



CORRELATION OF CARDIAC BIOMARKERS WITH APOLIPOPROTEIN B/A1 RATIO IN MYOCARDIAL INFARCTION

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ABSTRACT

Background- ApoB/apoA1 ratio has been considered as a very powerful marker for predicting the risk of cardiovascular disease in individuals across all age range. The present study was conducted to correlate the cardiac biomarkers levels with apolipoprotein B/A1 ratio in patients with MI so as to promote early identification of acute coronary event and reducing the mortality associated with MI.

Methodology- The present study was conducted as a facility based cross sectional study at LN Medical College and J.K. Hospital, Bhopal on all the patients diagnosed with MI. Patient's sample was subjected to estimation of three cardiac biomarkers CK MB, Troponin I and Myoglobin apart from other routine investigations as advised. Also, the sample obtained were subjected to estimation of ApoB, apoA1 and their ratio was estimated.

Results- A total of 267 cases of MI were enrolled with mean age of 56.2 ± 13.98 years and male:female ratio of 1.9:1. Troponin I showed a positive correlation with Apo B/Apo A1 in MI cases and the observed correlation was statistically insignificant ($p < 0.05$). However, we observed a positive correlation of Apo B/Apo A1 with CKMB and Myoglobin, but the observed correlation was statistically insignificant ($p > 0.05$).

Conclusions- Though, all the three biomarkers we studied, had good diagnostic accuracy, Troponin I was observed to be superior as it also correlated significantly with ApoB/A1 ratio indicating the role of Troponin I in not only diagnosis but also in predicting the risk of acute coronary event.

KEYWORDS : ApoB/ApoA1, cardiac biomarkers, myocardial infarction, correlation

INTRODUCTION

Acute Myocardial infarction is one of the most common cause of mortality globally. Majority of MI cases are secondary to some underlying coronary artery disease (CAD).^[1] Due to rapid demographic transition associated with urbanization and westernization, the incidence and proportions of MI along with cardiovascular mortalities are increasing significantly. In India the prevalence of MI is reported approximately a decade earlier when compared to developed nations. However, in India, the exact prevalence of MI and cardiovascular disease is not known but mortality due to cardiovascular disease were attributed in 28.1% cases in 2016.^[2] The prevalence of MI according to a self reported national survey in UK (2014) was 6,40,000 and 2,75,000 in males and females respectively.^[3] According to American Heart Association (AHA - 2019) the incidence of coronary events were reported in approximately 10,55,000 males and females in USA. In 2017, MI due to non obstructive coronaries (MINOCA) was observed in almost 5.9% cases and it was found to be more common in females as compared to males. The age of the first coronary event is estimated to be 65.6 years in males and 72 years in females. Mortality due to MI may be observed in approximately 30% cases.^[4]

American College of Cardiology and European cardiac societies released a consensus statement in 2007 for providing universal definition of myocardial infarction. This definition not only included ECG but also incorporated laboratory parameters and clinical history. According to this consensus definition, myocardial infarction was defined as an event which is characterized by raised or reduced blood test depicting damage to heart muscle (troponin I or T) with clinical diagnosis of MI.^[5] Various cardiac biomarkers are used in evaluation and diagnosis of MI which includes cardiac troponin (Trop T and Trop I), creatine kinase-MB (CKMB), homocysteine, myoglobin, Lactate dehydrogenase, C-reactive protein etc.^[6,7]

Apolipoproteins are also used for predicting the risk of cardiovascular disease. Apolipoprotein are component of lipoprotein particles, and among them ApoB/apoA1 ratio is

associated with cardiovascular disease and MI. Apolipoprotein B (apoB) represent atherogenic lipoprotein particles such as VLDL, IDL and LDL whereas Apolipoprotein A1 (ApoA1) reflect the high density lipoprotein levels, anti-oxidant and anti-inflammatory effects. ApoB manifests atherogenic and ApoA1 manifests antiatherogenic effects.^[8,9] Overall, apoB/apoA1 ratio has been considered as a very powerful marker for predicting the risk of cardiovascular disease in individuals across all age range.^[10] The present study was therefore conducted at a tertiary care centre in order to correlate the cardiac biomarkers levels with apolipoprotein B/A1 ratio in patients with MI so as to promote early identification of acute coronary event and reducing the mortality associated with MI.

Methodology

The present study was conducted as a facility based cross sectional study at Department of Biochemistry in collaboration with Department of Medicine LN Medical College and J.K. Hospital, Bhopal. The study was done on all the patients diagnosed with MI admitted during the study period of months i.e. from 1st March 2019 to 30th August 2021 and whose blood sample was received in Department of Biochemistry for estimation of cardiac biomarkers (CK MB, Trop I and Myoglobin). All the patients with muscle damage and chronic renal disease were excluded from the study.

