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ASSESSMENT OF TRIGLYCERIDE TO HIGH-DENSITY LIPOPROTEIN RATIO AS AN INDICATOR OF CORONARY ARTERY DISEASE AND ITS SEVERITY

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Contribution
NAS conceived the idea and designed the study. Data collection and manuscript writing was done by NAS, AK, MF, HA, JP, and KA. All the authors contributed equally to the submitted manuscript.

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ABSTRACT

Objectives: To evaluate the TG/HDL ratio test as a diagnostic tool for assessing the severity of CAD.

Methodology: This was a validation study conducted at the Indus Hospital, Karachi between March 2019 and March 2020. All patients irrespective of gender, aged above 18 years of age, who had chest pain or tightness radiating to the arms or shoulders, had shortness of breath, sweating or dizziness underwent an electrocardiogram (ECG) followed by coronary angiography in a catheterization lab were recruited in the study. Patients with a congenital heart disease or familial hyperlipidemia were excluded from the study. Lipid profiles were assessed by the principal author and were recorded in a predefined pro forma.

Results: The mean (SD) age of the subjects was 55.12 ± 9.93 years. A significant association of increasing TG/HDL ratio was observed with the severity of the illness ($p<0.0001$). The mean TG/HDL ratio was considerably varied in patients with mild to moderate, moderate to severe, and very severe disease from the control group and in the mean TG/HDL ratio of patients with mild to moderate from very severe disease patients ($p<0.05$).

Conclusion: The current study indicates a strong association of triglyceride to HDL-c ratio with severity of CAD. We recommend that TG/HDL ratio should be determined for CAD patients to assess the severity of CAD in addition to other lipoprotein products.

Keywords: coronary artery disease, cholesterol, High density lipoprotein, triglycerides

INTRODUCTION

Cardiovascular Disease (CVD) is a foremost cause of mortality globally. According to a recent report, cardiovascular diseases are estimated to increase substantially in the coming years.[1] Among them, Coronary artery disease (CAD) has been noted as the most vital cause. Numerous factors have been correlated with increased risk of CAD, including dyslipidemia. Dyslipidemia is defined as the irregular concentration of lipids and lipoproteins in the blood. Abnormally elevated levels of LDL-c (low-density lipoprotein), triglycerides (TG), and low level of HDL-c (high-density lipoprotein) have all been linked to coronary artery disease (CAD). HDL-c and TG are notable atherogenic markers and independent indicators of the disease.[2, 3]

More recently, it has been discovered that subfractions of lipid molecules also play a role in the progression of atherosclerosis. Smaller denser LDL-c molecules have more potential for atherogenesis compared to larger less dense particles. These heavier particles play significant role in disease progression. Similarly, the larger HDL2 particles which are less dense are protective while the smaller denser particles of HDL3 contribute in atherogenesis.[4, 5] The HDL2 correlates inversely with serum triglycerides and smaller denser LDL particle concentration.[6] The triglycerides concentration is inversely proportion to HDL-cholesterol ratio. Since carbohydrate is the vital component of diet among Pakistani population, therefore, high plasma levels of triglycerides and low levels of high-density lipoproteins (HDL-c) are a common consequential outcome. [7]

Furthermore, abnormally raised TG and low HDL-c contribute to metabolic syndrome and develops insulin resistance among patients. Both metabolic syndrome and insulin resistance are prevalent in South Asian countries and are major contributors of CAD in this region. [8]

Considering the importance of TG and HDL-c as non-invasive biomarkers in indicating the severity of the coronary artery disease, the current study was undertaken. This study evaluated the TG/HDL ratio test as an affordable and accessible diagnostic tool for assessing coronary artery disease and its severity in our local setting.

METHODOLOGY

This was a descriptive cross sectional study conducted at the Indus Hospital, Karachi between March 2019 and March 2020 for a duration of 12 months. The study was first approved by the ethical committee. All patients irrespective of gender, aged above 18 years of age, who had chest pain or tightness radiating to the arms or shoulders, had shortness of breath, sweating or dizziness underwent an electrocardiogram (ECG) followed by coronary angiography in a catheterization lab were recruited in the study.

