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Correlation of Triglyceride to HDL-C Ratio with Severity of Coronary Artery Lesion in Non-Diabetic Chronic Coronary Syndrome (CCS) Patients: A Cross-Sectional Analytical Study

Abu Bakar Siddique[*,1], Abdul Wadud Chowdhury[2], Kazi Nazrul Islam[3], Taslima Rahman[4], Sarower Polash[5], Sharowar Hossain Khan[6], Chinmoy Saha[7], Isha Abdullah Ali[8], Ahsanul Hoque[9], Goutom Chandra Bhowmik[10]

Affiliation:

[1]Junior Consultant, MD (Cardiology), FCPS (Medicine), Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh

[2]Professor and Director, MD (Cardiology), FCPS (Medicine), Department of Cardiology, National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh

[3]Associate Professor and Head, Department of Cardiology, Dhaka Medical College Hospital, Dhaka, Bangladesh

[4]Associate Professor, Department of Community Medicine, International Medical College, Gazipur, Bangladesh

[5]Junior Consultant, Department of Cardiology, Munshigonj General Hospital, Munshigonj, Bangladesh

[6]Assistant Surgeon, Department of Cardiology, Munshigonj General Hospital, Munshigonj, Bangladesh

[7]Assistant Professor, Department of Cardiology, Dhaka Medical College Hospital, Dhaka, Bangladesh

[8]Assistant Professor (Cardiology), Ibrahim Cardiac Hospital and Research Institute (ICHRI), Dhaka, Bangladesh

[9]Assistant Professor, Department of Cardiology, Dhaka Medical College Hospital, Dhaka, Bangladesh

[10]Junior Consultant, Department of Cardiology, Upazila Health Complex, Ishwardi, Pabna, Bangladesh

***Corresponding author:**
Abu Bakar Siddique, Junior Consultant, MD (Cardiology), FCPS (Medicine), Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.

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Abstract

Background: Raised Triglyceride level and low HDL-C level is the main lipoprotein pattern of Bangladeshi people. The aim of this study was to find out the correlation between TG/HDL-C ratio and CAD severity in non-diabetic CCS patients.

Methods: This cross-sectional analytical study was conducted among 89 non-diabetic patients with chronic coronary syndromes (CCS) undergoing coronary angiography (CAG) at Dhaka Medical College Hospital and the National Institute of Cardiovascular Diseases, Dhaka, from October 2019 to September 2020. Participants were categorized according to the triglyceride-to-high-density lipoprotein cholesterol (TG/HDL-C) ratio into Group A (TG/HDL-C ≤4; n=42) and Group B (TG/HDL-C >4; n=47). Coronary artery disease (CAD) severity was assessed by coronary angiography using the Gensini score and vessel score. The association between TG/HDL-C ratio and angiographic CAD severity was analyzed using appropriate statistical tests and multivariable logistic regression.

Results: High level of triglycerides and low level of HDL-C in Group B (p=<0.001). Total cholesterol was significantly higher in Group B (p=0.007). According to the Gensini score, no or mild CAD was more in group A 30 (71.4%), and moderate to severe CAD was more in group B 35 (74.5%). Vessel score explaining no critical disease or single vessel disease (SVD) were significantly higher in group A 31 (73.8%) and double vessel disease (DVD) or triple vessel disease (TVD) were significantly higher in group B 29 (61.7%). Both scores were significantly higher in Group B. Pearson's correlation found a strong association of the TG: HDL-C ratio with the Gensini score (r=0.798, p=<0.001). In multiple linear regression analysis, TG: HDL-C ratio was found to be significantly associated with a Gensini score>36 with an odds ratio of 18.94.

Conclusion: TG: HDL-C ratio significantly correlates with the severity of coronary artery lesions in non-diabetic CCS patients.

Keywords: TG: HDL-C ratio, CCS, Gensini score, Vessel score, CAD.

