Troponin -T as a prognostic and diagnostic marker for myocardial infarction

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Abstract

Over the past decade, there has been a progressive evolution of cardiac marker testing in patients with acute coronary syndromes. Myocardial infarction (MI) is the leading cause of death in the developed world. Biomarkers have an vital role in analysis, risk stratification, administrative running and medical assessment making in the setting of patients presenting with signs and symptoms of MI. Cardiac troponin (cTn) rose to prominence during the 1990s and has evolved to be the cornerstone for diagnosis of MI. Cardiac troponins are released from myocytes following myocardial damage and loss of membrane integrity. Troponin T are member of a group of cardiac regulatory proteins which function to regulate the calcium mediated interaction of muscle filaments actin and myosin resulting in contraction and relaxation of striated muscle. New algorithms integrating Brain natriuretic peptide (BNP), NT-proBNP, and more sensitive cTn assays footing potential for more rapid diagnosis of MI, allowing for appropriate management steps to be initiated and more efficient and effective utilization of healthcare resources.

Keywords: Myocardial infarction; Biomarkers; Troponin; Brain natriuretic peptide; Cardiac troponin

1. Introduction

Coronary artery disease remains the leading cause of mortality in the western world. Atherosclerosis is the major cause of coronary heart disease. The atherogenic process is far advanced by the time the clinical manifestation of coronary heart disease develops which includes sudden cardiac death.1 Coronary heart disease and its major manifestations myocardial infarction, which in turn results when blood supply is so much deprived sufficient to cause focal or massive necrosis of cardiac muscle was a medical rarity prior to first World War. WHO has declared CVD as a modern epidemic? MI is myocardial necrosis occurring as a result of critical imbalance between coronary blood supply and myocardial demand. Myocardial infarction is the “impairment of heart function due to inadequate blood flow to the heart compared to its need, caused by obstructive changes in the coronary circulation to the heart”. In more than 90% of cases, the cause of myocardial ischemia is reduced blood flow due to obstructive atherosclerotic plaque lesions in one of the three large coronary arteries or its branches.3

The possibility of suffering acute myocardial infarction in 40-60years age group is 8times higher than in people of a less advanced age. More than 50% of in hospital mortality from acute myocardial infarction occurs in subjects older than 65 years.4 Elderly patients with acute myocardial infarction have been reported to present with more atypical symptoms like atypical chest pain, dyspnea, and giddiness and also have highest rate of complication like CCF, cardio genic shock, arrhythmias with higher mortality. They are treated less aggressively than the younger.5, 6, 7, 8, 9.

Modifiable risk factors are serum lipids, lipoproteins, Hypertension (HTN), Diabetes
Mellitus (DM), smoking and tobacco chewing etc. Non modifiable risk factors are age, sex, genetics and family history. Interestingly over time, the patterns of MI presentation have changed as there is an increasing incidence of myocardial infarction without ST-segment elevation (NSTEMI), with concurrent decrease in the incidence of ST-segment elevation myocardial infarction (STEMI) 11. Earlier LDL was thought to be a marker for risk of the disease and was later replaced by HDL. Now attention has been directed towards identifying components of HDL. Because there was in consistency in correlation between HDL and risk of coronary heart disease12. The availability of serum cardiac markers with markedly enhanced sensitivity for myocardial damage enables to diagnosis AMI in about 1/3rd of patients who would not have fulfilled the criteria for myocardial infarction.

Troponin is a protein complex that confers calcium sensitivity to muscle. Troponin has three subunits cTnI, cTnT and Tnc. Cardiac Troponin T is a twin filament protein which takes part in cardiac muscle contraction. Cardiac Troponin T is not normally present in serum unless cardiac cell necrosis has occurred. Thus, it is more cardiac specific. Recent studies have shown that Cardiac Troponin T measurements acts as a specific and sensitive indicator of myocardial infarction and the prognostic value of the Cardiac Troponin T is independent of other risk factors such as age, sex and ECG abnormalities13. As assays for cTn have been evolved that are capable of reliably detecting smaller and smaller quantities in the blood, a dilemma has emerged as to how to use this new information. Several studies have attempted to answer this question and have shown that these lower concentrations of cTn have important prognostic significance and, more importantly, that intervention in these patients leads to improved clinical outcomes. Our present study was made an attempt to compare the levels of Troponin T in Myocardial infarction patients and evaluated the lipid profile in Myocardial infarction patients.