Severity of coronary artery disease was documented using the Coronary Artery Surgery Study (CASS) classification and clinical inspection by the consultant cardiologist. Patients with a congenital heart disease or familial hyperlipidemia were excluded from the study. Informed verbal and written consent were obtained from the study participants. For laboratory parameters such as HDL, LDL, TG, etc., a disposable sterile syringe of 5 ml was used to extract blood from cubital vein after preparing a sterile site. The sample collected was sent immediately to laboratory for analysis. Blood samples were taken at the time of admission. All sociodemographic, clinical, and laboratory data were documented by the principal author in a predefined proforma.

The patients were divided into three groups according to the findings of coronary angiography. Group A i.e., the normal category presented the patients having normal coronary arteries, non-obstructive CAD, or CAD in any vessel less than < 70%, exclusive of the left coronary artery. Group B or the mild to moderate category presented data of patients with single vessel coronary artery disease (SVCAD) > 70% and left Main (LM) < 50%. Group C or the moderate to severe CAD category consisted of patients with a two vessel CAD (2VCAD) involving two vessel CAD >70%, left main (LM) < 50% or three vessel CAD < 70%. Finally, group D included the very severe CAD patients having a three vessel CAD (3VCAD) > 70%, LM>50%, or both.

Data were entered and analyzed using SPSS version 26.0. Mean ± SD were computed for age and TG/HDL ratio. Frequency and percentage were computed for gender and severity of disease. Statistical Package for Social Sciences (SPSS v. 26) was used to assess the association between the mean TG/HDL ratio and the severity of disease with post hoc analysis depending upon Levene's test of homogeneity. P for trend analysis was done to assess trend in TG/HDL ratio according to severity of disease. P-value<0.05 was considered significant.

RESULTS

A total of 2212 patients with coronary artery disease were recruited in the study. 1613 (72.9%) of these patients were male patients while 599 (27.1%) were female patients. The mean age of the patients was 55.12 ± 9.93 years. 1213/2212 (54.8%) patients had moderate to severe disease, 533/2212 (24.1%) patients suffered from very severe disease, 258 (11.7%) patients had mild to moderate disease, and 208 patients (9.4%) were normal (Table 1).

The mean TG/HDL ratio was significantly varied in patients with mild to moderate, moderate to severe, and very severe disease from the control group. A significant difference was observed in the mean TG/HDL ratio of patients who had mild to moderate CAD compared to those with very severe disease (p<0.05). However, no statistically significant difference was seen in the mean TG/HDL ratio between the patients with moderate to severe and those with very severe disease (Table 2).

Table 1: The Characteristics of the Study Population (n=2212)

Characteristics	N	%
Gender		
Male	1613	72.9
Female	599	27.1
Disease status		
Normal	208	9.4
Mild-Moderate	258	11.7
Moderate-severe	1213	54.8
Very severe	533	24.1

It was found that patients in Group C (moderate to severe) and D (very severe) had significantly higher TG/HDL ratios as compared to Group A (non-obstructive CAD); 5.4 ± 4.7 and 5.8 ± 5.3 vs 4.7 ± 2.9, with p-values of 0.02 and 0.002, respectively. Similarly, compared to mild-moderate disease, Group D (very severe) disease had significantly higher ratios of TG/HDL (p=0.006). However, there was no significant difference between Group C (moderate to severe) and Group D (very severe) (Table 2).

Table 2: Comparison of TG/HDL ratio among severity of disease

Severity of Disease	N	Mean	Std. Deviation	Minimum	Maximum
Normal	208	4.7	2.9	1.06	22.27
Mild-Mod	258	4.9	2.8	1.09	19.48
Mod-severe	1213	5.4	4.7	.78	98.00
Very severe	533	5.8	5.3	1.19	88.95
Total	2212	5.4	4.5	.78	98.00
	Multiple comparisons (P-value)				
	Normal	**Mild-Mod**	**Mod-severe**	**Very severe**	

Normal	-	0.924	0.02*	0.002*
Mild-Mod	-	-	0.076	0.006*
Mod-severe	-	-	-	0.404

DISCUSSION

Previous literature has revealed the association of CAD with abnormally high cholesterol levels. [3, 9, 10] In a study by Nikkila et al., it was found that serum triglyceride was a better indicator of coronary artery disease compared to the total body cholesterol level. [11] The serum triglyceride concentration was substantially higher in patients with CAD than their healthy counterparts. Abnormally elevated levels of triglyceride considerably varied in patients with a single-, double-, three-vessel disease and those without CAD however, the total level of cholesterol did not significantly differ among the coronary artery disease patients or the control group.

