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Lipid ratio useful indicator in predicting risk of myocardial infarction in elderly normolipidemic patients: a report from a multi center study

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ABSTRACT

Objective: To evaluate the usefulness of lipid ratios in predicting coronary heart disease risk in normolipidaemic myocardial infarct (MI) patients and compare the findings with healthy controls. **Methods:** Lipid profile was determined in 1 021 normolipidaemic myocardial infarct patients and was compared with 1 021 age/sex-matched controls. Total cholesterol (TC), triglycerides (TG) and HDL-cholesterol (HDL-C) were analyzed enzymatically using kits obtained from Randox Laboratories Limited, Crumlin, UK. Plasma LDL-cholesterol (LDL-C) was determined from the values of TC and HDL-C using the friedwald's formula. The values were expressed as mean±SD and data from patients and controls were compared using students´ *t*-test. **Results:** TC, TC/HDL-C ratio, TG, LDL-C, 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 acute myocardial infarct patients as compared with controls. **Conclusions:** Establishment of lipid ratio from routine lipid profile assay could be very useful in predicting the future risk of acute mocardial infarction.

1. Introduction

Coronary heart disease (CHD) is still the leading cause of morbidity and mortality in the general population[1]. It is the leading cause of hospital deaths among adults in Asia and the number of deaths due to cardio vascular disease (CVD) has increased from 5.6 per 100 000 population in 1970 to 18.2 in 1992[2] and further is on the rise. This alarming increase implies a future increase in the financial burden associated with this disease and raises the possibility that age-adjusted death rates from coronary artery disease would be increased[3].

Autopsy studies have shown that early coronary atherosclerosis often begins in childhood and adolescence[4]. Further, hypercholesterolemia in adolescents correlated positively with changes in vasculature predictive of later CVD[5]. There is a tendency to persistence in ranks (tracking) for serum total and B-lipoprotein cholesterol with age[6].

Hypercholesterolemia in childhood is common in western countries with high rates of CHD[5]. India and Sri Lanka stand as a classical example to illustrate drastic changes that occur in societies during the industrialization and urbanization or the westernization of these countries[7].

The parental obesity influences childhood obesity through a mixture of genetic and environmental mechanisms[8]. Children with obese family members are several folds more likely to be obese, having increased preferences for high fat foods[9], but decreased physical activity[10] themselves than children whose family members are lean. Furthermore, adolescents with extreme obesity (BMI>40 kg/m^2) have significantly heavier parents than those with class I or II obesity (BMI<40 kg/m^2)[11].

It has been found that maternal obesity is the most significant predictor of obesity during childhood[12]. Thus the combination of having an obese mother and an earlier onset of obesity leads to higher BMI and weight at young adulthood[13].

Furthermore, adolescent obesity is associated with increased mortality and morbidity related to a variety of chronic diseases later in life and also reversal of obesity is associated with decreased metabolic risk in adulthood[11].

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Since the phenomenon of obesity, atherosclerosis and lipid profile act in conglomeration in causation of myocardial infarction (MI) which begins in early life, especially in children and adolescents with high levels of low density lipoprotein cholesterol (LDL-C)[14]. It is thereby recommended for every individual check their lipid profile at six-monthly intervals to categorize and alarm those individuals and families who present with a higher lipid ratio so that the future risk of MI can be well managed. Children and adolescents who are also overweight or obese should be screened[15]. Dyslipidemia characterized by elevated total cholesterol (TC), LDL-C and lowered high density lipoprotein cholesterol (HDL-C), is a conventional risk factor observed in myocardial infarction patients[16-18] and is the major cause of atherosclerosis. Our main aim in therapeutic target is to lower the LDL-C so that CVD could be efficiently prevented. In fact, these days more aggressive lowering of LDL-C levels by statins and LDL-apheresis is currently being practiced in the United States[19].