Introduction

Cardiovascular disease (CVD) is one of the most common causes of death worldwide. Cardiovascular diseases (CVD) are a group of disorders of the heart and blood vessels which include coronary artery disease (CAD), congenital heart disease, cerebrovascular disease, peripheral artery disease,

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and rheumatic heart disease. Among the cardiovascular death, 80% occur in low and middle-income countries (LMIC).[1] Rapid urbanization took place in Bangladesh in the past few decades due to its fast economic growth and recently, it has emerged as a developing country. Due to fast economic growth and rapid urbanization, non-communicable diseases (NCD) and associated mortality have been increasing last few decades in Bangladesh and near future chronic disease burden may rise due to a sedentary lifestyle.[2,3,4]

CCS are defined by the different evolutionary phases of CAD, excluding acute coronary syndromes (i.e. ACS). The most common clinical scenarios in CCS are stable angina, heart failure, recent revascularization, microvascular angina, on screening detection in case of asymptomatic patients.[5] Dyslipidemia is a group of conditions in which there are abnormal levels of lipids and lipoproteins in the blood. The prevalence of dyslipidemia in Bangladesh is 34%.[6] Prevalence of dyslipidemia in acute coronary syndrome is 60.7% in Bangladesh.[7] Dyslipidemia can directly impair endothelial cell function by local oxygen free radical production which can injure tissues and accelerate nitric oxide decay, reducing its vasodilator activity. Dyslipidemia is one of the major risk factors for coronary artery disease (CAD). Major predictors of CAD are High total cholesterol (TC), high Low-density lipoprotein cholesterol (LDL-C), high triglycerides (TG) and low high-density lipoprotein cholesterol (HDL-C).[8] Though there are many non-invasive markers of CAD severity, TG: HDL-C ratio was most strongly associated with the extent of coronary disease, as assessed by conventional coronary angiography (CAG).[9] Studies showed that, among the lipid variables TG/HDL-C ratio >4 is the most powerful independent predictor of CAD development.[10] Carbohydrate is the main diet of Bangladeshi people and high plasma concentrations of Triglycerides and low plasma concentrations of HDL cholesterol are consistent with the effects of these diets.[11] Though the consumption of rice and wheat has decreased, resulting in an overall decrease in monthly expenditure (59% to 41.33%) from cereal consumption, still rice and wheat consumption is quite high.[12-14] This may contribute to a high TG level in our people. Considering the above facts it is clear that TG/HDL-C ratio could be a very important, easy, non-invasive means of predicting the presence and extent of coronary atherosclerosis especially for the population of Bangladesh and other South-Asian countries. We aimed to study the association of TG: HDL-C ratio with CAD severity in non-diabetic CCS patients.

Materials and Methods

Study Design and Setting

This was a cross-sectional analytical study conducted among patients with chronic coronary syndromes (CCS). The study was carried out in the Department of Cardiology, Dhaka Medical College Hospital (DMCH), Dhaka and the National Institute of Cardiovascular Diseases (NICVD), Dhaka, during the COVID-19 pandemic. The study period extended from October 2019 to September 2020.

Study Population and Sampling

The study population comprised diagnosed CCS patients attending the indoor and outdoor cardiology services of DMCH and NICVD who underwent coronary angiography (CAG). Patients fulfilling the predefined eligibility criteria were recruited using a purposive sampling technique. Based on the triglyceride-to-high-density lipoprotein cholesterol (TG/HDL-C) ratio, participants were categorized into two groups: Group A (TG/HDL-C ≤4) and Group B (TG/HDL-C >4).

Eligibility Criteria

Patients aged ≥18 years with diagnosed CCS who underwent CAG during the study period were eligible. Patients with diabetes mellitus, acute coronary syndrome, previous percutaneous coronary intervention or coronary artery bypass grafting, valvular heart disease, chronic kidney disease, active malignancy or unwillingness to participate were excluded.

Sample Size

The calculated sample size was 100, based on previously reported differences in mean TG/HDL-C ratio between patients with normal coronary arteries and those with coronary artery disease, using a 5% level of significance and 90% statistical power. However, because of the COVID-19 pandemic and related limitations in patient recruitment, 89 patients were ultimately included. Of these, 42 were classified as Group A and 47 as Group B, according to the prespecified TG/HDL-C ratio cut-off of 4.

Study Procedure and Data Collection

Eligible participants underwent detailed clinical assessment, including demographic characteristics and cardiovascular risk factors such as smoking, hypertension, dyslipidemia, obesity, sedentary lifestyle and family history of premature coronary artery disease. Standard 12-lead electrocardiography and relevant investigations, including echocardiography, exercise tolerance testing where indicated, serum creatinine, serum electrolytes and fasting lipid profile were performed. Fasting lipid samples were obtained after at least 8 hours of fasting and analyzed in the DMCH clinical laboratory using a Dimension Xpand analyzer (Siemens) with Flex reagent cartridges. The TG/HDL-C ratio was calculated from the lipid profile and used for group classification.