2. Material and methods
The study was conducted during the period from December 2019 to February 2020 in the Department of Biochemistry, Bharath Institute of Higher Education and Research, Chennai Tamil Nadu. We maintained three study groups and ninety samples. The study design was carried out by cross sectional study. Ethical clearance was obtained from Institutional Ethics Committee conducted at the Bharath Institute of Higher Education and Research.

2.1. Collection of blood sample
The blood samples of the respondents were collected after an overnight fast, 1ml in sodium fluoride coated sugar tubes and 3ml in plain tubes between 8 am to 9 am. 1 ml of blood for postprandial blood sugar was collected 2 hrs after breakfast. The blood drawn was allowed to coagulate and the serum was separated by centrifuging and stored at -20°C until assayed.

2.2. Biochemical parameters
Fasting and postprandial plasma glucose, lipid profile, serum Troponin T, serum Urea and creatinine were the biochemical parameters estimated in the study population.

TROPONIN – T Immunoenzymometric assay was carried out by the micro CLIA plate provided in this kit has been pre-coated with an antibody specific to Human Tn-T.

2.3. Statistical analysis
The individual student’s t test was done to evaluate the significance of difference of means of two groups, using SPSS (statistical package for social science) statistical package, version 17. The data’s were also subjected to independent samples test (unpaired) where ever necessary to evaluate the significance of difference of mean of control and study groups using SPSS software. The values are presented as mean +SD and p value <0.05 was considered significant.

3. Results and discussion
Troponin-T levels in Myocardial Infarction Patients
Figure 1 shows the level of Troponin T in control and Tests group was found to be significantly (p < 0.001) increased in Myocardial Infarction patients when compared to control patients. The concentrations of Troponin T were expressed as mean ± SD.

3.1. Lipid Profile in STEMI and NSTEMI Patients

Table 1 shows the level of Total Cholesterol, Triglycerides, HDL, LDL and VLDL level in control and experimental group was found to be significantly (p < 0.05) increased in myocardial Infarction patients when compared to control patients. The concentrations of Total Cholesterol, Triglycerides, HDL, LDL and VLDL level were expressed as mean ± SD

| Particulars | Control Patients | Myocardial infarction Patients |
|-------------|------------------|-------------------------------|
| Total Cholesterol | 157 ± 10.8 | 279.8 ± 22.7 *a* |
| Triglycerides | 122 ± 12.5 | 197 ± 19.8 *a* |
| LDL | 111.8 ± 10.7 | 156.5 ± 15.7 *a* |
| HDL | 56.7 ± 5.8 | 25.8 ± 2.5 *a* |
| VLDL | 14.9 ± 1.8 | 44 ± 4.8 *a* |

MI is myocardial necrosis occurring as a result of critical imbalance between coronary blood supply and myocardial demand. Myocardial infarction is the "impairment of heart function due to inadequate blood flow to the heart compared to its need, caused by obstructive changes in the coronary circulation to the heart". In more than 90% of cases, the cause of myocardial ischemia is reduced blood flow due to obstructive atherosclerotic plaque lesions in one of the three large coronary arteries or its branches. Despite impressive strides in diagnosis and management over the last three decades, acute myocardial infarction continues to be a major public health problem in the industrialized world. Although the death rate of MI has declined by about 30% over the last decade, its development is still a fatal event in approximately one third of the patients.

Prospective epidemiological studies have identified several independent coronary risk factors including smoking, dyslipidemia, hypertension and diabetes mellitus. However half of all myocardial infarctions occur in persons in whom plasma lipid levels are normal. The recognition that atherosclerosis is an inflammatory process, several plasma markers of inflammation have also been evaluated as potential tools for prediction of the risk of coronary event.