Increased triglycerides (TG) and decreased HDL-C are considered to be a major risk factor for the development of insulin resistant and metabolic syndrome in South Asians. Although the TG/HDL-C ratio has been used as a clinical indicator for insulin resistance, results shown were inconsistent. The TG/HDL-C ratio is also widely used to assess atherogenic lipid. However, the utility of this ratio for predicting CHD risk still needs to be established. Since we have encountered MI patients with normal serum lipid profile, this study was undertaken to evaluate the usefulness of these lipid ratios in predicting CHD risk in normolipidaemic acute myocardial infarction (AMI) patients and to compare the results with healthy subjects.

2. Materials and methods

The study consisted of 1 021 elderly patients between 47-71 years (754 men and 267 women) with AMI were admitted to the Intensive Coronary Care Unit in Corporate Hospitals in India, Nepal and Sri Lanka. 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 1 021 age/sex-matched healthy volunteers (754 men and 267 women). The design of this study was approved by the Institutional Ethical Committee Board of the hospital, 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 $\geqslant$35 mg/dL, TC <200 mg/dL and TG <150 mg/dL[20]. Ten milliliters of blood were collected after overnight fasting for lipid profile. TC, TG, and HDL-C were analyzed enzymatically using kits obtained from Randox Laboratories Limited, Crumlin, UK. Plasma LDL-C was determined from the values of TC and HDL-C using the following formula[21].

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

3. Results

Serum parameters in AMI patients and controls were shown in Table 1. TC, TC/HDL-C, LDL-C, TG were significantly higher in AMI patients as compared with controls (Table 1). Significant difference for HDL-C between AMI and controls was observed (Table 1). On the other hand, LDL-C and LDL-C/HDL-C were higher in patients compared with controls (Table 1). No statistically significant difference was observed in TG/HDL-C among patients and 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-C, TG/HDL-C and LDL-C/HDL-C was shown in Table 2. Higher ratio of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C was observed in AMI patients compared with controls (Table 1, 2).

Table 1
Lipid profile in patients and healthy controls (mean±SD) (n=1 021).

Variables	Controls	Patients	95% *CI*
Age	62.13±2.56*	61.84±3.80*	61.67-62.00
Height (m)	1.57±0.28*	1.64±0.59*	1.61-1.66
Weight (kg)	67.84±3.26*	72.01±5.37*	71.77-72.24
BMI (kg/m^2)	26.35±1.98*	26.16±1.45*	26.09-26.22
TC (mg/dL)	177.53±47.52**	180.94±47.69**	178.86-183.01
HDL-C (mg/dL)	41.92±9.88**	42.83±10.73**	42.36-43.29
TG (mg/dL)	148.43±59.66**	146.87±59.66**	144.26-149.97
LDL-C (mg/dL)	105.64±40.14**	105.98±41.97**	110.05-111.90
TC: HDL-C	3.24±2.36**	4.40±2.72**	4.28-4.51
LDL: HDL-C	1.78±0.98**	2.66±1.45**	2.59-2.72
TG: HDL-C	2.87±1.26*	4.16±1.56*	4.09-4.32

*P<0.01; **P<0.001.

Table 2
Distribution pattern of TC/HDL-C, TG/HDL-C and LDL-C/HDL-C ratio in patients and healthy controls (mean±SD) (n=1 021).

Ratio		Controls	Patients
TC/HDL-C	2-3	2.67±0.35	-
	3-4	3.67±0.27	3.97±0.29
	4-5	4.39±0.26	4.94±0.26
	5-6	-	5.67±0.13
TG/HDL-C	1-2	1.36±0.24	-
	2-3	2.18±0.16	2.75±0.23
	3-4	-	3.62±0.16
	4-5	-	4.82±0.19
LDL-C/HDL-C	1-2	1.52±0.13	1.84±0.15
	2-3	2.33±0.24	2.87±0.19
	3-4	-	3.58±0.21
	4-5	-	4.51±0.22

4. Discussion

4.1. Observations of TC

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 patients with AMI [(180.94±47.69) mg/dL] was significantly (P<0.001) greater than that of the control subjects without AMI [(177.53±47.52) mg/dL].

A previous study has observed a greater value (189.70 mg/dL) for TC than the controls of the present study[22]. In a study of MI patients[23] a mean TC level (196.60 mg/dL) was reported and it was 5.3% higher than that of MI patients of the present study.