All participants underwent coronary angiography during hospitalization. Angiographic findings were independently assessed by two cardiologists using visual estimation.

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Coronary artery disease severity was evaluated using the vessel score and Gensini score. For analytical purposes, a Gensini score of ≤36 was categorized as no/mild CAD, whereas a score of >36 was considered moderate-to-severe CAD. All information was recorded using a structured questionnaire and preformed data collection checklist.

Statistical Analysis

Data were analyzed using SPSS version 22. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Student's t-test was used to compare continuous variables and the chi-square test was used for categorical variables. Pearson's correlation coefficient was applied to assess correlations between continuous variables, while point-biserial correlation was used where appropriate for categorical variables. Multivariable logistic regression analysis was performed to determine the independent association between TG/HDL-C ratio and angiographic severity of CAD. Results were reported with a 95% confidence interval (CI) and a p-value <0.05 was considered statistically significant.

Results

Demographic, risk factors and CCS variables

Demographic variables were similarly distributed between the 2 groups. The minimum age of the respondents was 27 years and the maximum age was 75 years. The mean age in group A was 51.1±9.6 years and in group B was 52.6±10.8 years. Male to female ratio was 4:1. Variables of risk factors and CCS presentation were balanced between 2 groups except hypertension and obesity which were significantly higher in group B (Table 1).

Table 1: Baseline demographic, CAD risk factors and CCS presentation (n=89)

Variables	Group A (n=42)		Group B (n=47)		p-value
	No.	%	No	%	
Age group (years)					
<30	2	4.8	0	0	
30-39	1	2.4	5	10.6	
40-49	14	33.3	12	25.5	
50-59	15	35.7	17	36.2	0.192^{ns}
60-69	9	21.4	8	17	
≥70	1	2.4	5	10.6	
Gender					
Male	32	76.2	40	85.1	0.285^{ns}
Female	10	23.8	7	14.9	
Risk factors					
Hypertension	20	47.6	36	76.6	.005^{s}
Obesity (BMI>27kg/m^2)	13	31	26	55.3	.021^{s}
Smoking	22	52.4	31	66	.204^{ns}
Sedentary habit	18	42.9	27	57.4	.169^{ns}
Dyslipidemia	9	21.4	14	29.8	.369^{ns}
Family History of Premature CAD	4	9.8	4	8.8	.868^{ns}
Old MI	25	59.52	29	61.7	
CSA	17	40.48	18	38.3	0.217^{ns}

Data were expressed as frequency and percentage

Chi-squared Test (χ^2) was done to observe association.

ns = not significant, s= significant

Group A: patients with TG: HDL-C≤4

Group B: patients with TG: HDL-C>4

BMI>27kg/m^2(Obese)

BMI≤27kg/m2 (Non-obese)

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Biochemical and angiographic variables

High level of triglycerides, and low level of HDL cholesterols in Group B (p= <0.001) as expected but similar distribution of LDL cholesterol in both groups (p=0.375). Total cholesterol was also significantly higher in Group B (p= 0.007) (Table 2). According to the Gensini score, no or mild CAD was more in group A 30 (71.4%), and moderate to severe CAD was more in group B 35 (74.5%). Vessel scores explaining no critical disease or single vessel disease (SVD) were significantly higher in group A 31 (73.8%) and double vessel disease (DVD) or triple vessel disease (TVD) were significantly higher in group B 29 (61.7%) (Table 3).

TG: HDL-C ratio, age, female sex, and sedentary habits were found to have a significant positive correlation with the Gensini score. The scatter plot diagram showed a linear positive relationship between the TG/HDL-C ratio and the Gensini score. The coefficient of determination (r^2) was 0.636 which means 63.6% variability of the Gensini score was associated with the TG/HDL-C ratio and the remaining 36.4% due to other factors. A multivariate logistic regression model was constructed with the TG: HDL-C ratio, Total cholesterol, hypertension and obesity as independent variables and the Gensini score as dependent variable. TG: HDL-C ratio was found to be significantly associated with Gensini score>36. These are presented in Table 4 and Table 5.

