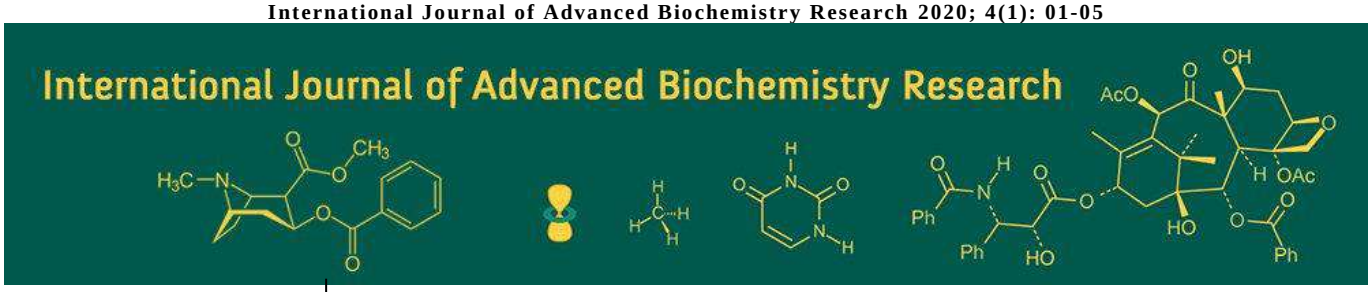

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A prospective observational study on effects of acute myocardial infarction on cholesterol and cholesterol ratios: At a tertiary care centre

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Abstract
Background: Myocardial infarction generally occurs with the abrupt decrease in coronary blood flow that follows a thrombotic occlusion of a coronary artery previously narrowed by atherosclerosis.
Aim & Objectives: To study the effect of acute myocardial infarction on the ratios of total cholesterol to HDL (High Density Lipoprotein) cholesterol and of LDL (Low Density Lipoprotein) cholesterol to HDL (High Density Lipoprotein) cholesterol.
Methodology: This is a hospital based prospective study done in Intensive coronary care unit &Medical Wards of Mamatha Institute of Medical Sciences &Hospital, Hyderabad during period of January 2019-October 2019.
Results: Eighty patients who were admitted with confirmed diagnosis of acute myocardial infarction fulfilling the criteria are enrolled in the study. Eighty one percent (81%) of the patients studied were men. Hypertension was present in Thirty (30%) percent, twenty-five (25%) percent were diabetic, thirty-two (37%) percent of were smokers, fourteen (14%) percent of the patients had family history of coronary artery disease. Non-ST elevation myocardial infarction was diagnosed in twenty (18%) patients, eighty-two (82%) of the patients were diagnosed to have ST elevation myocardial infarction. Sixteen (18%) of the patients studied were obese. Acute myocardial infarction significantly reduces the total serum cholesterol levels and increases the serum triglyceride levels. But the acute myocardial infarction has no significant effect on the cholesterol ratios (LDL cholesterol / HDL cholesterol ratios and cholesterol / HDL cholesterol ratio).
Conclusion: We conclude, after 24 hours of acute myocardial infarction assessment of cholesterol ratios will be more appropriate than assessing total cholesterol levels.

Keywords: Cholesterol ratio, acute myocardial infarction, triglycerides, LDL

Introduction
Coronary artery disease remains the most common cause of death despite significant advancement in its prevention and treatment [1].
Myocardial infarction generally occurs with the abrupt decrease in coronary blood flow that follows a thrombotic occlusion of a coronary artery previously narrowed by atherosclerosis. The injury is facilitated by factors such as cigarette smoking, hypertension, dyslipidemia, diabetes and a number of other factors [2].
Acute myocardial infarction (MI) is one of most common diseases among the developing countries. Mortality rate of MI is approximately 30% and for every 1 in 25 patients who survive the initial hospitalization, dies in first year after MI. Indians are 4 times more prone to acute MI as compared to people of other countries due to combination of genetic and lifestyle factors that promote metabolic dysfunction.
Aggressive management of the risk factors is one of the crucial elements in the treatment of patients with coronary artery disease. Serum markers that are used for cholesterol risk assessment and management are total cholesterol, low density lipoprotein (LDL) cholesterol level and high-density lipoprotein (HDL) cholesterol level.
Patients with acute myocardial infarction should have plasma lipid levels determined within 24 hours of the onset of symptoms of acute infarction [3].
The studies like Mulligan *et al.* (1984), and many other studies have questioned the validity of the plasma lipid levels measures beyond 24 hours from the onset of myocardial infarction[4].

