

ORIGINAL RESEARCH**Correlation between Triglyceride/HDL Cholesterol Ratio and Angiographic Severity of Coronary Artery Disease**

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Received: 14 September, 2022

Accepted: 18 October, 2022

Abstract

Background: Coronary artery disease is a leading cause of mortality and morbidity worldwide^(1,2). Dyslipidemia is a well-established risk factor for atherosclerosis which is a lipid driven disease. Given the gravity of the problem caused by CAD, it becomes vital to conduct an extensive research on predictors of CAD, which may serve as potential therapeutic targets for the treatment and prevention of the disease in the population. Atherogenicdyslipidemia i.e., a triad of elevated levels of Triglycerides and LDL (sdLDL) and low levels of HDL is an established risk factor for atherosclerosis and the resultant CAD.sdLDL is a sub fraction of LDL that is more atherogenic and a good predictor of atherosclerosis⁽³⁾. However the estimation of sdLDL is expensive and difficult to assess. Ratio of Triglyceride to HDL Cholesterol, reflects the interaction between atherogenic and protective lipoproteins. Hence it has now emerged as a surrogate marker for sdLDL and a predictor of atherosclerosis.

This study aims to determine the correlation between Ratio of Triglyceride to HDL Cholesterol and the angiographic severity of CAD.

Materials and Methods: This cross sectional study was conducted in the Department of Cardiology, KIMS Hubballi during the period of September 2019 to December 2021. 170 patients presenting with features suggestive of acute coronary syndrome, admitted to KIMS Hubli were included in the study. After detailed clinical history and examination routine investigations and fasting lipid profile were estimated. Subsequently patients were subjected to coronary angiography via the trans femoral approach using standard techniques and scored by Gensini score.

Results: In our study, the ages of subjects ranged from 31 to 80 years, with mean age being 58.84(10.37)years. The mean age among Males was 57.13±11.34, and that among Female group was 62.12±7.21. Most patients ranged in the age group of 61 to 70 years. Among 170 participants, 112 (65.9%) were males, whereas 58 (34.1%) were females. Male : female ratio

was 2:1.60% of the study population was diabetic, while 62.4% of the population had hypertension. 51.7% had a history of tobacco smoking, 48.3% had a history of tobacco chewing, while 55.2% of the participants had a history of alcohol use. TG/HDL-C ratio showed a positive correlation with severity of coronary artery disease as evidenced by number of vessels, degree of stenosis And Gensini score. Maximum proportion of patients showing multiple vessel and triple vessel disease, chronic total occlusions, LAD stenosis were in High TG/HDL-C range. The ratio also showed a positive correlation with traditional risk factors for atherosclerosis like diabetes, hypertension, smoking.

Conclusion: TG/HDL-C ratio is a reliable indicator of metabolic interaction between lipoproteins and predicts individuals at high risk for atherosclerosis and the resultant CAD. It can be easily calculated from fasting lipid profile alone and gives comprehensive information regarding atherogenicity and can be effectively used for disease prevention and treatment.

Keywords: Dyslipidemia, Dyslipidemia, triglycerides, HDL Cholesterol.

Introduction

Coronary artery disease has become a major cause of mortality and morbidity across the globe. At the turn of 21st century, cardiovascular diseases have emerged as the leading cause of mortality in India.⁽¹⁾ This transition in epidemiology is mainly due to increased prevalence of CVD and its risk factors. These diseases tend to affect the population in the most productive years of their lives, leading to catastrophic social and economic repercussions. The situation in India is particularly alarming, owing to earlier age of onset, rapid progression and high mortality rate⁽²⁾. Inadequate resources, lack of effective screening programs and poor economy have only compounded the problem. CAD occurs in Indians 5-10 years earlier compared to other populations across the world, and the main impact of this unusual phenomenon is on the active workforce of the country aged 35-65 years.^[4] In India, the highest burden of ACS in the world is observed, and both the prevalence and incidence among Indians are high.^[4,5] Sedentary lifestyle, westernization of food habits, increasing prevalence of diabetes mellitus, South Asian ethnicity contribute to the increasing incidence of ACS in India.^[5] India has a high prevalence of diabetes mellitus, 2-3 times the recorded prevalence in Western countries, relative to every other region in the world. An estimated 19.3 million individuals in India alone had diabetes in 1995, which is showing an upward trend and this is projected to hit 57.2 million in 2025. Factors such as Diabetes, hypertension, age, family history, tobacco smoking have been shown to have an impact on CAD incidence. Atherogenic dyslipidemia comprises a triad of increased triglycerides, small dense LDL particles and reduced HDL levels. It is typically seen in patients with obesity, metabolic syndrome, insulin resistance and type 2 diabetes mellitus and has emerged as an important marker for CVD risk in these patients. One of the major predisposing factors to atherosclerosis is abnormal lipoprotein metabolism, which is prevalent in about 70% of the patients with premature CAD.