Table 2: Comparison of lipid profiles between two groups (n = 89)

Lipid Parameters	Group A (n=42)	Group B (n=47)	p value	Total (n=89)
	Mean±SD	Mean±SD		Mean±SD
Triglycerides (mg/dl)	144±38	260±73	<.001	205±83
HDL cholesterol (mg/dl)	45±9	37±7	<.001	41±9.4
LDL cholesterol (mg/dl)	103±37	111±47	0.375	107±42
Total cholesterol (mg/dl)	158±41	183±43	0.007	171±44

Data were expressed as frequency and percentage
Chi-squared Test (χ^2) was done to observe association.
ns = not significant
s= significant
Group A: patients with TG:HDL-C≤4
Group B: patients with TG:HDL-C>4

Table 3: Angiographic severity of coronary artery disease by Gensini score and Vessel score (n=89)

Variables	Group A (n=42)		Group B (n=47)		P value
	No.	%	No.	%	
Gensini score					
≤36	30	71.4	12	25.5	<0.001[s]
>36	12	28.6	35	74.5	
Vessel score					
No critical disease or Single vessel disease (SVD)	31	73.8	18	38.3	0.002[s]
Double vessel disease (DVD) or Triple vessel disease (TVD)	11	26.2	29	61.7	<0.001[s]

s=significant

Table 4: Bivariate analysis of variables with Gensini score in patients with CCS (n=89).

Variables	Correlation co-efficient (r)	Significance
TG: HDL-C ratio[a]	0.798	<.001[s]
Age[a]	0.315	.003[s]
Sex (female)[b]	-0.227	.032[s]
Sedentary habit[b]	0.226	.033[s]
Hypertension[b]	0.066	.542[ns]
Obesity[a]	0.034	.753[ns]
Smoking[b]	0.18	.092[ns]
Family history of premature CAD[b]	0.037	.729[ns]
Dyslipidemia[b]	0.15	.159[ns]

a= Pearson correlation; b= point biserial; ns=non-significant; s=significant

Table 5: Predictors of coronary artery disease by multivariate logistic regression (n=89)

Variables of interest	Standardized coefficient(β)	p-value	Odds Ratio (OR)	95% CI of OR
TG:HDL-C ratio	2.941	<0.001	18.94	5.427-66.070
Total Cholesterol	0.47	0.416	1.6	0.516-4.964
Hypertension	-0.976	0.11	0.38	0.114-1.249
Obesity	-0.773	0.169	0.17	0.153-1.388

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Discussion

We observed no or mild CAD was predominant in group A and moderate to severe CAD was predominant in group B. That means CAD severity increased when TG: HDL-C ratio was >4. The mean age of the total population was 51.8±10.2 years. A multicenter study showed a mean age of 49.7±12.8 years among stable angina patients which was similar to our study.[15] Two recent studies showed mean age 60±8 years and 58.8±10.5 years.[16,17] Probably their mean age was higher due to increased life expectancy in those countries. The male-to-female ratio was 4:1. Studies found that stable angina was more common in males than females.[15,16] Probably, due to hormonal defense CCS is less in menstruating females. Among the cardiovascular risk factors, hypertension and obesity were significantly higher in Group B patients. Study conducted in a tertiary care hospital in Bangladesh showed a raised BMI (47.6%) in the high coronary artery disease group whereas we found 55.3% in group B respondents.[18] A recent nationwide study of risk factor analysis found that the prevalence of HTN was 15.1%, Dyslipidemia 34.3%, obesity 16.02% and smoking 40.56%.[6] Probably our small sample size can't explain these. A recent study showed similarity with our fasting lipid profile findings.[19]