The studies have demonstrated that acute myocardial infarction results in a transient decline in the serum cholesterol levels, which becomes apparent after 24 hours of onset of myocardial infarction and may last for 2 to 3 months [5].

Therefore in situations in which plasma lipid levels are not determined within 24 hours of the onset of myocardial infarction symptoms, the cholesterol measurements are usually deferred until the effect of acute infarction is fully resolved which may result in an inappropriate delay in the management of hyper cholesterolemia based on Brugada & Wenger *et al*. study [3].

The ratios of total cholesterol to HDL cholesterol and of LDL cholesterol to HDL cholesterol also can be used as predictors of acute coronary events [6].

The purpose of the present study is to determine whether the acute myocardial infarction affects the values of the serum cholesterol ratios as it does with absolute serum cholesterol Levels.

Methodology

Patients and methods

The study was conducted at the Intensive coronary care unit and medical wards of Mamatha Institute of Medical Sciences & Hospital during the period of January 2019-October 2019. Eighty patients who were admitted with a confirmed diagnosis of acute myocardial infarction were enrolled in the study.

Inclusion criteria

The diagnosis of acute myocardial infarction was made if patients had ischemic type chest pain for ≥ 30 minutes with evidence of ST – segment elevation of ≥ 1 mm in two anatomically contiguous leads on the ECG or the appearance of a new left bundle branch block.

- Patients who had symptoms suggestive of acute myocardial infarction but did not meet the ECG diagnostic criteria, needed to have serum creatinine – kinase MB levels that were more than twice the upper limit of normal.

Exclusion criteria

1. Symptoms suggestive of acute myocardial infarction ≥ 12 hours.
2. Hospital stays of < 4 days.
3. Already receiving lipid – lowering medications.

All the patients were followed from the day of admission to the day of discharge.

Lipid measurements

Besides clinically examination and routine investigation, the serum lipid profile was measured within the first 24 hours of the onset of symptoms of myocardial infarction and again at day 4 post myocardial infarction.

The serum total cholesterol, triglyceride levels were measured by enzymatic colorimetric test using reagents on Mindray BS -240 pro automated clinical chemistry analyzer and HDL cholesterol is measured by precipitation assay.

- The LDL cholesterol value was calculated by using the Fried Ewald formula.
- LDL cholesterol = total cholesterol –HDL cholesterol – (triglyceride/5) The cholesterol ratios then were calculated by using the total cholesterol /
- HDL cholesterol and LDL cholesterol / HDL cholesterol ratios. All the blood samples were 12 hours fasting samples.

Statistical analysis

Continuous variables were expressed as the mean ± standard deviation (SD) and the categoric variables were expressed as a percentage. The student‘s t‘ test was used to compare lipid values and ratios between day 1 post M I and day 4 post M I. A two tailed _P ‘value of < 0.05 was considered to be significant.

Table 1: Clinical characteristics of study population

Total number of cases studied = 80		
S. No	**Characteristics**	**No. of Patients (Percentage)**
1	Hypertension	30%
2	Diabetic mellitus	25%
3	Smoker	32%
4	Positive family history	14%
5	Non-ST elevation Myocardial infarction	18%
6	ST elevation myocardial infarction	82%
7	Obesity	18%

Observation in lipid profile

1. All serum lipid levels changed significantly between day 1 post myocardial infarction (within 24 hours) and day 4 post myocardial infarction.
2. On day 1 post myocardial infarction the mean total cholesterol value is 192.20.
3. On day 4 post myocardial infarction, the mean total cholesterol value is 175.50.

Mean Cholesterol Value – D1
Post Myocardial infarction = 192.20
Mean Cholesterol Value – D4
Post Myocardial infarction = 175.50
On day 1 of post – myocardial infarction, the mean triglyceride value was 124.98.
On day 4 of post – myocardial infarction, the mean triglyceride value was 143.22
Day-1 Post Myocardial Infarction Mean Triglyceride Value=128.78
Day-4 Post Myocardial Infarction Mean Triglyceride Value=145.25

Observation in lipid profile

Regarding the Cholesterol ratios, the ratio at total cholesterol to High Density Lipo protein cholesterol (Cholesterol / HDL ratio) on day – 1 post myocardial infarction and day 4 post myocardial infarction were 4.280 and 4.400 respectively.

