 0.91 p = <0.01	r = 0.13 p = <0.01	r = 0.30 p = <0.01	-	r = 0.88 p = <0.01	r = -0.01 P = 0.07
Non-HDL-C	**r = 0.95 p = <0.01**	**r = 0.47 p = <0.01**	**r = 0.04 p = 0.27**	**r = 0.88 p = <0.01**	**-**	**r = 0.29 p = <0.01**
TC:HDL-C	r = 0.07 p = 0.05	r = 0.36 p = <0.01	r = -0.63 p = <0.01	r = -0.01 p = 0.07	r = 0.29 p = <0.01	-

r value = Pearson's correlation coefficient, p value < 0.01 is highly significant.

Figure I
ROC for non-HDL-C as variable for risk of CVD defined by TC/ HDL-C ratio



DISCUSSION

The role of LDL-C in the development and progression of atherosclerosis is well established. LDL-C remains the primary target of dyslipedemia management in accordance to NCEP-ATP III guidelines[2]. Along with LDL-C, other lipid parameters like triglycerides and triglyceride-rich lipoproteins are also implicated in cardiovascular diseases[7]. Hence, the atherogenic potentials of other lipoproteins are ignored. Non-HDL-C estimates all proatherogenic lipoproteins and could account for the residual risk being carried by the patients[8]. Therefore this study was interested in finding the association of non-HDL-C with risk of cardiovascular disease defined by an established index namely TC/ HDL-C ratio. Further, non-HDL-C can be calculated in hypertriglyceridemic (TGL > 400 mg/dl) conditions where LDL-C estimation with Friedwald's formula is less accurate and inappropriate[9]. The study revealed sensitivity and specificity of non-HDL-C as 70.9% and 71.5% respectively with the optimized cut-off value of 137 mg/dl and OR of 6.08. On ROC analysis, non-HDL-C had

an AUC of 0.78. These emphasize the strong association of non-HDL-C with risk of CVD when defined on basis of TC/ HDL-C ratio. This study showed that mean non-HDL-C values were significantly ($p<0.01$) high in patients with risk defined by TC/ HDL-C ratio both in males and females. Non-HDL-C showed a significant positive correlation with TC/ HDL-C ratio. Thus this study shows that non-HDL-C can differentiate patients with and without risk of CVD similar to an established lipid profile index TC/ HDL-C ratio. The cut-off value of non-HDL-C optimized for sensitivity and specificity was found to be 137 mg/dl to that of the value proposed by NCEP ATP- III i.e. 130 mg/dl[2]. The findings of this study are in agreement with other studies that suggest the usage of non-HDL-C as a lipid parameter for assessing the cardiovascular disease risk[10,11].

CONCLUSION

Non-HDL-C showed significantly higher values in individuals with risk of CVD when defined by TC/ HDL-C ratio. This study suggests the use of non-HDL-C as a parameter for identifying individuals with CVD risk.

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CONFLICT OF INTEREST

There is no conflict of interest whatsoever arising out of publication of this manuscript.

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