

The Relationship/Association of Triglyceride and Severity of Coronary Artery Disease: Is Triglyceride Really a Risk Factor for Coronary Artery Disease?

KAJAL KUMAR KARMOKER¹, KHANDAKER AISHA SIDDIKA¹, MOHAMMAD WALIDUR RAHMAN¹, BIJOY DATTA¹, MOHAMMAD BAZLUR RASHID¹, GOLAM RAHMAN MALLICK¹, NIRANJAN KUMAR SANA.²

¹Department of Cardiology, National Institute of Cardiovascular diseases (NICVD), Dhaka, Bangladesh, ²Department of Biochemistry and Molecular Biology, Rajshahi University, Rajshahi, Bangladesh.

Address of Correspondence: Dr. Kajal Kumar Karmoker, Associate Professor, Department of Cardiology, National Institute of Cardiovascular diseases (NICVD), Dhaka, Bangladesh. E mail: drkajal71@gmail.com

Abstract:

Worldwide, the major cause of mortality and morbidity is coronary artery disease (CAD). In the pathogenesis and progression of atherosclerosis, lipid and its metabolites play an important role. The aim of the study was to find out the association of triglyceride (TG) level on the severity of coronary artery disease (CAD) in patients with ischemic heart disease (IHD). In this cross-sectional study, 431 patients with ischemic heart disease were enrolled after taking informed written consent. TG level were categorized into normal (< 150 mg/dl), borderline (150-199 mg/dl) and high (≥200 mg/dl). Patients with ischemic heart disease (IHD) were stratified according to TG level. Severity of CAD was assessed by the Gensini score. Most of the patients (33.4%) belonged to the age group 51–60 years. The mean age was 51.31±10.30 years. The majority (74.5%) of patients were male. Among risk factors, 205 (47.6%) patients were smokers, followed by hypertension 190 (44.1%) and diabetes mellitus 175 (40.5%). The association of TG with the whole spectrum of IHD was found statistically significant ($p < 0.05$). Moderate to severe CAD was found to be higher in the high TG level group compared with the other groups and was statistically significant.

Key Words: Triglyceride, Coronary Artery Disease, Gensini Score.

University Heart Journal 2022; 18(2): 101-105

Introduction:

Cardiovascular diseases (CVDs) account for maximum death worldwide. CVDs were responsible for 32% of all global deaths in 2019.¹ Heart attack and stroke were responsible for 85% of these deaths.¹ More than three quarters of CVD deaths take place in low- and middle-income countries.¹ 38 % of the total non-communicable diseases death in 2019 was due to CVDs.¹ The exact prevalence of coronary artery disease in Bangladesh is not known. Recent data indicates the coronary artery disease prevalence is 1.85% to 3.4% in the rural population and it is 19.6% in the urban population.² The clinical presentations of coronary artery disease include silent ischemia, stable coronary artery disease, acute coronary syndrome, heart failure, and sudden death.³ Dyslipidemia is one of the major risk factors of ischaemic heart diseases and the role of total cholesterol especially LDL-Cholesterol is well established in the pathogenesis of atherosclerosis and ischemic heart disease.⁴ The term “atherogenic lipid profile” has been introduced to describe

a common form of dyslipidemia, characterized by three lipid abnormalities: increased serum triglyceride (TG) level, decreased concentration of high-density lipoprotein (HDL), and the presence of modified low-density particles (LDL).^{5,6} TG rich lipoproteins also could lead to higher incidence of CV diseases, so serum TG level should be lower. The specific cutoff points around which the association with TGs and CVD risk have not been systematically evaluated. Various quantitative scoring systems have been used to define angiographic severity of coronary artery disease. Gensini score is a widely accepted angiographic severity scoring system.⁷

The aim of this study was to assess whether increased TGs level are really a risk factor for coronary artery disease.

Methods:

This cross sectional study was performed in the Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh during the period of March 2018 to February 2021. 431 Patients with

IHD were included in this study. Patients undergoing CAG for evaluation of coronary arteries in valvular heart diseases, congenital heart diseases, other non-cardiac surgery, CKD, known case of Carcinoma, acute infective episode were excluded from this study. Before enrollment, informed written consent was taken from each patient. Detailed history was taken and clinical examination was performed and data were recorded in predesigned structured data sheet. Demographic data such as age, sex, occupation was recorded. Risk factors profile including smoking, hypertension, diabetes, dyslipidemia and family history of coronary artery disease was noted. On admission venous blood was obtained from all patients. Serum creatinine, random blood sugar and other relevant investigations for coronary angiogram were performed. Blood sample was taken for fasting lipid profile on the day of CAG. 12 lead resting ECG was done. Transthoracic echocardiography was done on the day before coronary angiogram and left ventricular ejection fraction (LVEF) was measured. Coronary angiogram was done by conventional method in the same hospital setting. Presence and severity of coronary artery disease was assessed by visual estimation by two cardiologists and severity was graded by the Gensini score. According to the Gensini score CAD is categorized as mild (1-10), moderate (> 10-50) and severe (> 50).