Observation in lipid profile

The ratio at low density lipoprotein cholesterol to high density lipoprotein cholesterol (LDL/HDL ratios) on day – 1 post myocardial infarction and day- 4 post myocardial infarction were 2.820 and 2.700 respectively.

Table 2: Comparison of serum lipid values on Day 1, Day 4

Serum lipids	Within 24 hrs of Myocardial infarction	Day-4 post Myocardial infarction	Z 'and P' Values
Total cholesterol (mg/dl)	192.20±17.75	175.50±23.05	7.44
Triglycerides (mg/dl)	128.78±39.25	145.25±35.64	5.03
Total cholesterol / HDL cholesterol ratio	4.28±0.38	4.40±0.38	0.34
LDL cholesterol / HDL cholesterol ratio	2.82±0.40	2.70±0.38	0.06

The values are expressed as mean ± standard deviation. If z 'is > 1.96 and if_ P' is < 0.05 then the change is significant.

Discussion

Coronary artery disease remains the most common cause of death despite significant advancements in its prevention and treatment. Aggressive management of the risk factors is one of the crucial elements in the treatment of patients with coronary artery disease.

Atherosclerosis has multifactorial etiology but abnormality in lipoprotein metabolism is one of the key factors in its development, which is an important risk factor in development of cardiovascular disease [7].

Epidemiological studies have conclusively linked high levels of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) and low levels of high-density lipoprotein cholesterol (HDL-C) with CHD incidence and mortality (Yokokawa *et al*., 2011) [8]. Early treatment of hyperlipidemia following acute myocardial infarction (AMI) provides potential benefits and reduces the morbidity and mortality of CHD. Many studies in the past few decades have shown that acute myocardial infarction results in a significant decrease in the serum levels of total cholesterol, LDL cholesterol, and HDL cholesterol [9]

The acceptable time for the measurement of plasma lipids after an acute myocardial infarction is within 24 hours after the onset of symptoms and the plasma lipid levels measured beyond 24 hours are mostly considered to be invalid. Acute MI causes rapid decline in serum levels of total cholesterol, LDL-cholesterol; HDL-cholesterol.

The levels of lipid and lipoproteins change during acute illness that cause delay in treatment choice [10]

Acute myocardial infarction like any other tissue injury, initiates various local and systemic reactions[11].The local response includes vasodilation, leucocyte infiltration and chemotaxis, monocyte and macrophage activation and cytokine release [12].

The cytokines act on the systemic targets, including the liver to generate changes in the concentration of various heterogenous plasma proteins, collectively known as acute – phase reactants including lipoproteins [13, 14].

During tissue necrosis acute phasic changes occur that alter the lipid profile levels post-acute coronary events. Modifications of serum lipids after AMI include reductions in TC, LDL and HDL, in the range of 10 - 20%, with reciprocal increases in triglyceride (TG) approximating 20-30% (Miller 2008) [15]. Several mechanisms accounting for these changes include the acute phase response associated with up-regulation of LDL-receptor (R) activity and reduction in several pivotal HDL regulatory proteins.

From many clinical studies it is clear that phasic changes do occur in patients following AMI and therefore there is a recommendation for detection of hyperlipidemia in patients with AMI that the serum lipids should be assessed either within 24 hours after infarction or after 2-3months of AMI[16]

Besides alterations in the lipoproteins, acute phase response is also associated with changes in serum concentration of inflammatory markers. There is an intra-cardiac inflammatory response in AMI that appears to be the result of the evolution of myocardial necrosis, as shown by higher C-reactive protein (CRP) and interleukin (IL)-6 levels in patients with major adverse cardiac events [17].

In the present study, there is significant changes in TC levels in AMI patients. On day 1 post myocardial infarction the mean total cholesterol value is 192.20.

On day 4 post myocardial infarction, the mean total cholesterol value is175.50. On day 1 of post – myocardial infarction, the mean triglyceride value was 128.78.

