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Original article

Serum TC/HDL-C, TG/HDL-C and LDL-C/HDL-C in predicting the risk of myocardial infarction in normolipidaemic patients in South Asia: A case-control study

Arun Kumar[1], Ramiah Sivakanesan[2]

[1] *Manipal College of Medical Sciences, Pokhara, Nepal*
[2] *Faculty of Medicine, University of Peradeniya, Sri Lanka*

Abstract

Dyslipidemia the major cause of atherosclerosis are suggested to act synergistically with non-lipid risk factors to increase atherogenesis. Low-density lipoprotein cholesterol (LDL-C) is the main therapeutic target in the prevention of CVD. Increased triglycerides (TG) and decreased high-density lipoprotein (LDL-C) are considered to be a major risk factor for the development of insulin resistant and metabolic syndrome. Although the TG/HDL-C ratio has been used in recent studies as a clinical indicator for insulin resistance, results were inconsistent. The TG/HDL-C ratio is also widely used to assess the lipid atherogenesis. How ever the utility of this rate for predicting coronary heart disease (CHD) risk is not clear. We encountered myocardial infarct patients with normal serum lipid concentration so this study was undertaken to evaluate the usefulness of these lipid ratios in predicting CHD risk in normolipidemic AMI patients and to compare the results with healthy subjects. The aim of the present study was to evaluate serum TC/HDL-C, TG/HDL-C and LDL-C/HDL-C in myocardial infarct subjects with normal lipid profile. To study this, lipid profile was determined in 165 normolipidemic acute myocardial infarction patients and 165 age/sex-matched controls. Total cholesterol, triglycerides, and HDL-cholesterol were analyzed enzymatically using kits obtained from Randox Laboratories Limited, Crumlin, UK. Plasma LDL-cholesterol was determined from the values of total cholesterol and HDL- cholesterol using the friedwalds formula. The values were expressed as means ± standard deviation (SD) and data from patients and controls was compared using students t-test. The results and conclusion of the study were: Total cholesterol, TC: HDL-C ratio, triglycerides, LDL-cholesterol, LDL: HDL-C ratio were higher in MI patients ($p<0.001$). HDL-C concentration was significantly lower in MI patients than controls ($p<0.001$). Higher ratio of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C was observed in AMI patients compared to controls.

Keywords: TC/HDL-C; TG/HDL-C; LDL-C/HDL-C; acute myocardial infarction; normal lipid profile

INTRODUCTION

Atherosclerosis begins in early life, especially in children and adolescents with high levels of low density cholesterol (LDL-C)[1]. It is recommended to conduct a full lipid profile on children and adolescents who present with a higher risk family history, including familial hypercholesterolemia, cardiovascular disease (CVD), Diabetes or early heart attack and stroke. Children and adolescents who are also overweight or obese should be screened[2]. Dyslipidemia the major cause of atherosclerosis are suggested to act synergistically with non-lipid risk factors to

Correspondence to: Dr. Arun KumarAssistant Professor, Department of BiochemistryManipal College of Medical Sciences, Pokhara, Nepalemail: arun732003@gmail.com

increase atherogenesis. Low-density lipoprotein cholesterol (LDL-C) is the main therapeutic target in the prevention of CVD. Indeed, more aggressive lowering of LDL-C levels by drugs and LDL-Apheresis is now being practiced in United States[3].

Dyslipidemia characterized by elevated TC, LDL-C and lowered HDL-C, is a conventional risk factor observed in myocardial infarction patients[4, 5, 6, 7, 8, 9, 10, 11]. Increased triglycerides (TG) and decreased high-density lipoprotein (LDL-C) are considered to be a major risk factor for the development of insulin resistant and metabolic syndrome. Although the TG/HDL-C ratio has been used in recent studies as a clinical indicator for insulin resistance, results were inconsistent. The TG/HDL-C ratio is also widely used to assess the lipid atherogenesis. However the utility of this rate for predicting coronary heart disease (CHD) risk is not clear. Since we have encountered myocardial infarct patients with normal serum lipid concentration, this study was undertaken to evaluate the usefulness of these lipid ratios in predicting CHD risk in normolipidemic AMI patients and to compare the results with healthy subjects.

MATERIALS AND METHODS

Setting design and patients

The study consisted of 165 patients (123 men and 42 women) with AMI, admitted to the intensive cardiac care unit, Sharda hospital, India. The diagnosis of AMI was established according to diagnostic criteria: chest pain, which lasted for $\leqslant$ 3 hours, ECG changes (ST elevation of $\geqslant$ 2 mm in at least two leads) and elevation in enzymatic activities of serum creatine phosphokinase and aspartate aminotransferase. The control group consisted of 165 age/sex-matched healthy volunteers (123 men and 42 women). The design of this study was pre-approved by the institutional ethical committee board of Chaudhary Charan Singh University, and informed consent was obtained from the patients and controls.