LDL seems to be the major target of oxidative modification, making it particularly atherogenic. Oxidation of LDL particles plays a major role in the initiation and progression of CAD and is facilitated by macrophages, endothelial cells and smooth muscle cells. In vitro studies show that basal expression of TLR 4 by macrophages is up regulated by oxLDL⁽⁶⁾. A considerable heterogeneity exists among LDL, and it is found that these modified sub fractions of LDL are more atherogenic than the LDL-C itself. Besides the traditional fasting serum lipid measurements, there exist a number of alternative measures to assess lipoprotein sub fractions. The techniques employed include nuclear magnetic resonance (NMR), ultracentrifugation gradient gel electrophoresis, ion mobility method.⁽⁴⁾ However due to the complicated detection methods and high cost, the use of these methods to detect lipid sub fractions is limited. Hence a number of comprehensive indices have been developed for the

prediction of atherosclerosis and the resultant coronary artery disease and studies show that these indices are considered to be better predictors of CAD than the lipid profile itself.⁽⁵⁾ It describes the interaction between atherogenic (TG) and protective lipoproteins (HDL-C).⁽⁷⁾ Studies have shown that TG/HDL-C ratio inversely correlates with the LDL particle size and serves as a reliable marker for the prediction of atherosclerosis and the resultant CAD.

Materials & Methods

This cross sectional study was conducted in the Department of Cardiology, KIMS Hubballi during the period of September 2019 to December 2021.

170 patients presenting with features suggestive of acute coronary syndrome, admitted to KIMS Hubli were included in the study. Patients having renal, hepatic dysfunction, patients on lipid lowering drugs and hormonal therapy were excluded from the study. After detailed clinical history and examination routine investigations and fasting lipid profile were estimated using standard techniques. TG/HDL-C ratio was divided into 3 groups ie, Optimum (<3), Intermediate (3.1 to 3.8) and High (>3.8). Subsequently patients were subjected to coronary angiography via transfemoral route using standard techniques. The results were scored by Gensini scoring system.

Statistical Analysis

Data was entered into Microsoft Excel sheet and was analysed using SPSS 22 version software. Categorical data was expressed in the form of Frequencies and proportions. Statistics were calculated by univariate analysis with Chi square and non prametric ANOVA (Kruskal – Wallis). Continuous data was represented as mean and standard deviation. P Value: (probability of the result being true) of <0.05 was considered statistically significant after assuming all the rules of statistical tests.