Both Vessel score and Gensini score were significantly higher in group B patients. We found significantly high double or triple vessel disease in group B. A study on ACS patients showed high vessel scores in respondents with TG: HDL-C ratio>4.[20] So, TG: HDL-C ratio is a good marker of atherogenic dyslipidemia. Mean± SD of the Gensini score in our study was 48.1±35.8. Aditya Sudjana et al,. found a Gensini score of 51±36 which is similar to our study.[16] In bivariate analysis, we found a significant positive correlation of the TG: HDL-C ratio with the Gensini score which means CAD severity increases with raised TG: HDL-C ratio. Many studies showed a similar result.[10,16,17] In multivariate logistic regression model TG: HDL-C ratio was found to be significantly associated with Gensini score>36 (OR=18.94, CI=5.427-66.070, p=<0.001). These results support previous studies.[10,17,21] A study only on Persian males showed strong relationship of TG: HDL-C ratio with coronary lesions after excluding diabetes and after adjusting with confounding variables.[22] Da Luz et al., and Conkbayir C et al., showed that the TG/HDL-C ratio was associated with the severity of coronary lesions assessed by using the Friesinger index.[10,17] All these studies used stable angina pectoris patients as their study population and Conkbayir C et al., and Aditya Sudjana et al., excluded diabetic patients in their study.[17,16] The results of this study have demonstrated that coronary artery lesions were observed significantly more in patients with TG: HDL-C ratio>4 and this correlation remained statistically significant even after adjustment for other significant cardiovascular risk factors.

Conclusion

In this study, the TG: HDL-C ratio was significantly associated with CAD severity which was measured by Gensini score and vessel score. TG: HDL-C ratio can be used as a marker of CAD severity as it is non-invasive, faster, easier, cheaper and widely available. Whether TG: HDL-C ratio represents a risk marker or a risk factor for coronary artery disease remains to be elucidated.

Limitations and Recommendations:

- The sample size was less due to the COVID pandemic and purposive sampling was done instead of random sampling. Therefore, further clinical study with a larger sample size involving multiple centers is recommended.
- Statin consumption was not included as a confounding variable in this study.
- Lipid-lowering agents and non-pharmacological measures like lifestyle modifications and dietary changes should be advised for all patients of IHD to achieve a better lipid profile with a low TG: HDL-C ratio.

Declarations

Ethics Approval and Consent to Participate

The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Ethical approval was obtained from the Ethical Review Committee of Dhaka Medical College Hospital, Dhaka, Bangladesh, before commencement of the study. All participants were informed about the objectives and procedures of the study and written informed consent was obtained before enrollment and data collection.

Consent for Publication

Written informed consent was obtained from all participants for the use of their anonymized clinical and angiographic data for scientific publication. No personally identifiable information is presented in this manuscript.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available because they contain participant-level clinical information and are subject to institutional confidentiality requirements. The data may be made available from the corresponding author on reasonable request, subject to appropriate ethical and institutional approval.

Competing Interests

The authors declare that they have no competing interests or conflicts of interest related to this study.

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Author contributions

Professor Dr. Abdul Wadud Chowdhury

- Design the study, data interpretation and analysis of data
- Revised the article and approved the final version of the article
- Accountable fot all aspects of the work and resolved any issues related to its accuracy or integrity.

Dr. Abu Bakar Siddique

- Corresponding author
- Design the study, data collection, interpretation and analysis of data
- Revised the article and approved the final version of the article
- Accountable fot all aspects of the work and resolved any issues related to its accuracy or integrity.

Dr. Kazi Nazrul Islam

- Contribute to the concept, design the study, data collection, interpretation and analysis of data
- Revised the article
- Accountable fot all aspects of the work and resolved any issues related to its accuracy or integrity.

Dr. Taslima Rahman

- Design the study, data collection, interpretation and analysis of data
- Accountable fot all aspects of the work and resolved any issues related to its accuracy or integrity.

Dr. Sarower Polash

- Design the study, data collection, interpretation and analysis of data
- Revised the article and approved the final version of the article
- Accountable fot all aspects of the work and resolved any issues related to its accuracy or integrity.

Dr. Sharowar Hossain Khan

- Design the study, data collection, interpretation and analysis of data
- Accountable for all aspects of the work and resolved any issues related to its accuracy or integrity.

Dr. Chinmoy Saha

- Design the study, data collection, nterpretation and analysis of data
- Accountable fot all aspects of the work and resolved any issues related to its accuracy or integrity.

Dr. Isha Abdullah Ali

- Design the study, data collection, interpretation and analysis of data
- Accountable fot all aspects of the work and resolved any issues related to its accuracy or integrity

Dr. Md. Ahsanul Hoque

- Design the study, data collection, interpretation and analysis of data
- Accountable fot all aspects of the work and resolved any issues related to its accuracy or integrity

Goutom Chandra Bhowmik

- Design the study, data collection, interpretation and analysis of data
- Accountable fot all aspects of the work and resolved any issues related to its accuracy or integrity

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