On day 4 of post – myocardial infarction, the mean triglyceride value was 145.25. Regarding the Cholesterol ratios, the ratio at total cholesterol to High Density Lipoprotein cholesterol (Cholesterol / HDL ratio) on day – 1 post myocardial infarction and day 4 post myocardial infarction were 4.280 and 4.400 respectively. The ratio at low density lipoprotein cholesterol to high density lipoprotein cholesterol (LDL/HDL ratios) on day – 1 post myocardial infarction and day- 4 post myocardial infarction were 2.820 and 2.780 respectively.

By statistical analysis of lipid values and ratios between day 1 and day 4, a two tailed - P‖ value of <0.05 was considered to be significant.

By day 4 to 5 post myocardial infarction, there is a significant decrease in serum concentrations of apoprotein A-1and apoprotein –B reflecting the maximum decrease in the serum cholesterol level by the time [18].

While the serum cholesterol level decreases after an acute myocardial infarction, serum triglyceride level increases. This paradoxical rise in serum triglycerides is due to an increase in serum – C reactive protein level which may increase to levels that are several hundred – fold higher than baseline 4 days after and myocardial infarction[19].

The C- reactive protein binds selectively with very LDL and interferes with its catabolism thereby increasing the serum triglyceride concentration.[20] First time Biorck *et al*. (1957) [21] reported that serum cholesterol levels decreased during MI. Since then, a wide range of changes in the serum lipid and lipoproteins following acute coronary events have been reported.

The results observed in present study are consistence with study by Amit Kumar Shrivastava *et al.* (2015) [22] which included 400 patients with AMI who were admitted within 24 h of onset of symptoms. The proportion of hypertension was 42% and diabetes mellitus was 25%, smoking:30%, family history 21%, alcohol 29% in AMI patients. Baseline serum levels of TC, TG and LDL-C (P = 0.039) were significantly higher in AMI patients as compared to the controls, whereas HDL-C was significantly higher (P< 0.001) in the control group. In AMI patients, all serum lipid levels changed significantly between day 1 post-MI (i.e., within 24 h) - day 7 post-MI. From day 1 to day 2 post-MI, serum TC levels, LDL-C levels, and HDL-C levels decreased significantly ($p < 0.001$). On the contrary, the serum TG levels increased significantly ($p < 0.001$) on day 1 to day 2.

Sheetal S Ghodke *et al.* (2012) [23] total 80 cases were studied in the age group 30 to 80 years and status was compared with 80 age and sex matched healthy controls in the same age group. A significant elevations were found in the levels of total cholesterol, LDL cholesterol and LDL cholesterol / HDL cholesterol ratio(P<0.001)these results indicates that the high levels of total cholesterol and LDL cholesterol / HDL cholesterol ratio are associated with risk of myocardial Infarction in adult and detection of this ratio still could be useful for cholesterol risk assessment in patients with acute myocardial Infarction.

On contrary Kumar *et al.* (2009) [24] observed significantly higher total cholesterol (TC)and triglyceride (TG)levels and lower high-density lipoprotein cholesterol (HDL)levels in AMI patients. In a series of 50 male AMI patients, serum LDL levels and the ratio of LDL to HDL were different among the two groups; however, serum HDL levels were significantly decreased in AMI group. The risk of AMI was associated with an increase in LDL and a decrease in HDL in both Asians and non-Asians. Lower Concentrations of serum HDL and higher serum TG were found to be independent risk factors, while serum LDL was not associated with AMI.

In the present study hypertension was seen in 30%, In study by Idemudia and ugwuja[25](2009) reported that the association between hypertension and dyslipidemia is well established and both may add up to increase patients susceptibility to the development of coronary heart disease. Of the 150 hypertensive patients, 54% were females in the age range of 50- 59 years, 53.6% were males (40-49) years. Hypertensive patients have significantly higher lipid profile with no significant difference in HDL levels

In present study obesity is in 18%and smokers are 32%, Observations in Wilsgaard and Arnesen (2004) [26] study reported steady increase in body weight is becoming major health problem. They assessed the association between 8-year change in bodyweight and serum lipids in an population based study of men and women aged 20-61 years. Significant associations between body mass index and HDL, Total cholesterol, TGs, were observed in all 10-year age group both in men and women. The association between BMI change and serum lipid change was strongest for persons who were consistent smokers or non-smokers at each survey.