3.2. Presentation of MI according to age

In the present study shows age wise distribution of controls and Myocardial Infarction cases. It included healthy controls with mean age of 48.8 ± 5.3 years and Myocardial Infarction cases with mean age of 56.7 ± 6.2 years. In patients with STEMI male and female percentage in the present study was (66% and 50%) was comparable with Mutlu et al (67% and 51.2%) and L. Newby et al (66% and 50.2%). In patients with NSTEMI, males and female percentage in the present study was 26.6% and 57.1% comparable with Mueller et al.
3.3. Presentation of MI

About 18.33% of patients with myocardial infarction presented without chest pain (atypical symptoms) on initial evaluation. The patients experiencing MI without chest pain tended to be older (mean age 64 vs 59) remaining 81.66% of patients with myocardial infarction with chest pain. Chest pain has been reported as the cardinal clinical feature among patients who present with a myocardial infarction. The WHO requires the presence of chest pain as one of the cornerstones features in its diagnosis of myocardial infarction. The rapid early action for coronary treatment study, a randomized controlled clinical trial sponsored by National Institute of health was designed in Part to test the effect of educating the public about the symptoms of MI and benefits of early treatment.

3.4. Presentation according to ECG in MI patients

The present guidelines pertain to patients presenting with ischemic symptoms and persistent ST-segment elevation on the electrocardiogram (ECG). Most of these patients will show a typical rise in biomarkers of myocardial necrosis and progress to Q-wave myocardial infarction. Separate guidelines have recently been developed by another Task Force of the ESC for patients presenting with ischemic symptoms but without persistent ST-segment elevation and for patients undergoing myocardial revascularization in general. We have documented a pronounced gender difference with females far outnumbering men in the incidence of atypical presentation. (Though statistically not significant may be because of small sample size) This is similar to the results found in the study conducted by Muller RT et al.

3.4.1. Proportion of MI according to blood pressure status

In the present study, 57.9% of hypertensive patients presented with STEMI compared to the NSTEMI hypertensive group (31.71%). 68.29% of non-hypertensive patients presented STEMI compared with NSTEMI (31.71%). The study by S Bhagat et al (55%), Paul M Ridker et al (55.8%) and Kunihiro Kinjo et al present a similar trend of incidence. The hypertension is one of the strong risk factor for cardiovascular disease. Before JNC 7 was published these persons were considered to have normal blood pressure and were not recognized as potential candidates for cardiovascular intervention or risk reduction. But we now know, that person with hypertension are at increased risk of cardiovascular events.

3.4.2. Proportion of MI according to diabetic status

In the present study, 75% of Diabetic patients presented with STEMI compared to the NSTEMI diabetic patients (25%). 87.5% of non-diabetic patients of STEMI compared with NSTEMI non-diabetic patients (12.5%). Diabetic and non-diabetic STEMI myocardial infarction patients were significantly (p<0.001) increased when compared with NSTEMI patients.

Ridker et al, showed a Diabetic and non-diabetic STEMI patients were significantly (p<0.001) increased when compared with NSTEMI patients. Diabetes mellitus is an established risk factor in CAD. The role of DM in endothelial dysfunction has been proven beyond doubt.

3.4.3. Troponin -T in myocardial infarction patients

Acute Coronary Syndrome (ACS) is a term used to describe a group of conditions resulting from insufficient blood flow to the heart muscle. These conditions range from atypical chest discomfort and nonspecific electrocardiographic changes to a large ST-segment elevation, myocardial infarction and cardiogenic shock. Troponin T are member of a group of cardiac regulatory proteins which function to regulate the calcium mediated interaction of muscle filaments actin and myosin resulting in contraction and relaxation of striated muscle. Troponin T is almost exclusive to the myocardium, with small amounts expressed in skeletal muscle. Insufficient blood flow and oxygen supply to the heart muscle causes necrosis of the myocardium and subsequent release of Troponin T into the bloodstream.

Daubert et al. reported 2010 Troponin T in the bloodstream rises to detectable levels after 4-6 hours, peaks at 10-12 hours and can be detected for up to 14 days post infarction. In the present study, patients with elevated Troponin -T levels on admission had higher incidence of death (15.1%). It was comparable to that of the study by Newby et al. (10%). The other complication was not comparable to that of the study by Newby et al. Olaitidoye AG, et al. showed Troponin T shows prognostic significance for acute myocardial infarction or death in the same patients with myocardial infarction patients. The marker is a sensitive and specific, as confirmed by meta-analysis, and this supports a role in risk stratification.

