

# Serum lipid profile abnormality in predicting the risk of myocardial infarction in elderly normolipidaemic patients in South Asia: A case-controlled study

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## Abstract

**BACKGROUND:** The major cause of atherosclerosis, dyslipidaemic, acts synergistically with non-lipid risk factors resulting increase in atherogenesis. Increased (TG) and decreased high-density lipoprotein (HDL-C) and the increased TG/HDL-C ratio are considered as major risk factors in the development of Insulin resistance and metabolic syndrome. The accuracy of TG/HDL-C ratio in predicting coronary heart disease (CHD) risk is not properly established by recent research.

**AIM:** The study was undertaken to evaluate the usefulness of lipid ratios TC/HDL-C, TG/HDL-C and LDL/HDL-C in predicting CHD risk in normolipidaemic patients with myocardial infarction and to compare the results with healthy subjects.

**SETTING & DESIGN:** Lipid Profile was determined in 165 normolipidaemic Acute Myocardial Infarction patients and compared them with 165 age/sex-matched controls.

**MATERIAL & METHODS:** 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 friedwald's formula.

**STATISTICS:** The values were expressed as means  $\pm$  standard deviation (SD) and data from patients and controls was compared using students 't'-test.

**RESULTS AND CONCLUSION:** Total cholesterol, TC/HDL-C ratio, Triglycerides, LDL-cholesterol, LDL-C/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.

## 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 of 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 characterized by elevated TC, LDL-C and lowered HDL-C, is a conventional risk factor observed in myocardial infarction patients (3,4,5,6,7,8,9,10) and is 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. Indeed, more aggressive

lowering of LDL-C levels by statins and LDL-Apheresis is now being practiced in United States (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 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 ratio for predicting coronary heart disease (CHD) risk is not clear. Since we have encountered myocardial infarction patients with normal serum lipid concentration, this study was undertaken to evaluate the usefulness of these lipid ratios in predicting CHD risk in normolipidaemic AMI patients and to compare the results with healthy subjects.

**MATERIALS AND METHODS**

Setting Design and Patients: The study consisted of 165 elderly patients between 48-69 years (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 ≤ 3 hours, ECG changes (ST elevation of ≥ 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 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.

Normolipidaemic subjects were judged by the following criteria: LDL <130 mg/dl, HDL ≥ 35 mg/dl, Total cholesterol (TC), <200 mg/dl; and triglycerides (TG), <150 mg/dl. 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<sup>13</sup>:

**Figure 1**

$$\text{LDL-cholesterol} = \frac{\text{TC} - \text{TG} - \text{HDL-cholesterol}}{5} \text{ (mg/dl)}$$

**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 1-2). 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).

The analysis based on the ratio of TC/HDL-cholesterol, TG/HDL-cholesterol and LDL-cholesterol/HDL-cholesterol is shown in Table-3. Higher ratio of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C was observed in AMI patients compared to controls (Table 2-3).

**Figure 2**

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)
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)

\* ratio † (mg %)

**Figure 3**

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

Variables	Controls (n=165)	Patients (n=165)	P-value (95%CI)
TC: HDL-C*	3.39 ± 0.36	4.57 ± 0.58	<0.001(4.48-4.65)
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 %)

**Figure 4**

Table 3: Distribution pattern of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C ratio in patients and healthy controls (mean  $\pm$  SD)

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

## DISCUSSION

### OBSERVATIONS OF TOTAL CHOLESTEROL

The lipid profile pattern in normolipidaemic patients with AMI and normal healthy control were studied and the variation in patterns was compared. The mean TC level of the control subjects compared with AMI (186.44  $\pm$  13.95 mg/dl) was significantly ( $p < 0.001$ ) greater than that of subjects without AMI (168.58  $\pm$  12.16 mg/dl).

A previous study have observed a greater value (189.70 mg/dl) for TC than the controls of the present study (Goswami, et al., 2003)<sup>14</sup>). In a study of MI patients<sup>15</sup>) a mean TC level of (196.60 mg/dl) was reported and it was 5.3% higher than the TC of MI patients of the present study.

Higher values for TC (196.60 mg/dl)<sup>15</sup>) and (215.70 mg/dl)<sup>16</sup>) have been reported by previous studies in AMI patients than the subjects without AMI. These values were 5.3% and 15% greater than the values reported in the present study for MI patients.

The TC levels observed (199.80 mg/dl) were slightly higher than the present study have been reported by Sivaraman et

al., 2004<sup>17</sup>) in patients with acute coronary syndrome. They also reported a significant higher values ( $p < 0.001$ ) when compared to the controls in their study.

Similarly, significant differences ( $p < 0.001$ ) were observed in young CAD patients compared with control<sup>3</sup>). The result of the present study was in agreement with their observation.

Lower levels of TC (181mg/dl) in MI patients than observed in the present study have been reported by Shindhe, et al., 2005<sup>18</sup>), Rajashekhar, et al., 2004<sup>7</sup>) and Kharb, et al., 2003<sup>19</sup>) in studies on Indian population.