Results

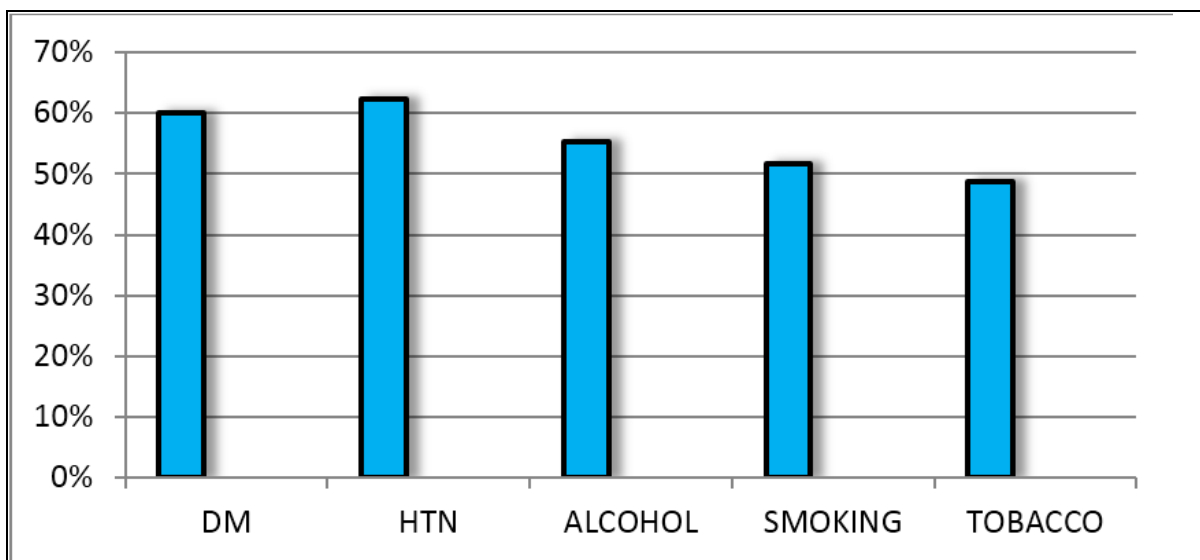
Among 170 participants, 112 (65.9%) were males, whereas 58 (34.1%) were females. Male:female ratio was 2:1. The ages of subjects ranged from 31 to 80 years, with mean age being 58.84(10.37)years. The mean age among Males was 57.13±11.34, and that among Female group was 62.12±7.21. Most patients ranged in the age group of 61 to 70 years. In our study , 102 (60%) of the patients were diabetic . among males, 54.5% and among females 70.7% were diabetic. 106 (62.4%) of the patients were hypertensive. Among males, 61.6% and among females 63.8% were hypertensive. In this study , 51.7% had a history of tobacco smoking, 48.3% of the patients had a history of tobacco chewing and 55.2% of the patients had a history of alcohol use.

		Number	Percentage
AGE	31 TO 40 Yrs.	15	8.8
	41 TO 50 Yrs.	23	13.5
	51 TO 60 Yrs.	49	28.8
	61 TO 70 Yrs.	60	35.3
	71 TO 80 Yrs.	23	13.5
SEX	MALE	112	65.9
	FEMALE	58	34.1
DM	YES	102	60
	NO	68	40
HTN	YES	106	62.4
	NO	64	37.6
SMOKING	YES	87	51.7
	NO	83	48.3
ALCOHOL	YES	94	55.2
	NO	76	44.8
TOBACCO CHEWING	YES	83	48.3
	NO	87	51.7

Table 1: Demographic profile of the patients in our study

Risk Factor	Number	Percentage
Diabetes mellitus	102	60
Hypertension	106	62.4
Alcohol consumption	94	55.2
Smoking	87	51.7
Tobacco chewing	83	48.8

Table 2: Distribution of risk factors in the present study

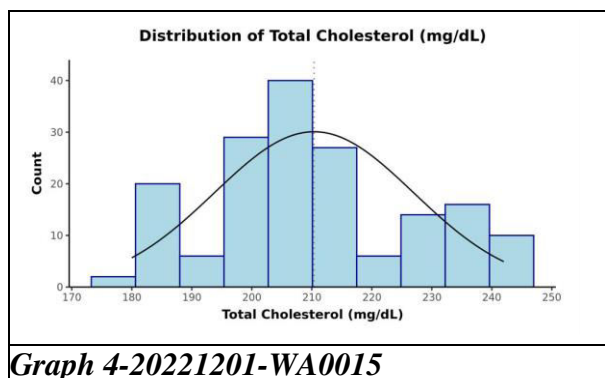


Graph 1: Distribution of risk factors in the present study

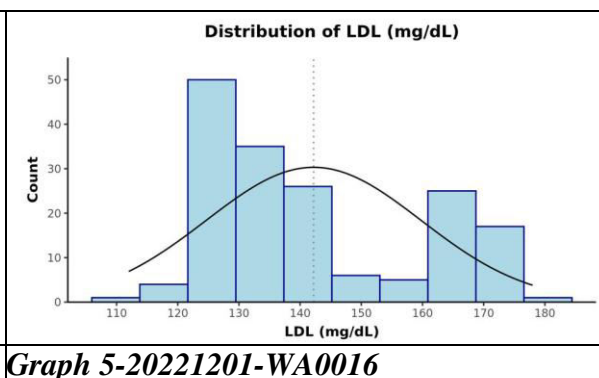
Chi square test was use to study the association between TG/HDL-C ratio and a positive correlation was seen between high TG/HDL-C ratio and Diabetes Mellitus, Hypertension, consumption of alcohol and tobacco.