Even though there are no certain guidelines on the specific levels of TG in association with CAD, recent literature indicates a strong relationship between unbalanced serum triglycerides and increased incidence of CAD. [12]

In the current study we assessed the ratio of TG and HDL-c as an affordable test to determine the severity of CAD. The study revealed that the higher the TG/HDL ratio, the more severe the disease was. The association between the TG/HDL ratio and the severity of disease was statistically significant ($p<0.05$). We found a relationship of triglycerides to HDL-cholesterol as a strong independent gauge of the severity of the coronary disease.

The Strong Heart Study by Lee J et al., assessed the association between dyslipidemia and risk of coronary artery disease in a prospective longitudinal study on American Indians. [13] The study reported that low levels of serum HDL-c and high levels of triglycerides are associated with an increased [1.32 folds HR (95% CI 1.06–1.64)] risk of coronary heart disease. Another study by Hadaegh et al. reported similar findings indicating that Iranian men with TG/HDL-c ratio of higher than or equal to 6.9 (top quartile) had augmented risk of acquiring metabolic syndrome and chronic heart disease compared to those with lower ratio of TG/HDL-c. [14]

Considering the complex and labor-intensive methods of assessing the LDL subfractions which are technically advanced and not accessible, these tests are not commonly used in the clinical setting. Therefore, a cheap and easy test such as the TG/HDL-c ratio is a promising prospect in assessing the risk for cardiovascular disease and its severity among patients. [15-17] In an article, Ference et al., explored the correlation of variants that lower triglycerides in the lipoprotein lipase (LPL) gene and variants that lower low density lipoprotein (LDL) in the LDL receptor gene (LDLR) with the risk of cardiovascular disease (CVD). [18] It was found that the clinical outcome of lowering the serum concentration of TG was similar to lowering the low-density lipoprotein (LDL-c) levels in the plasma. In contrast, a secondary analysis of AIM HIGH Study revealed that the only plasma concentration of HDL3-c was inversely associated with cardiovascular events ($p=0.04$). The other lipoprotein fractions (HDL2-c, HDL-c, LDL-TG) were not significantly correlated with any cardiovascular events ($p>0.05$). [19]

It is important to advocate dietary and lifestyle modifications in patients who have a high TG to HDL-c ratio since both triglyceride and HDL-c are established predictors of adverse cardiac outcome. Our study findings also concur with the findings of previous studies signifying the relationship between dyslipidemia and increased risk of CAD. [20-23] Certain diets including medium-chain triglycerides have been shown to enhance satiety and hence decrease food intake. [24] Similarly, mild to moderate intensity exercise is another inexpensive method to control the triglyceride concentration as well as plasma HDL-c levels. [25]

In short, clinicians should recommend patients reduce the intake of saturated fats, carbohydrates, products with trans fatty acids, and increased intake of fruits and vegetables. Evidence has shown that improved diet and lifestyle modifications can slow coronary plaque progression, reduce the risk of cardiovascular disease, and lower the mortality rate.

In this study there were various limitations such as previous history and risk factors of patients was not known. We generalized all the patients according to SVCAD, 2VCAD, 3VCAD and LM (+/-) but overlooked proximal lesions of LAD, Ostial lesion or bifurcation or trifurcation lesions. It shows no significant comparison between moderate to severe and very severe disease because very severe lesions such as LM+ SVCAD, LM+2VCAD were included in mod to severe group.

CONCLUSION

The current study indicates a strong association between triglyceride to HDL-c ratio with severity of coronary artery disease (CAD). We recommend that TG/HDL ratio should be determined for CAD patients to assess the severity of coronary artery disease (CAD) in addition to other lipoprotein products.

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