Inclusion criteria were patients with a diagnosis of AMI with normal lipid profile. Patients with diabetes mellitus, renal insufficiency, current and past smokers, hepatic disease or taking lipid-lowering drugs or antioxidant vitamin supplements were excluded from the study. Normolipidemic subjects was judged by the following criteria: LDL <160 mg/dl, HDL $\geqslant 35$ mg/dl, Total cholesterol (TC), <200 mg/dl; and triglycerides (TG), <150 mg/dl[12]. Ten milliliters of blood was collected after overnight fasting for lipid profile.

Lipid profile TC, TG, and HDL-cholesterol were analyzed enzymatically using kits obtained from Randox Laboratories Limited, Crumlin, UK. Plasma LDL-cholesterol was determined from the values of total cholesterol and HDL- cholesterol using the following formula[13]:

$$\text{LDL-cholesterol} = \text{TC} - \frac{\text{TG}}{5} - \text{HDL-cholesterol}$$

(mg/dl)

RESULTS

Serum parameters in AMI patients and control are shown in Table 1. Total cholesterol, its ratio to HDL-cholesterol (TC/HDL-C), LDL-cholesterol, triglycerides was significantly higher in AMI patients compared with control (Table 1-2). Significant difference for HDL-cholesterol between AMI and control was observed (Table-1). On the other hand, LDL-cholesterol and its ratio to HDL-cholesterol (LDL-C/HDL-C) were higher in patients compared with controls (Table-1). No statistically significant difference was observed in TG/HDL-C ratio among patients with controls. Also, significantly lower HDL-C concentration was observed in AMI patients than in the controls ($p<0.001$). Lowering of HDL-cholesterol is a known phenomenon in MI subjects[11].

The analysis based on the ratio of TC/HDL-cholesterol, TG/HDL-cholesterol and LDL-cholesterol/HDL-cholesterol is shown in Table-2. Higher ratio of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C was observed in AMI patients compared to controls.

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Table 1: lipid profile in patients and healthy controls (mean ± SD)

Variables	Controls(n=165)	Patients(n=165)	P-value (95% CI)
Age	60.55±3.98	61.84±3.80	0.0037(61.26-62.42)
Total Cholesterol	168.58±12.16	186.44±13.95	<0.001(184.31-188.56)
HDL-Cholesterol	50.51 ± 6.78	41.27 ± 4.62	<0.001(40.56-41.97)
TC: HDL-C*	3.39 ± 0.36	4.57 ± 0.58	<0.001(4.48-4.65)
Triglycerides	107.84 ± 11.51	128.96 ± 12.19	<0.001(127.10-130.82)
LDL-Cholesterol	83.59 ± 11.95	119.37 ± 14.05	<0.001(17.22-21.51)
LDL:HDL-C*	1.90 ± 0.31	2.93 ± 0.51	<0.001(2.85-3.00)
TG: HDL-C*	2.17 ± 0.35	3.16 ± 0.49	0.3149(3.086-3.234)

* ratio ? (mg %)

Table 2: Distribution pattern of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C ratio in patients and healthy controls (mean ± SD)

Ratio	Controls(n=165)	Patients(n=165)
TC/HDL-C		
2-3	2.90 ± 0.09(n=28)‖	
-3-4	3.44 ± 0.25(n=129)	3.70 ± 0.20(n=31)
4-5	4.19 ± 0.22(n=8)	4.53 ± 0.27(n=90)
5-6	–	5.26 ± 0.23(n=44)
TG/HDL-C		
1-2	1.77 ± 0.13(n=56)	
-2-3	2.38 ± 0.23(n=109)	2.65 ± 0.27(n=59)
3-4	–	3.42 ± 0.26(n=99)
4-5	–	4.22 ± 0.19(n=7)
LDL-C/HDL-C		
1-2	1.71 ± 0.17(n=106)	1.86 ± 0.15(n=5)
2-3	2.23 ± 0.21(n=59)	2.57 ± 0.27(n=81)
3-4	–	3.32 ± 0.21(n=74)
4-5	–	4.11 ± 0.12(n=5)

DISCUSSION

The MI patients for the present study were selected with normal lipid profiles, but their mean serum TC concentration was significantly higher ($p<0.001$) than the controls (Table 1). Goswami, et al., in 2003 14) conducted a study on lipid profiles of normal individuals in the age group 21-70 years in Kolkata. Their study observed mean TC to be 189.7 mg/dl which was 12.5% higher than controls (168.6 mg/dl) of the present study. Earlier studies conducted[15] on coronary heart disease patients with respect to lipid profiles compared to the controls. The mean serum TC levels observed was 196.6 mg/dl which was 5.3% higher than the present study, but no significant difference was observed.