Metabolic Profile	Mean ± SD Median (IQR) Min-Max Frequency (%)
BMI (Kg/m ²)	24.65 ± 1.65 24.40 (23.20-26.20) 21.80 - 28.20
BMI	
18.5-22.9 Kg/m ²	41 (24.1%)
23.0-24.9 Kg/m ²	75 (44.1%)
25.0-29.9 Kg/m ²	54 (31.8%)
HbA1c (%)	7.23 ± 1.34 7.05 (6.10-8.17) 5.50 - 11.20
HbA1c	
<6.5%	65 (38.2%)
6.5-8%	57 (33.5%)
>8%	48 (28.2%)
Total Cholesterol (mg/dL)	210.37 ± 16.62 208.00 (198.00-218.00) 180.00 - 242.00
Total Cholesterol	
<200 mg/dL	48 (28.2%)
≥200 mg/dL	122 (71.8%)
LDL (mg/dL)	142.21 ± 17.56 136.50 (128.00-161.00) 112.00 - 178.00
LDL (≥100 mg/dL)	170 (100.0%)
HDL (mg/dL)	36.01 ± 5.35 36.00 (32.00-39.75) 25.00 - 48.00
HDL	
<40 mg/dL	127 (74.7%)
≥40 mg/dL	43 (25.3%)
Triglyceride (mg/dL)	173.71 ± 32.01 188.00 (140.00-202.00) 120.00 - 215.00
Triglyceride	
<150 mg/dL	61 (35.9%)
≥150 mg/dL	109 (64.1%)
TG/HDL-C Ratio	5 ± 1.52 5.22(2.6-7.4)
TG/HDL-C Ratio Category	
Low	23 (13.5%)
Intermediate	38 (22.4%)
High	109 (64.1%)

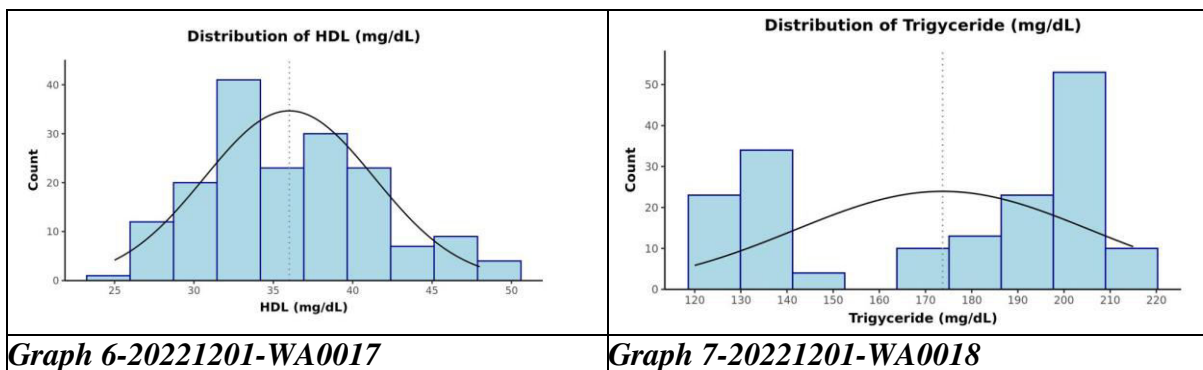
Table 3: Summary of Metabolic parameters in our study