Though the TC levels of the subjects selected in the present study were within the normal lipid profile, the mean levels of TC in MI subjects was greater in the present study and it was in agreement with the observations of the previous studies though they have reported greater or lower levels of TC in subjects with MI than the TC levels in the present study.

### OBSERVATIONS OF HIGH DENSITY LIPOPROTEIN-CHOLESTEROL

The mean serum HDL-C level observed in patients with MI in the present study (41.3 mg/dl) was significantly lower ( $p < 0.001$ ) than the values observed in controls (50.5mg/dl). In a study on normolipidaemic subjects in the age group 21-70 years it has been reported mean HDL-C levels of 52.9 mg/dl, which is 28.1% higher than the observations of the present study<sup>14</sup>).

HDL-C levels similar to the present study have been reported (39.5mg/dl)<sup>15</sup>) (42.11mg/dl)<sup>6</sup>) in patients with heart disease. Similar levels of HDL-C was reported in many studies<sup>4,10,16,18</sup>). Therefore, most of the research evidences supported drastic lowering of HDL-C levels in AMI patients.

### OBSERVATIONS OF TRIGLYCERIDES

Triglyceride (TG) values observed in MI patients was (129mg/dl) significantly higher when compared with controls (107.8mg/dl). A similar level of TG have been reported<sup>14,18</sup>) in normolipidaemic AMI patients as observed in the present study. However 22.3% and 18% higher levels of HDL-C in MI patients was observed and reported by coworkers<sup>15,16</sup>) respectively.

Furthermore, significantly higher levels of TG (149 mg/dl) (15.5%)<sup>19</sup>) and (140.5 mg/dl) 8.5%<sup>8</sup>) have been observed compared with the observations of the present study.

The findings of the above data confirms that elevated TG levels are associated with the incidence of heart diseases and that is even so when they are within the normal levels.

### **OBSERVATIONS OF LOW DENSITY LIPOPROTEIN-CHOLESTEROL**

The mean serum level of LDL-C in the patients was (119.4mg/dl) significantly greater than control (83.6 mg/dl). In a study of healthy subjects with age group of 21-70 years, significantly higher value was reported and it was very much similar to the LDL-C level of the MI patients of the present study <sup>14</sup>).

In the studies of patients with a history of MI, greater values were reported by several researchers <sup>6,18</sup>) where as some have reported <sup>10</sup>) lower values of LDL-C than the present study. However similar levels of LDL-C in MI patients were also reported in several studies <sup>8,15,16</sup>)

### **OBSERVATIONS OF TC/HDL-C RATIO**

The TC/HDL-C ratio in MI patients (4.6) was significantly ( $p<0.001$ ) higher compared with controls (3.4). Similar TC/HDL-C ratio (3.6) has been observed in normolipidaemic subjects of the age group 21-70 years by Goswami, et al., 2003 <sup>14</sup>). Lower ratio of TC/HDL-C were observed in AMI patients in study conducted elsewhere <sup>15</sup>).

Similar ratio (4.6) was reported in MI patients by study conducted elsewhere <sup>10,16,19,20</sup>). Higher ratio compared to the present study has been reported in MI patients <sup>8,16,18</sup>). A cut of level of 3.3 has been suggested <sup>12</sup>).

These data indicate though the TC levels were within the normal level; the TC/HDL-C ratio was elevated significantly in MI patients indicating the importance of assessing TC/HDL-C ratio even in normolipidaemic subjects.

### **OBSERVATIONS OF LDL-C/HDL-C RATIO**

Increased LDL-C and reduced HDL-C are considered to be highly atherogenic. Thus the increased level of LDL-C/HDL-C would indicate an increased risk of developing atherosclerosis. A cut of level of 1.6 has been suggested <sup>12</sup>).

The present study observed significantly higher ratio (2.9) in AMI patients compared with control (1.9).

Results reported on the ratio were inconsistent, as some studies reported higher ratios <sup>6,15</sup>), similar ratio <sup>15</sup>) and lower ratios <sup>21</sup>) of LDL-C/HDL-C compared to the present study.

### **OBSERVATIONS OF TG/HDL-C RATIO**

Increased TG and decreased HDL-C are also thought to be atherogenic and thus increased ratio of TG/HDL-C would indicate an increased atherogenic risk. The present study observed significantly ( $p<0.001$ ) higher ratio (3.2) in MI patients compared with control (2.2). A slightly higher ratio (2.5) has been reported in healthy subjects earlier <sup>14</sup>). The data reported in previous studies in MI patients were inconsistent to the present study. Some studies have reported higher ratios <sup>8,15,16,17,19, 21</sup>) whereas some reported similar ratios as observed in our study <sup>18</sup>). As per NCEP ATP-111 a cut of level of 2.5 has been suggested <sup>12</sup>).

The present study concludes the importance of assessing the lipid ratios even in a normal individual as it is one of the atherogenic factors for development of myocardial infarction and other coronary complications. The practice of computing the ratio should be practiced even in a normal health check up packages.

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