Statistical analysis

Data analysis was performed using SPSS version 23. Frequency and percentage were computed for categorical variables like gender, risk factors, diagnosis and angiographic findings. Mean and standard deviation were computed for quantitative variables and were analyzed by independent sample t test. The Chi-Square test and Spearman rho correlation coefficient test were used to compare the Gensini score between the groups divided according to the risk scores. Statistical significance was defined as a p value < 0.05.

Results:

This cross sectional study was performed in the department of cardiology in National Institute of Cardiovascular Diseases (NICVD), Dhaka, from March 2018 to February 2021. A total of 431 patients with ischemic heart disease who underwent coronary angiogram were enrolled in this study. This study was aimed to correlate TG level with the severity of coronary artery disease in patients with ischemic heart disease.

The age of the study population ranged between 25 to 75 years, with a mean of 51.31 ± 10.3 years (Table 1). Most

of the patients were in 51- 60 years age group. Majority (74.5%) patients were male (Table 1).

Table-I
Demographic characteristics of the study population (n= 431)

Demographic Characteristics	Frequency	Percent (%)
Age (Years)		
<30 years	14	3.2
31-40 years	65	15.1
41-50 years	131	30.4
51-60 years	144	33.4
61-70 years	72	16.7
>71 years	05	1.2
Mean \pm SD	51.31 \pm 10.30	
Range(min- max)	(25-75)	
Sex		
Male	321	74.5
Female	110	25.5

n= total number of patients

Data are presented as percentage (%).

Among the risk factors, smoking was highest 205 (47.6%) followed by hypertension 190 (44.1%), diabetes mellitus 175 (40.5%), family history of ischemic heart disease 88 (20.4%), 87 (20.27%) previous history of angina (Table 2)

Table-II
Distribution of the study population by risk factors (n= 431)

Risk factors	Frequency	Percent (%)
Smoking	205	47.6%
Hypertension	190	44.1%
Diabetes Mellitus	175	40.6%
Dyslipidemia	129	29.9%
Family history of IHD	88	20.4%
Previous history of Angina	87	20.2%

n= total number of patients

Data are presented as percentage (%).

184 (42.7%) patients presented with ST elevation Myocardial Infarction (STEMI), 113 (26.2%) patients had Chronic Stable Angina (CSA), 74 (17.2%) had Non ST elevation Myocardial Infarction (NSTEMI), and 60 (13.9%) patients had Unstable Angina (UA) (Figure 1).

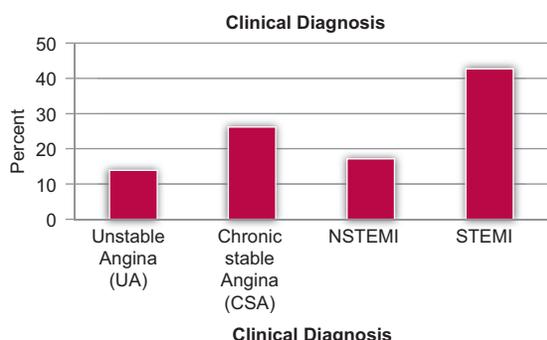


Fig.-1: Distribution of the study population by Clinical Spectrum of ischemic heart disease (n = 431)

Majority of the patients 191 (44.3%) had hypertriglyceridemia (table 3)

Table-III

Distribution of the study population by Triglyceride Level (n = 431)

Triglyceride (TG) Level	Frequency	Percent (%)
Normal TG (<150 mg/dl)	124	28.8
Borderline high TG (150-199 mg/dl)	116	26.9
High TG (200-499 mg/dl)	191	44.3
Total	431	100.0

n= total number of patients.

Data are presented as percentage (%).