The study was approved by Institute's ethical committee. After obtaining consent from participants fulfilling inclusion criteria, detailed history regarding sociodemographic variables, clinical history, comorbid conditions, duration between onset of symptoms and hospitalisation, addiction, lifestyle etc. was obtained and entered in questionnaire. All the patients were then subjected to general and systemic examination with cardiovascular examination in detail. Patient's sample was subjected to estimation of three cardiac biomarkers CK MB, Troponin I and Myoglobin apart from other routine investigations as advised. Also, the sample obtained were subjected to estimation of ApoB, apoA1 and their ratio was estimated.

STATISTICAL ANALYSIS – Data was compiled using MS

Excel and analysed using IBM SPSS software version 20. Categorical data was expressed as frequency and proportions whereas continuous data was expressed as mean and standard deviation. Correlation of Trop I, CKMB and myoglobin with ApoB/ Apo A1 ratio was done using Pearson Correlation and curve estimation in both case and control group. P value less than 0.05 was considered statistically significant.

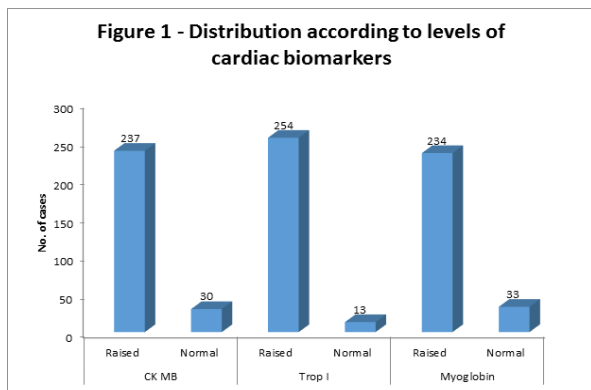
RESULTS

During the study period, a total of 267 cases of MI were enrolled with mean age of 56.2± 13.98 years.

Table 1 – Distribution according to baseline variables

Baseline variables	Frequency (n=267)	Percentage
Age (years)	<30	10
	31 – 40	34
	41 – 50	45
	51 – 60	77
	> 60	101
Gender	Male	177
	Female	90

Majority of patients belonged to elderly age group (37.8%) and 66.3% patients were males with male:female ratio of 1.9:1.



The mean CKMB in the MI patients was 46.78 ± 49.19 IU/L and these levels were raised in 237 (88.8%) cases with MI. The mean troponin I levels in case with MI whereas mean myoglobin levels were 106.97±22.34. Overall, Troponin I and myoglobin levels were raised in 254 (95.1%) and 234 (87.6%) patients respectively.

Table 2– Mean levels of apolipoproteins in both groups

Apolipoprotein	Mean	SD
Apo A ₁	97.34	7.14
Apo B	92.19	5.36
Apo B/A ₁	0.95	0.05

The mean ApoA1 levels in patients with MI were 97.34±7.14 mg/dL whereas mean ApoB levels were 92.19±5.36 ng/dL.. The mean ApoB/Apo A1 ratio was 0.95±0.05.

Table 3- Correlation of ApoB/A1 ratiowithcardiac biomarkers

ApoB/A1 ratio	R	R Square	Adjusted R Square	Std. Error of the Estimate	F value	P value
CKMB	0.080	0.006	0.003	47.725	1.7	0.19
Troponin I	0.215	0.046	0.043	2.300	12.8	0.01 *
Myoglobin	0.076	0.006	0.002	18.902	1.5	0.21

In present study, Troponin I showed a positive correlation with Apo B/Apo A1 in MI cases and the observed correlation was statistically insignificant (p<0.05). However, we observed a positive correlation of Apo B/Apo A1 with CKMB and Myoglobin, but the observed correlation was statistically insignificant (p>0.05).

DISCUSSIONS

Myocardial infarction or heart attack is one of the most common cardiac emergency encountered in day to day practice and is associated with higher morbidity as well as mortality.⁽¹¹⁾ Myocardial infarction with prolonged duration may lead to cardiac cell death as well as necrosis of the cardiac musculature. Early and timely diagnosis of MI and its immediate management are the key strategies in reducing the morbidity and mortality associated with acute myocardial infarction.⁽¹¹⁾ Though ECG is effective in establishing the definitive diagnosis of myocardial infarction with good accuracy, but the ECG changes take time to manifest. For reducing the mortality and preventing permanent changes in myocardium, it is imperative to diagnose myocardial infarction early and treat accordingly. The role of various cardiac biomarkers such as cardiac troponin (Troponin T and Troponin I), myoglobin, creatine kinase-MB (CKMB), Lactate dehydrogenase, homocysteine, C-reactive protein etc. have been suggested for early identification of MI but their diagnostic accuracy is variable depending upon duration since cardiac injury or symptoms and time of evaluation.⁽¹¹⁾ The ideal Cardiac biomarkers must be highly sensitive and specific, which could be detected as early as possible during the pathogenetic process of the disease.^(6,7) The present study was conducted at tertiary care centre with the aim to study the correlation of three cardiac biomarkers with ApoB/ ApoA1 ratio.