In the present study 25% patients were diabetic 30% were hypertensive. Main objective of the study by seyoum *et al.* (2003) [27] was to analyze lipid levels in type 1 and type II diabetic patients.535 were males and 47% were females. There were 46.4% type 1 and 53.6% typeII patients. Hypercholesterolemia and hypertriglyceridemia were seen in 18.5% and 14.2% of the patients. Total cholesterol was significantly higher in females than in males and in type II than in type I patients (P<0.01, P<0.001, respectively).

A low serum HDL cholesterol level is considered to be an independent cardiovascular risk factor that leads to the development of atherosclerosis and related cardiovascular events. High serum levels of HDL are associated with reduced risk for the development of atherosclerotic disease. HDL Particles are believed to be antiatherogenic, secondary to their capacity to drive reverse cholesterol transport and antagonize pathways of inflammation, thrombosis, and oxidation [28].

All serum lipid levels changed significantly between day 1 post-MI (ie, within 24 h) and day 4 post-MI. From day 1 post-MI to day 4 post-MI, serum total cholesterol levels LDL cholesterol levels and HDL cholesterol level decreased significantly. On the contrary, the serum triglyceride levels increased significantly on day 1 post-MI on day 4 post-MI however, the cholesterol ratios remained unchanged between day 1 post-MI and day 4 post-MI. The ratio of total cholesterol to HDL cholesterol was on day 1 post- MI and on day 4 post-MI (change was not significant), and the ratio of LDL cholesterol to HDL cholesterol was on day 1 post-MI and on day 4 post-MI (change not significant).

The present study analysis suggest that the cholesterol ratios could be used to determine cholesterol risk in patients who experienced acute myocardial infarctions and may have an advantage in situations in which the absolute total and fractionated cholesterol levels are longer applicable because of the effect of the acute myocardial infarction. (Beyond 24 hours after the onset of acute myocardial infarction).

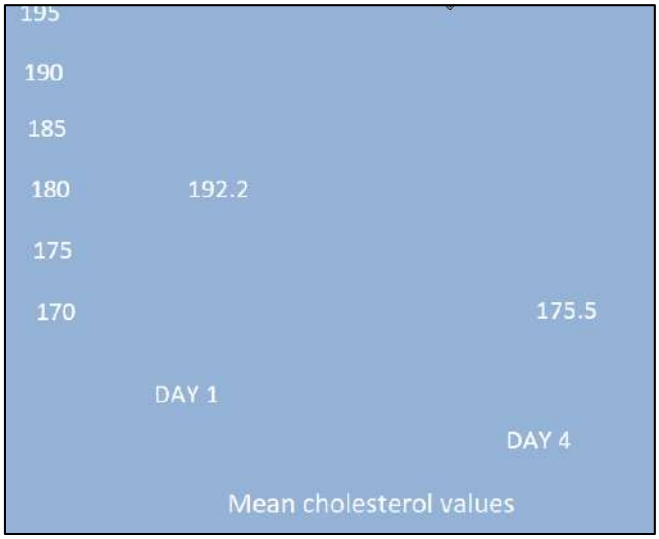

Fig 1: Comparision of Mean cholesterol values

Day 1- Chol/HDL -4.280
Day 2- Chol/HDL-4.400

Fig 2: Cholesterol/HDL ratio

Conclusion

Following acute myocardial infarction the total serum cholesterol level falls significantly and the triglyceride level rises significantly. Therefore measurement of absolute levels of serum cholesterol and triglycerides following acute myocardial infarction are not valid in risk assessment 24

hours after infarction. But acute myocardial infarction does not affect the cholesterol ratios. (Cholesterol / HDL and LDL / HDL cholesterol ratios) even 24 hours after infarction. Therefore following acute myocardial infarction, the cholesterol ratios are valid and very useful in risk assessment. Considering that phasic changes in serum lipid and lipoprotein levels occur after 24 hours of ACS, the findings of this study emphasize the need for assessment of the lipid profile of patients to be made at admission, so as to identify patients at a higher potential risk Exact knowledge regarding baseline serum lipids and lipoprotein levels as well as their varying characteristics can be used to guide selection of lipid lowering medication.

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Conflict of Interest: The authors declare that they have no conflict of interest in this study

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