A retrospective study conducted[6] on the association of modifiable risk factor among patients with CAD, observed higher TC (194.6 mg/dl) compared to controls, which was similar to the findings of the present study.

In a study conducted[16] on the lipid profile pattern in MI patients was 215.7 mg/dl which was 15% higher compared to the present study. Another study conducted[10] on lipid profile parameters in patients of coronary artery disease, observed a higher TC lev-

els (206.2mg/dl) compared to the present study. In another study conducted[17] on lipid profile pattern in CHD patients, showed higher TC compared to the present study. Sivaraman, et al., (2004)[18] evaluated lipid profile in patients of acute coronary syndromes. The study observed higher levels of TC (199.8 mg/dl) as observed in the present study and the differences in lipid profile parameters was significant ($p < 0.001$) when compared to healthy controls.

In another study conducted[4] on lipid profile in young patients with angiographically proven CAD. The aim of their study was to analyze the lipid profile in young patients with CAD. They observed higher mean serum TC levels and the differences was highly significant ($P < 0.001$). The reported findings were coinciding with the findings of the present study.

Study conducted[19] on MI patients, observed lower TC 181 mg/dl compared to the present study. The difference in values was significant ($P < 0.05$). The present study also observed a higher TC levels in MI patients and the differences was highly significant ($P < 0.0001$). In another study[8] determined the lipid profile and their association with CHD in South Indian population. They observed lower TC (179.5 mg/dl) in CHD patients compared to the present study. Kharb[20] studied the lipid profile in AMI patients and observed lower levels of TC (179 mg/dl) compared to the present study. In another study (Das, et al., 2002)[21] determined the lipid profile in CAD patients. Their study observed significantly higher levels of TC (200 mg/dl) in CAD patients compared to the current study. The findings of the present study was also agreeable to the findings of the above mentioned studies where the present study also observed a significantly higher levels of TC in MI patients compared to the healthy controls even the present study all the patients with myocardial infarction were within the normal TC levels.

Observations of serum high density cholesterol (HDL-C)

The mean serum HDL-C observed in MI patients in the present study was 41.3 mg/dl compared to the controls (50.5 mg/dl) and was significant ($p < 0.001$). Study conducted[14] on lipid profiles of normal individuals in the age group 21-70 years in Kolkata. Their study observed mean serum HDL-C to be 52.9 mg/dl which was 28.1% higher than controls (41.3mg/dl) of the present study. The present study found the results to slightly vary from the observations of Goswami, et al., (2004)[14]. It could be due to differences in sample size as the previous study was conducted on a large population of 1396 subjects and with varied age from 21-70 years compared to present study where 330 subjects including patients and controls. Moreover our subjects had higher range from 48-69 years. Earlier studies conducted[15] on lipid profile pattern in coronary heart disease patients observed mean serum HDL-C was 39.5 mg/dl which was almost similar to the observed values of the present study and no significant difference was observed. A retrospective study conducted[6] on the association of modifiable risk factor among patients with CAD, the mean serum HDL-C observed in patients was 42.11 mg/dl was 2% higher compared to the present study.

The HDL-C levels observed in the present study are similar to those of the earlier studies conducted elsewere[10,16,18].

In another study conducted[4] on Lp(a) and lipid profile in young patients with angiographically proven CAD. The aim was to analyze the lipid profile in young patients with CAD. The mean serum HDL-C levels were almost similar to the findings of the current study.

Even the studies conducted[19, 8, 20, 21] also showed lower HDL-C levels in MI patients compared to controls which was similar to present study. The observations made from all the above mentioned studies in MI patients reveals that HDL-C levels is drastically lowered in MI patients which could be an additional risk for patients.

Observations of TC/ HDL-C ratio

In the present the TC/HDL-C ratio observed in MI patients was 35.3% higher compared to controls, showing 4.6 in MI patients and controls showing 3.4. The differences in the ratio between MI patients and the controls was highly significant ($P < 0.001$) (Table 1).

Goswami, et al., in 2003[14] conducted a study on lipid profiles of normal individuals in the age group 21-70 years in Kolkata. They observed the TC/HDL-C ratio 3.6 which was almost similar to the controls of the present study.