The observed mean Troponin-T values of first day of Normal and myocardial infarction patients were 0.014 ± 0.001 and 2.27±0.26 respectively. In second day observed mean Troponin-T values of Normal and myocardial infarction patients
were 0.013 ± 0.001 and 21.81±0.15 and in third day observed mean Troponin-T values of Normal and myocardial infarction patients were 0.014 ± 0.001 and 0.69±0.06. The Levels of Troponin T in myocardial infarction patients were significantly increased in three days (p>0.001) when compared with normal control groups. In the present study, The Levels of Troponin T in myocardial infarction patients were significantly increased in three days (p>0.001) when compared with normal control groups.

3.5. Lipid profile in myocardial infarction patients

In the present study, the mean total cholesterol, triglycerides and LDL cholesterol levels were significantly greater in cases as compared to controls. The mean HDL-cholesterol was significantly lower in cases. However there was no significant difference in mean VLDL levels between cases and controls (p>0.05). In myocardial infarction patients the levels of cholesterol, triglycerides, LDL and HDL levels were significantly (p>0.05) increased when compared with control.

Dyslipidemia has been proven as one of the major risk factor for MI. Both VLDL – cholesterol and LDL-cholesterol are associated with atherogenic process, and there is increasing evidence that HDL-cholesterol prevents atherogenesis. The current trend in management of dyslipidemia is based on the executive summary of the third report of the National Cholesterol Education Program (NCEP). Accordingly the basic principle of prevention of the intensity of risk reduction should be adjusted to person’s absolute risk. This involves identification of all the risk factors associated with MI in a patient. The cutoff values for lipid parameters depend on the total risk factors present.

In line with the present study case control studies reported within India have also reported high total cholesterol, HDL cholesterol and triglyceride levels in patients suffering from MI. Vashist et al from Delhi studied 702 clinically documented CHD and 186 normal healthy controls and reported that total LDL-cholesterol, and triglyceride levels were significantly higher in cases while HDL cholesterol level was not different. Our present study showed there is significant increase in Total Cholesterol levels compared to controls. Our study is in accordance with Sabari Da, Suman B Sharma and Masoud Pezeshkian. O Metwalli in his study involving 58 patients and 30 controls found significant increase in TG levels. They suggested increased TG level may be due to genetic/nutritional /acquired abnormalities of lipoprotein especially VLDL which causes alteration in TG levels. Nigam PK found increasing trend of TG levels with significant increase in day 3 compared to day 1 in cases compared to controls in Indian population. The mechanism of increase in TG after MI may be due to elevated flux of fatty acids and impaired removal of LDL from the plasma. Another mechanism may be the effect of β blockers. However, Surjit Singh showed no significant increase in TG in cases compared to controls.

In our present study, there was significant increase in LDL levels compared to controls. Our results were in accordance with Suman Sharma, Sabari Das, Christ and Paul Holvoet. Since TG brings significant change in LDL particle size, density, distribution and composition producing small dense LDL which is more atherogenic. They suggested oxidation of LDL plays important role in atherogenesis. In our study, we found significant decrease in HDL levels compared to controls. Results were in accordance with Framingham Study, Palani samyan Suman Sharma found significant decrease in HDL levels along with increase in TC, TG and LDL in patients with acute MI.

4. Conclusion

Patients of acute myocardial infarction admitted in Balaji Medical College and Research Institute from June 2019 to December 2019 were studied. The diagnosis was done using the clinical features. A total of 50 cases were studied. The participants of the study were men and women between 40-60 yrs., Patients attending Emergency department, cardiology OPD and ICU in Balaji Medical College diagnosed as myocardial infarction will be included in the study with consent of patient and attenders.

- The incidence of MI is high in male in the age 50-60 years compared to 40-50 years.
- There is no case of MI in females of age group 40-50 years
- There is significant increase in Trop T in MI when compared to controls.
- There is a significant increase in Total cholesterol, Triglycerides and LDL levels and significantly decreases in HDL in myocardial infarction patients.

The data obtained from the present study suggest that prognostic and Diagnostic marker of Troponin- T may be an important markers for the myocardial in.
Compliance with ethical standards

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Disclosure of conflict of interest
Authors have declared that no competing interests exist.

Authors’ contributions
All the Authors have equal contributions in designing, executing and preparation of manuscript.

Statement of informed consent
Informed consent was obtained from all individual participants included in the study.

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