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

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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 51.3±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.

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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).

| 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 ± SD                  | 51.31 ±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)

| 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).
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)

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 | Normal TG level | High TG level | P =.02 |
|---------------|-----------------|---------------|--------|
| 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. 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. 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. 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.

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