Earlier studies conducted[15] on coronary heart disease patients with respect to lipid profiles com-

pared to the controls, the ratio of TC/HDL-C observed was 3.8 in MI patients which were lower than the ratio observed in the present study. A retrospective study conducted [6] on the association of modifiable risk factor among patients with CAD, observed TC/HDL-C ratio 4.6 in patients, which was similar to the findings of the present study. In a study conducted[16] on the relationship of plasma homocysteine and lipid profiles in MI patients, observed TC/HDL-C ratio 5.2 which was higher than the present study. Another study conducted[10] on lipid profile parameters in patients of coronary artery disease, observed TC/HDL-C ratio 4.8 which was almost similar to the ratio observed in the present study. Sivaraman, et al., (2004)[18] evaluated lipid profile in patients of acute coronary syndromes. The study observed TC/HDL-C ratio 5.3 which was higher than the ratio observed in the present study.

Study conducted[19] on MI patients, observed TC/HDL-C ratio 4.7 in patients which was similar to the present study. In another study[8] determined the lipid profile and serum antioxidant levels and their association with CHD in South Indian population. They observed TC/HDL-C ratio 5.1, which was higher than the ratio observed in the present study. Kharb (2003)[20] studied the lipid profile in AMI patients and observed TC/HDL-C ratio 4.6, similar to the observations of the present study. The ratio of TC/HDL-C is crucial in determining the risk of cardiovascular problems as observed from the findings of the above mentioned studies. These observations regarding the HDL-C and TC:HDL-C ratio thus emphasis the fact that despite subjects maintaining normal concentration of total cholesterol, low HDL-C and elevated ratio are more than adequate to increase the risk of developing MI. Thus an individual with normal serum total cholesterol concentration cannot be content of being free of cardiovascular problems.

Observations of Triglycerides (TG)

The Triglycerides (TG) values observed in MI patients was 129 mg/dl which was 21% higher than controls (107.8 mg/dl). Goswami, et al., in 2003[14] on lipid profiles study in normal individuals in the age group 21-70 years in Kolkata, observed the mean serum TG (132 mg/dl) which was almost similar to the present study. Earlier studies conducted[15] on coronary heart disease patients with respect to lipid profiles compared to the controls. The mean serum TG observed in MI patients was 157.8 mg/dl which was 22.3% higher than the observed TG levels of the present study. In a study conducted[16] on the relationship of plasma homocysteine and lipid profiles in MI patients, the mean serum TG levels observed was 152.8 mg/dl which was 18% higher than the mean serum TG levels observed in the present study.

Sivaraman, et al., (2004)[18] evaluated lipid profile in patients of acute coronary syndromes. The study observed similar TG levels (125.9 mg/dl) compared to the present study. Study conducted[19] on MI patients, observed the mean serum TG in patients was 149 mg/dl which was 15.5% higher than the TG levels observed in the present study. In another study[8] determined the lipid profile and serum antioxidant levels and their association with CHD in South Indian population. The mean serum TG observed in MI patients was 140.5 mg/dl which was 8.5% higher than the TG levels of the present study. Kharb (2003)[20] studied the lipid profile in AMI patients and observed 12.4% higher levels of TG (145 mg/dl) compared to the present study. In all the above mentioned study it was observed that the TG levels were higher in MI patients compared to healthy controls and similar findings was also observed in the present study.

Observations of Low density lipoprotein cholesterol (LDL-C):

The mean serum LDL-C in MI patients was 119.4 mg/dl which was 42.8% higher compared to controls (83.6 mg/dl). Goswami, et al., in 2003[14] conducted a study on lipid profiles of normal individuals in the age group 21-70 years in Kolkata. The mean serum LDL-C observed in their study was 115.6 mg/dl which was 30.4% higher than the LDL-C levels (83.6mg/dl) observed in the present study. The variations in the fining of the present study could be due to differences in sample size as the previous study[14] was conducted on a large population of 1396 subjects and with varied age from 21-70 years compared to present study where 330 subjects including patients and controls. Moreover our subjects had higher range from 48-69 years. Earlier studies conducted[15] on lipid profile pattern on coronary heart disease patients compared to the controls. The