Nearly half 213 (49.4%) of the patients had moderate stenosis, 99 (23%) of the patients had severe stenosis, and 119 (27.6%) of the patients had mild stenosis (Figure 2)

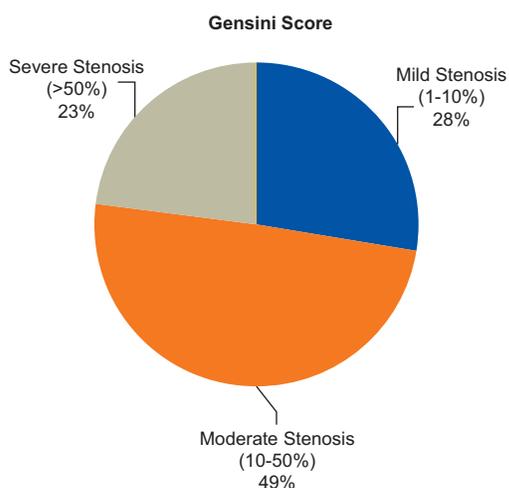


Fig.-2: Distribution of the study population by Gensini score (n=431)

Severe CAD was found higher in high TGs group compared with the other groups and was statistically significant (Table 4)

Table-IV

Relationship of TG level with the severity of coronary artery disease as assessed by the Gensini Score (n= 431)

Gensini Score	TG level		P =.02
	Normal TG level	High TG level	
Mild (1-10)	103 (23.8%)	16 (3.5%)	
Moderate (>10-50)	56 (12.9%)	147 (56.6%)	
Severe (>50)	23 (5.3%)	76 (39.8%)	
Total	192	239	

Data were analyzed by Chi-square test.

P value < 0.5 was considered as statistically significant

In the table 5, the results of Spearman’s correlation coefficient shows that the relationship between Triglyceride (TG) Level with clinical spectrum of ischemic heart disease. There is a strong significant positive correlation between Triglyceride (TG) Level with clinical diagnosis of ischemic heart disease (r=.171, p=0.01)

Table-V

Relationship of TG with clinical spectrum of ischemic heart disease (n= 431)

Clinical Spectrum of IHD	Triglyceride (TG) Level	
	r	p
IHD	.171**	.001

** . Correlation was significant at the 0.01 level (2-tailed).

Discussion:

The aim of the study was to find out the correlation of increased TG level on the severity of CAD in patients presenting with IHD. Lipid disorder was thought to be the main culprit behind the atherosclerosis but recent advances has suggested the role of inflammation and the underlying cellular and molecular mechanisms that contribute to atherogenesis.^{8,9,10} In this present study, it was observed that the age of the population ranged between 25 to 75 years, with a mean of 51.31 ± 10.3 years. Most of the patients were in 51- 60 years age group. Majority (74.5%) patients were male. Similar observation also found in other studies.^{11,12} In this study, among the risk factors, the highest 205 (47.6%) patients were smokers followed by hypertension 190 (44.1%), diabetes mellitus 175 (40.5%), family history of ischemic heart disease 88 (20.4%), 87 (20.27%) had previous history of angina. These findings were similar to the previous studies.¹¹⁻¹⁴ In this study out

of 431 patients, 113 (26.2%) patients had chronic stable angina, 60 (13.9%) had unstable angina, 74 (17.2%) had NSTEMI and 184 (42.7%) had STEMI. The present study shows that out of 431 patients, 124 (28.8%) had normal TG, 116 (26.9%) had borderline TG level and 191 (44.3%) had high TG level. Out of three groups most of the patients had high TG level. This study demonstrates that high TG levels are associated with severity of CAD. Our findings are also consistent with other studies.^{15, 16, 17} But the role of elevated TG as a CAD risk has been strongly debated for a long time. The exact level at which risk begins to increase is unclear. When lipid guidelines for CVD prevention first emerged, elevated TGs were defined as >250 mg/dL.¹⁸⁻²⁰ Subsequently the National Cholesterol Education Program Adult Treatment Panel to modify this definition to >150 mg/dL.^{21, 22} This new definition is consistent with trends observed for TGs in publications of the National Health and Nutrition Examination Survey.^{23, 25} The exact threshold above which CVD risk increases is less clear; other work has shown increasing risk with elevated TGs above 88 mg/dL and above 133 mg/dL.^{26, 27} Moreover, a growing body of evidence shows that TGs or more specifically, TG rich lipoproteins and their remnants, are indeed associated with an increased risk for atherosclerosis and CAD via different mechanisms including the excessive release of free fatty acids, the production of pro-inflammatory cytokines, fibrinogen and coagulation factors and impairment of fibrinolysis.^{15, 28, 29} The complexity of this entire issue and the many uncertainties and controversies regarding TGs as a risk factor for CAD have likely occurred because elevated TGs are very often associated with decreased HDL cholesterol and increase number of small, dense LDL particles which are considered highly atherogenic.³⁰ Other study showed that high TGs, even in subjects with favorable HDL cholesterol levels, may identify a subset of individuals at an increased risk for CAD.³¹ Some study showed that the macrovascular and microvascular changes are also associated with higher TGs levels in patients with type 2 Diabetes mellitus even in good control of LDL cholesterol, and also contributing in diabetic nephropathy and retinopathy.³² Most recent genetic studies showed that the causal association between TGs and cardiovascular disease especially those involving lipoprotein lipase and CVD risk.³³ In this study, it was observed that out of 431 patients, Gensini scoring revealed moderate stenosis in majority cases 213(49.42%), severe stenosis 99 (23%), and mild stenosis in 119 (27.6%) patients. In our study, while correlating increased TG level with the Gensini score, it was found that moderate to severe CAD was found higher