Graph 4-20221201-WA0015



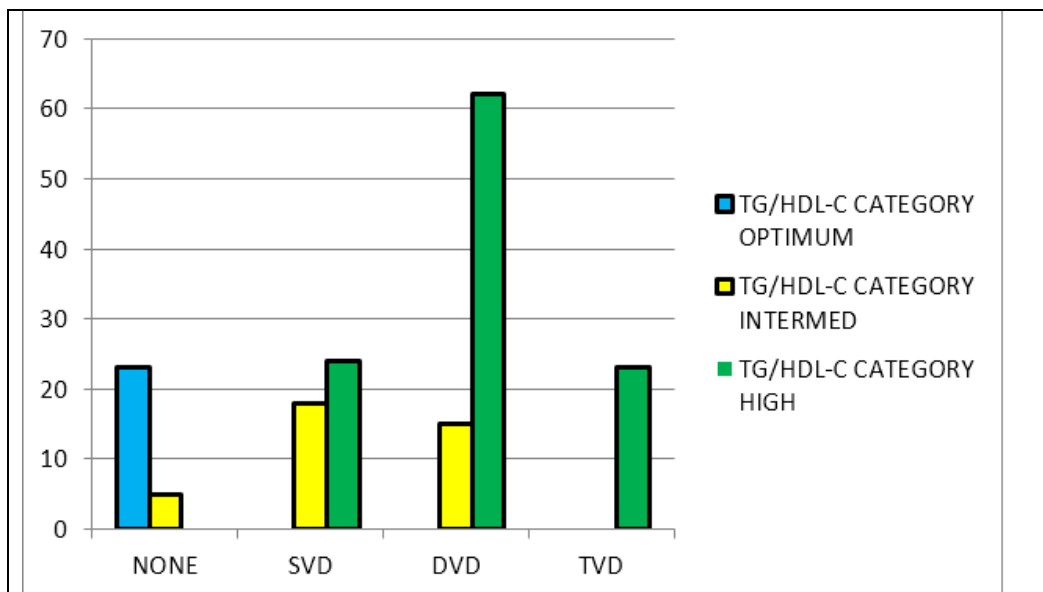
Graph 5-20221201-WA0016



Association between TG/HDL-C ratio and severity of coronary artery disease as assessed by number of vessels involved and Gensini score showed a positive correlation. There was a significant difference between the various groups in terms of distribution of Number Of Vessels Involved ($\chi^2 = 156.342, p = <0.001$). Strength of association between the two variables (Bias Corrected Cramer's V) = 0.67 (High Association). Participants in the Low TG/HDL-C ratio category had normal coronaries. Participants in the group TG/HDL-C ratio Category: Intermediate had the largest proportion of patients with SVD. Participants in the group TG/HDL-C ratio Category: High had the largest proportion of patients with DVD.

Number Of Vessels Involved	TG/HDL-C Category			Total	χ^2	P Value
	Optimum	Intermediate	High			
None	23 (100.0%)	5 (13.2%)	0 (0.0%)	28 (16.5%)	156.342	<0.001
SVD	0 (0.0%)	18 (47.4%)	24 (22.0%)	42 (24.7%)		
DVD	0 (0.0%)	15 (39.5%)	62 (56.9%)	77 (45.3%)		
TVD	0 (0.0%)	0 (0.0%)	23 (21.1%)	23 (13.5%)		
Total	23 (100.0%)	38 (100.0%)	109 (100.0%)	170 (100.0%)		

Table 4: Association Between TG/HDL-C Ratio Category and Number Of Vessels Involved (n = 170)