mean serum LDL-C levels observed was 117.2 mg/dl which was similar to the findings of the present study. A retrospective study conducted[6] on the association of modifiable risk factor among patients with CAD, the mean serum LDL-C observed was 130 mg/dl which higher 8.7 % higher than LDL-C levels observed in the present study. In another study conducted[16] on the relationship of plasma homocysteine and lipid profiles in MI patients, observed LDL-C levels to be 110.3 mg/dl which was slightly lower than present study. Another study conducted[10] on lipid profile parameters in patients of coronary artery disease, the mean serum LDL-C observed was 107.7 mg/dl which was also slightly lower than LDL-C levels observed in the present study. Sivaraman, et al., (2004)[18] evaluated lipid profile in patients of acute coronary syndromes also observed 15% higher mean serum LDL-C levels (137.1 mg/dl) compared to the present study. In another study[8] determined the lipid profile and serum antioxidant levels and their association with CHD in South Indian population. The mean serum LDL-C levels observed in their study were 113.1 mg/dl which was similar to the present study. Observations from the above mentioned studies reveal that the LDL-C concentration to be higher in MI patients compared to controls.

Observations of LDL-C/HDL-C ratio

The LDL-C/HDL-C ratio in MI patients was 2.9, which were 52.6% higher than controls (1.9). Goswami, et al., in 2003[14] conducted a study on lipid profiles of normal individuals in the age group 21-70 years in Kolkata. The LDL-C/HDL-C ratio observed in their study was 2.2 which were 15.8 % higher than the LDL-C/HDL-C observed among the controls of the present study. Earlier studies conducted[15] on lipid profile among coronary heart disease patients compared to the controls, observed LDL-C/HDL-C ratio 3.0 which was almost similar the findings of the present study. A retrospective study conducted[6] on the association of modifiable risk factor among patients with CAD, observed LDL-C/HDL-C ratio 3.1 which was slightly higher than the values observed in the present study. In a study conducted[16] on the relationship of plasma homocysteine and lipid profiles in MI patients, observed LDL-C/HDL-C ratio 2.3 which was 26% higher than the observations of the present study. Another study conducted[10] on lipid profile parameters in patients of coronary artery disease, the LDL-C/HDL-C ratio 2.0 which was 45% lower than the ratio observed in the present study.

In another study[8] determined the lipid profile and serum antioxidant levels and their association with CHD in South Indian population. The LDL-C/HDL-C ratio observed in their study was 3.3 which 13.8% higher than the observed ratio of the present study. In another study[21] determined the antioxidants and lipid profile in CAD patients. The LDL-C/HDL-C ratio observed was 2.6 which was 1.2% lower than observed in the present study. Observations made from the above studies reveal a lower ratio of LDL-C/HDL-C is beneficial and it is indicative of atherogenic lipid profiles. The higher the ratio the higher is the risk of MI or any cardiovascular disease.

Observations of TG/HDL-C ratio:

The mean TG/HDL-C ratio in MI patients was 3.2 which were 45.5% higher than controls (2.2). Goswami, et al., in 2003[14] conducted a study on lipid profiles of normal individuals in the age group 21-70 years in Kolkata. The study observed mean TG/HDL-C ratio 2.5 in controls which was slightly higher than the ratio observed in the present study. The variations could be due to differences in sample size as the previous study was conducted on a large population of 1396 subjects and with varied age from 21-70 years compared to present study where 330 subjects including patients and controls. Moreover our subjects had higher range from 48-69 years. Earlier studies conducted[15] on coronary heart disease patients with respect to Lp(a) and lipid profiles compared to the controls. The mean TG/HDL-C ratio observed in patients was 4.0 which were 25% higher than the ratio observed in the present study. In a study conducted[16] on the relationship of plasma homocysteine and lipid profiles in MI patients, the observed mean TG/HDL-C ratio was 3.6 which was 12.5% higher than the observations of the present study. In another study conducted[17] on lipid profile pattern in CHD patients, the mean TG/HDL-C ratio observed was 3.9 which was 22% higher than the ratio observed in the current study. Sivaraman, et al., (2004)[18] evaluated lipid profile in patients of

acute coronary syndromes. The mean TG/HDL-C ratio observed in the study was 3.3 which were almost similar to the present study.

Study conducted[19] on antioxidants and lipid profile pattern in MI patients, the observed mean TG/HDL-C ratio was 3.9 which were 22% higher than the observations of the present study. In another study[8] determined the lipid profile and serum antioxidant levels and their association with CHD in South Indian population. The observed mean TG/HDL-C ratio was 4.0 which were 25% higher than the current study. Kharb (2003)[20] studied the lipid profile in AMI patients; the mean TG/HDL-C ratio observed in their study was 3.7 which was 15.6% higher ratio than observed in the current study. In another study[21] determined the lipid profile in CAD patients, the observed mean TG/HDL-C ratio was 4.2 and it was 31.2% higher than the ratio observed in the present study.

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