In India, the age of patients presenting with MI has been identified as a decade earlier as compared to Western population with average age of presentation at 65.6 years and 72 years in males and females respectively. Overall, the mortality rate due to MI is estimated to be approximately 30% globally with mortality rate of approximately 28.1% in India.^(3,4) In present study, mean age of patients with MI was 56.2±13.98 years and maximum cases belonged to elderly age group (37.8%). Similarly, mean age of patients with MI in a study by Korkmaz et al was 55± 15 years.⁽¹²⁾ However, mean age of patients with MI in a study by Hoh et al was 60.95±11.52 years.⁽¹³⁾ Similar findings were documented by Sharma et al, in which the authors concluded that the mean age of patients with heart disease is 53 years in Indian population approximately 5- 10 years earlier than the World.⁽¹⁴⁾ Coronary artery disease and MI are usually considered as disorder of elderly and advanced age. There are certain risk factors which are associated with myocardial infarction and cardiac diseases. With the increase in life expectancy and advancement in medical technology, the proportion of elderly and dependent population has increased significantly. Westernization, changes in lifestyle and dietary habits has also increased the exposure to modifiable risk factors. All these factors might be the associated factors associated presentation of MI at younger age.

In present study, majority of patients with MI were males with male:female ratio of 1.9:1. This could be attributed to cardioprotective effect of estrogens in premenopausal females. These findings were supported by findings of Canto et al in which the authors concluded that MI in women usually manifest at advanced age and females are less symptomatic, i.e. they are less likely to present with chest pain or discomfort.⁽¹⁵⁾ The findings of our study were also concordant to the findings of Korkmaz et al, in which 55% cases with MI were males.⁽¹²⁾

The standard cutoff values were taken for individual cardiac biomarkers in our study to assess the activity of these cardiac biomarkers in presence or absence of MI. In our study, assessment of cardiac biomarker assays was done at the time of admission irrespective of time duration since onset of symptoms or myocardial injury. We observed that majority of

patients presented after 6 hours of onset of symptoms and mean duration since onset and hospitalization was 10.3 ± 3.6 hours for cases with myocardial infarction. The MB isoform of creatinine kinase isoenzyme (previously called creatinine phosphokinase) has been shown to be a cardiac biomarker with good diagnostic accuracy if tested within first 24 hours after injury.^[16] The level start rising after 4 to 6 hours of myocardial injury and remain elevated till 1 to 2 days.^[2] The cardiac biomarker myoglobin is a heme protein which can be detected as early as within first three hours following myocardial injury and/ or onset of symptoms. The enzyme is eliminated rapidly by the renal system.^[17] Troponins are the regulatory protein which are composed of three isoforms-troponin C, troponin I and Troponin T. Of them, Troponin C does not act as cardiac biomarkers but play a very important role in calcium binding. On the other hand Trop T as well as Trop I inhibit binding of tropomyosin binding and ATPase activity respectively.^[18] Both these cardiac troponins have higher sensitivity and specificity for predicting the myocardial infarction and outcome of patients with MI.^[19]

In present study, we also aimed to assess the correlation ApoB/apoA1 ratio with cardiac biomarkers. Apolipoproteins are component of lipid metabolism (lipoproteins) that helps in assessment of cardiovascular risks. Among various apolipoproteins, the ratio of ApoB/apoA1 is particularly associated with myocardial infarction and cardiovascular diseases. Overall, Apo A represent cardioprotective lipoprotein particles i.e. HDL and Apo B represent atherogenic lipoprotein particles such as VLDL, IDL and LDL.^[8,9] Overall in our study, Apo A1 as well as Apo B levels were significantly higher in cases with MI as compared to controls and the ratio of Apo B/A, was also significantly higher in MI as compared to non MI group ($p < 0.05$). Amongst various cardiac biomarkers, we documented statistically significantly positive correlation of ApoB/ A1 with only troponin I in MI patients ($r = 0.215$, $p < 0.05$). These findings were supported by findings of Zhu et al where the authors observed ApoB to be significantly associated with adverse cardiovascular event with hazard ratio of 1.349 ($p < 0.05$). Also the authors documented significant correlation of ApoB with VTI and CIMI.^[20] To best of our knowledge, none of the previous studies have assessed the correlation of ApoB/A1 with various cardiac biomarkers. The present study is unique to assess such association.

CONCLUSIONS

Though, all the three biomarkers we studied, had good diagnostic accuracy, Troponin I was observed to be superior as it also correlated significantly with ApoB/A1 ratio indicating the role of Troponin I in not only diagnosis but also in predicting the risk of acute coronary event.

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