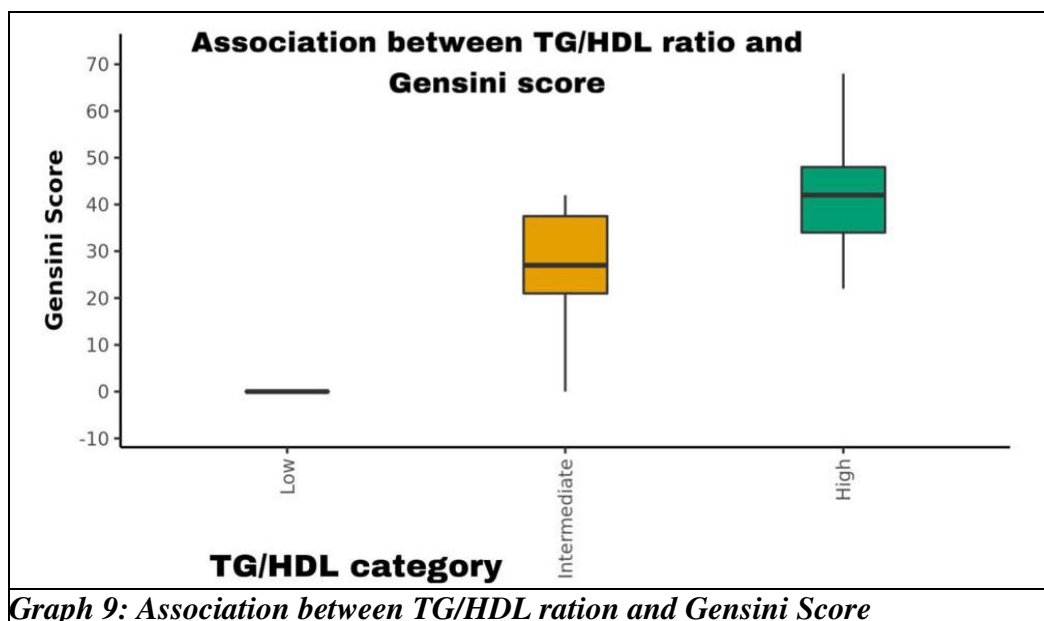


Graph 8: Association Between TG/HDL-C Ratio Category and Number Of Vessels Involved (n = 170)

Gensini Score	TG/HDL-C Category			Kruskal Wallis Test	
	Low	Intermediate	High	χ^2	p value
Mean (SD)	0.00 (0.00)	26.00 (11.97)	45.08 (15.76)	91.245	<0.001
Median (IQR)	0 (0-0)	27 (21-37.5)	42 (34-48)		
Range	0 - 0	0 - 42	22 - 98		

Table 5: Comparison of the 3 Subgroups of the Variable TG/HDL-C Ratio in Terms of Gensini Score (n = 170)

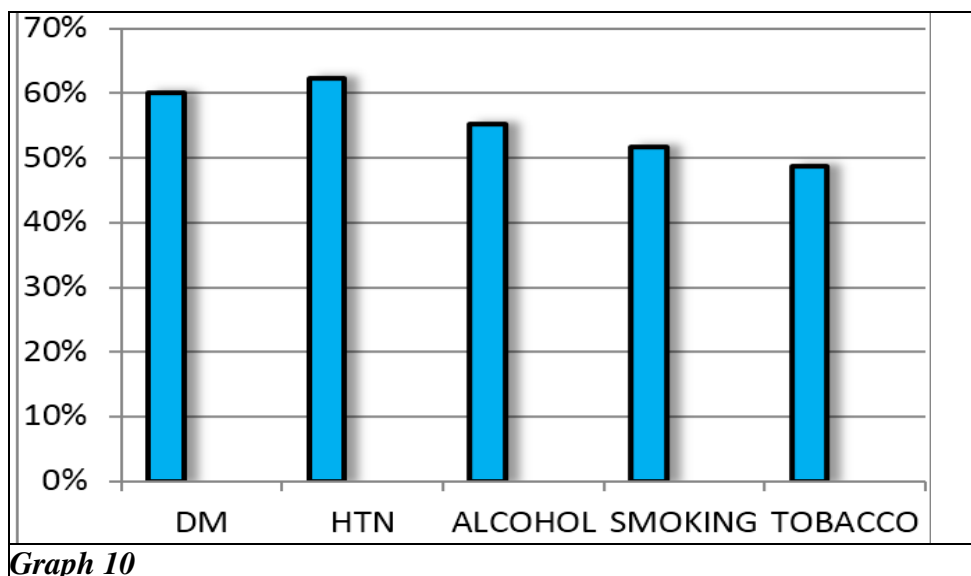
The variable Gensini Score was not normally distributed in the 3 subgroups of the variable AIP Category. Thus, non-parametric tests (Kruskal Wallis Test) were used to make group comparisons. Gensini score was the highest in the group with high TG/HDL-C ratio (45.08). There was a significant difference between the 3 groups in terms of Gensini Score ($\chi^2 = 91.245$, $p = <0.001$), with the median Gensini Score being highest in the TG/HDL-C Category: High group. The Box-and-Whisker plot below depicts the distribution of Gensini Score in the 3 groups. The middle horizontal line represents the median Gensini Score, the upper and lower bounds of the box represent the 75th and the 25th centile of Gensini Score respectively, and the upper and lower extent of the whiskers represent the Tukey limits for Gensini Score in each of the groups.