Higher values for TC (196.60 mg/dL)[23] and (215.70 mg/dL) have been reported by previous studies in AMI patients[24]. These values were 10.3% and 22% 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 which is reported by Sivaraman *et al*[25] in patients with acute coronary syndrome. They also reported a significant higher values (P<0.001) when compared with the controls in their study.

Similarly, significant differences (P<0.001) were observed in young cardio arterial disease (CAD) patients compared with controls[24]. The result of the present study was in agreement with their observation.

Lower levels of TC (181 mg/dL) in MI patients than observed in the present study have been reported in studies on Indian population[26,27].

The TC levels of the subjects selected in the present study were within the normal lipid profile but the mean levels of TC in MI subjects were 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 that of in the present study.

4.2. Observations of HDL-C

The mean serum HDL-C level observed in patients with MI in the present study [(42.83±10.73) mg/dL] was significantly higher (P<0.001) than the values observed in controls [(41.92 ±9.88) mg/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[22].

HDL-C levels similar to the present study have been reported (39.5 mg/dL)[23] and (42.11 mg/dL)[29] in patients with heart disease. Similar levels of HDL-C were reported in many studies[24,26]. Therefore, most of the research evidences supported drastic elevation of HDL-C levels in AMI patients.

4.3. Observations of TG

TG value observed in MI patients [(148.43±59.66) mg/dL] was significantly higher when compared with controls [(146.87± 59.66) mg/dL]. Similar levels of TG have been reported[22,26] in normolipidemic AMI patients as observed in the present study. However, 22.3% and 18% higher levels of TG in MI patients were observed and reported by coworkers[23,24], respectively.

Furthermore, significantly higher levels of TG (149 mg/dL, 15.5%)[27] and (140.5 mg/dL, 8.5%)[30] have been observed compared with the observations of the present study.

The findings of the above data confirm that elevated TG levels are associated with the incidence of heart diseases in normolipidaemic AMI patients with body mass index (BMI) positively correlated with serum TG.

4.4. Observations of LDL-C

The mean serum level of LDL-C in the patients [(105.98 ± 41.97) mg/dL] was significantly greater than control [(105.64± 40.14) 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[22].

In the studies of patients with a history of MI, greater values were reported by several researchers[26] whereas some have reported[31] lower values of LDL-C than the present study. However, similar levels of LDL-C in MI patients were also reported in several studies[23,24].

4.5. Observations of TC/HDL-C

The TC/HDL-C in MI patients (4.40±2.72) was significantly (P<0.001) higher compared with controls (3.24±2.36). Similar TC/HDL-C (3.6) has been observed in normolipidaemic subjects of the age group 21-70 years by Goswami *et al*[22]. Lower TC/HDL-C was observed in AMI patients in study conducted elsewhere[23].

Similar ratio (4.6) was reported in MI patients by study conducted elsewhere[24,27,28]. Higher ratio compared with the present study has been reported in MI patients[24,26]. A cut of level of 3.3 has been suggested[20].

Though the TC levels were within the normal level, the TC/HDL-C was elevated significantly in MI patients indicating the importance of assessing TC/HDL-C even in normolipidaemic subjects.

4.6. Observations of LDL-C/HDL-C

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[20].

The present study observed significantly higher ratio (2.66 ±1.45) in AMI patients compared with control (1.78±0.98).

Results reported on the ratio were inconsistent, as some studies reported higher ratios[23], similar ratio[23] and lower ratios[27] of LDL-C/HDL-C compared with the present study.

4.7. Observations of TG/HDL-C

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 (4.16±1.56) in MI patients compared with control (2.87±1.26). A slightly higher ratio (2.5) has been reported in healthy subjects earlier[22]. The data reported in previous studies in MI patients were inconsistent to the present study. Some studies have reported higher ratios[23-27] whereas some reported similar ratios as observed in our study[26]. As per NCEP ATP-111 a cut of level of 2.5 has been suggested[20].

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 the development of MI and other coronary complications. The practice of computing the ratio should be practiced even in a normal health check up packages.

Conflict of interest statement

We declare that we have no conflict of interest.

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