in high TG level group compared with the normal TG level groups and was statistically significant. Similar results were also observed by other studies.^{13, 15, 17, 34-36} Some study reported that increased TG may help to more adequately identify and better treat the highest risk of patients with atherosclerosis.^{12, 14} After considering the above scenario the increased TGs level are really a risk factor for CAD.

Conclusion

In conclusion our study showed that increased TGs level are predictors for CAD and provide additional information regarding the risk of presenting multi-vessels coronary stenosis.

References:

1. Cardiovascular diseases WHO World Health Organization 2021 doi: <https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-cvds>
2. Saquib N, Saquib J, Ahmed T, Khanam M. and Cullen MR. Cardiovascular diseases and type 2 Diabetes in Bangladesh. A systematic review and meta-analysis of studies between 1995 and 2010. BMC Public Health 2012;12(1):434.
3. Hamm CW, Bassand JP, Agewall S, Bax J, Boersma E, Bueno H, et al. ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. The Task Force for the management of acute coronary syndromes (ACS) in patients presenting without persistent ST-segment elevation of the European Society of Cardiology (ESC). European Heart Journal 2011; 32(23): 2999-3054.
4. Bouzidi N, Messaoud MB, Maatouk F, Gamra H, Ferchichi S. Relationship between high sensitivity C-reactive protein and angiographic severity of coronary artery disease. Journal of Geriatric Cardiology 2020; 17:256-63.
5. Oberman A, Kreisberg RA. Hypertriglyceridemia and Coronary Heart Disease. JCE & M 2000; 85(6):2098-2105.
6. Miller M, Seidler A, Moalemi A, Pearsom TA. Normal Triglyceride Levels and Coronary Artery Disease Events: The Baltimore Coronary Observational Long-Term Study. J Am Coll Cardiol 1998;31:1252-57.
7. Gensini Gu. A more meaningful scoring system for determining the severity of coronary artery disease. Am J Cardiol 1983; 51: 606.
8. Ross R. Atherosclerosis-an inflammatory disease. N Engl J Med 1999; 340: 115-26.
9. Libby P, Ridker P, Maseri A. Inflammation and atherosclerosis. Circulation 2002; 105: 1135-43.
10. Glass CK, Witztum JL. Atherosclerosis: the road ahead. Cell 2001; 104: 503-16.
11. Razbam MM, Eslamic M, Bagheradeh A. The relationship between serum levels of hs-CRP and coronary lesion severity. Clujul Medical 2016; 89(3): 352-64.
12. Muhammad R, Masood A, Zaffar J, Butt U. Correlation of Razbam MM, Eslami M, Bagherzadeh A. The relationship mean HbA1c