Discussion

Despite the fact that small, dense LDL particles are an established risk factor for cardiovascular disease, the assessment of their subfractions by current methods have been too technically demanding to be applicable in a routine clinical laboratory. The usual techniques include density gradient ultracentrifugation⁽⁸⁾ non-denaturing gradient gel electrophoresis (NDGGE),⁽⁹⁾ and nuclear magnetic resonance (NMR) spectroscopy,⁽¹⁰⁾ which have the disadvantages of being labor-intensive, technically demanding, expensive, or slow to produce results. As a result, these precise and accurate techniques are not widely used in clinical settings. Thus, developing surrogate markers of lipid particle profiles are of great clinical and economic importance. Of particular interest are ratios that have atherogenic particles in the numerator and HDL-c or its constituents in the denominator. The ratio of total cholesterol to HDL-c^(11,12) and, to a lesser extent, the ratio of LDL-c to HDL-c⁽¹³⁾ have been shown to be better predictors of CAD than lipid alone. The ratio TG/HDL-c, initially proposed by Gaziano et al,⁽¹⁴⁾ is an atherogenic index that has proven to be a highly significant independent predictor of myocardial infarction, even stronger than TC/HDL-c and LDL-c/HDL-c. The Copenhagen Male Study showed triglycerides on their own to be another strong risk factor, but it found that stratifying triglyceride levels by HDL-c levels led to more accurate detection of increased risk of coronary disease.

In our study, the ages of subject ranged from 30 to 80 years, with mean Age being 58.84 ± 10.37 . The mean age among Males was 57.13 ± 11.34 , and that among Female group was 62.12 ± 7.21 . In Bangladesh, Rahman et al⁽¹⁵⁾ found that, the mean age was 50.21 ± 8.01 years and most of the patients were found in the age range of 40 to 59 years, which closely resembles the present study. On the other hand, Penalva et al,⁽¹⁶⁾ da Luz et al⁽¹⁷⁾ and Gimeno-Orna et al⁽¹⁸⁾ have observed the mean age were 68 ± 8 years, 57.2 ± 11.1 and 64.8 ± 9.06 years respectively. The mean BMI in our study was 24.65 ± 1.65 . Bolibar et al⁽¹⁹⁾ found the mean (\pm SD) BMI was 26.2 ± 2.9 kg/m² in ACS patients, which is comparable with the current study. On the other hand, Bampi et al⁽²⁰⁾ and Flohlich, Gimeno-Orna et al have observed higher mean BMI in patients with IHD in their studies. Regarding traditional risk factors for CAD, Hypertension was the most common risk factor noted in our study. This observation is in comparison with other similar studies by Wei Ni et al and Bharadwaj et al⁽²¹⁾, which had 52.9% and 56% of hypertensive patients respectively.



The mean Triglyceride level in our study was 173.71 ± 32.01 (borderline range). Similar results were obtained in studies by Rismawati et al⁽²²⁾ and Luz et al, who found mean triglyceride levels of 151.2mg/dl and 167.9mg/dl respectively. The mean HDL-C in our study was 36.01 ± 5 mg/Dl. The result is similar to other studies by Rismawati et al and Sharma et al where the mean HDL level was 35.7mg/dl and 38.38mg/dl respectively. The mean TG/HDL C ratio in our study was 5 ± 1.52 . In our study, 16.5% of the patients had normal coronaries, 24.7% of the patients had single vessel disease and 58.8% of the patients had multiple vessel disease, with DVD being the commonest finding. The findings are similar to study by Amin MR et al which showed 16.9% patients with no vessel involvement, 36.4% with SVD, 23.7% DVD and 22.8% TVD. In Bolibar et al⁽²³⁾ and Rahman⁽¹⁵⁾ study, almost similar result has been found.

Conclusion

In evaluation of patients with CAD, the evaluation of fasting lipid profile has been an integral part of the clinical work up. However, even in the pretext of apparently normal levels of lipid parameters, CAD still persists. TG/HDL C ratio, a better indicator of metabolic interaction between lipoproteins, predicts individuals at high risk for atherosclerosis and the resultant CAD. It can be easily calculated from fasting lipid profile alone and gives comprehensive information regarding atherogenicity and can be effectively used for disease prevention and treatment.

Therefore, TG/HDL C ratio can be advocated for :

- Inclusion in routine lipid profile
- As a monitoring index to plan lipid lowering strategies as a mode of primary prevention.
- As a tool to predict the severity of CAD and stratification of patients to direct needful therapy.

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