- levels with severity of coronary arteries disease in diabetics. *Pak Heart J* 2014; 47(4): 184-87.
13. Ahmed M, Islam MM, Rahman Ma, et al: Association of C-Reactive Protein and HbA1c in the Severity of Coronary Artery Disease in Patients with Ischemic Heart Disease. *Cardiovasc.j*.2018;11(1):53-58.
 14. Seyedian SM, Ahmadi F, Dabagh R, Davoodzadeh H. Relationship between high-sensitivity C-reactive protein serum levels and the severity of coronary artery stenosis in patients with coronary artery disease. *ARYA Atheroscler* 2016; 12(5): 231-37.
 15. Reiner Z: Are Elevated Serum Triglycerides Really a Risk Factor for Coronary Artery Disease? *Cardiology* 2015;131:225-27
 16. Roshan MM, Soltanipour S, Mirbolouk F et al. The Association between TG/HDL-C Ratio and Severity of Coronary Artery Disease in the North of Iran. *World heart journal* 2019;11(3).
 17. Haihang L, Dong Z, Changsheng M et al: Association of CRP Levels with the severity of Coronary Artery Disease. *Heart (British Cardiac Society)*. 2010 Castelli WP. Epidemiology of triglycerides: a view from Framingham. *Am J Cardiol*. 1992;70(19):3H-9H.
 18. Castelli WP. Epidemiology of triglycerides: a view from Framingham. *Am J Cardiol*. 1992;70(19):3H-9H.
 19. Assmann G, Schulte H. The Prospective Cardiovascular Munster (PROCAM) study: prevalence of hyperlipidemia in persons with hypertension and/or diabetes mellitus and the relationship to coronary heart disease. *Am Heart J*. 1988;116(6 Pt 2):1713-24.
 20. Assmann G, Schulte H, von Eckardstein A. Hypertriglyceridemia and elevated lipoprotein(a) are risk factors for major coronary events in middle-aged men. *Am J Cardiol*. 1996;77(14): 1179-84.
 21. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA*. 2001;285(19):2486-97.
 22. Stone NJ, Bilek S, Rosenbaum S. Recent National Cholesterol Education Program Adult Treatment Panel III update: adjustments and options. *Am J Cardiol*. 2005;96(4A):53E-59E.
 23. Miller M, Stone NJ, Ballantyne C, et al. Triglycerides and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation*. 2011;123(20):2292-2333.
 24. Carroll MD, Lacher DA, Sorlie PD, et al. Trends in serum lipids and lipoproteins of adults, 1960-2002. *JAMA*. 2005;294: 1773-81.
 25. Cohen JD, Cziraky MJ, Cai Q, et al. 30-year trends in serum lipids among United States adults: results from the National Health and Nutrition Examination Surveys II, II, and 1999-2006. *Am J Cardiol*. 2010;106(7):969-75.
 26. Pedersen SB, Langsted A, Nordestgaard BG. Nonfasting Mild-to-Moderate Hypertriglyceridemia and Risk of Acute Pancreatitis. *JAMA Intern Med*. 2016;176(12):1834-42.
 27. Lawler PR, Kotrri G, Koh M, et al. Real-world risk of cardiovascular outcomes associated with hypertriglyceridaemia among individuals with atherosclerotic cardiovascular disease and potential eligibility for emerging therapies. *Eur Heart J*. 2020;41(1):86-94.
 28. Navar AM. The evolving Story of Triglycerides and Coronary Heart Disease Risk. *JAMA* 2019; 321(4): 347-49
 29. Reiner Z, De Bacquer D, Kotseva K, Prugger C, De Backer G, Wood D; EUROASPIRE III Study Group: Treatment potential for dyslipidaemia management in patients with coronary heart disease across Europe: findings from the EUROASPIRE III survey. *Atherosclerosis* 2013;231:300-07
 30. Fruchart J-C, Sacks F, Hermans MP, et al: A call to action to reduce residual vascular risk in dyslipidemic patients. A position paper by the Residual Risk Reduction Initiative (R²I). *Diabetes Vasc Dis Res* 2008;4:319-35.
 31. Egeland GM, Iglund J, Sulo G, Nygard O, Ebbing M, Tel GS.: Non-fasting triglycerides predict incident acute myocardial infarction among those with favourable HDL-cholesterol: cohort Norway. *Eur J Prev Cardiol* 2014, E-pub ahead of print.
 32. Berk BC, Weintraub WS, Alexander RW. Elevation of C-reactive protein in "active" coronary artery disease. *Am J Cardiol* 1990; 65: 168-172.
 33. Liuzzo G, Biasucci LM, Gallimore JR, Grillo RL, Rebuzzi AG, Pepys MB, et al. The prognostic value of C-reactive protein and serum amyloid A protein in severe unstable angina. *N Engl J Med* 1994; 331: 417-24.
 34. Haverkate F, Thompson SG, Pyke SD, Gallimore JR, Pepys MB. Production of C-reactive protein and risk of coronary events in stable and unstable angina: European Concerted Action on Thrombosis and Disabilities Angina Pectoris Study Group. *Lancet* 1997; 349: 462-66.
 35. Tataru MC, Heinrich J, Junker R, Schulte H, von Eckardstein A, Assmann G, et al. C-reactive protein and the severity of atherosclerosis in myocardial infarction patients with stable angina pectoris. *Eur Heart J* 2000; 21:1000-1008.
 36. Masood A, Jafar SS, Akram Z. Serum high sensitivity C-reactive protein levels and the severity of coronary atherosclerosis assessed by angiographic ginsini score. *JPak Med Assoc* 2011; 61(4): 325-27.