

EVALUATION OF CARDIAC BIOMARKERS AND RISK FACTORS TO ASSESS MYOCARDIAL INFARCTION

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Abstract

Background: Myocardial infarction (MI) is a sever emergency and the life threatening condition if left untreated, it may be a cause of death.

Objective: This study was conducted to (i) observe patients of different age groups who are mostly affected from the MI in Southern Punjab, Pakistan and (ii) evaluate various cardiac biomarkers (Troponin-T, CPK, CKMB, AST and LDH enzymes) for the detection of MI and the role of risk factors especially hypertension, age factor and diabetes.

Methodology: This study was carried out at Ch. Pervaiz Elahi Institute of Cardiology (CPEIC) Multan, Pakistan. One hundred (100) patients who were suffering from severe chest pain (one of the risk factor) were selected from the Emergency Department of the hospital. All the history of the patient including age, sex and family history regarding cardiac or hypertensive disease was taken on special designed Performa (one of the experimental tool) and blood samples were collected to test cardiac biomarkers in Main Laboratory by kit method.

Results: The mean values of the systolic, diastolic blood pressure and pulse rate of infracted patients (129.2 ± 21.4 , 83.9 ± 11.4 and 84.8 ± 16.7) were compared with mean values of that of the control group of patients (119.33 ± 8.28 , 79.67 ± 5.7 and 76.90 ± 12.90) which showed significant ($p < 0.05$) increase in blood pressure and the pulse rate of the infracted patients. All the enzymes levels were significantly ($p < 0.05$) higher in the MI patients. Troponin-T (0.351 ± 0.52), CPK (499 ± 85.5), CKMB (45 ± 4.78), AST (60.3 ± 7.5) and LDH (542 ± 292) were significantly ($P < 0.05$) higher from the control (0.014 ± 0.005), (90.3 ± 26.2), (20.77 ± 3.6), (20.3 ± 6.19) and (373.4 ± 56.6), respectively.

Conclusion: Patients in the age group of 40-59 are mostly affected from the myocardial infarction. All the cardiac biomarkers have their importance because in some cases the Troponin-T was negative but the patient was suffering from MI but in the early diagnosis of MI, Troponin-T is superior to the other enzymes.

Keywords: Biomarkers, Myocardial infarction, Risk factors, Troponin-T.

INTRODUCTION

Immediately after an acute coronary occlusion, blood flow ceases in the coronary vessels beyond the occlusion except for small amounts of collateral flow from surrounding vessels. The area of muscle that has either zero flow or so little flow that it cannot sustain cardiac muscle function is said to be infarcted, and the condition is known as myocardial infarction (MI) [White 2009].

Myocardial infarction accounts for one third of the mortality which can be attributed to coronary artery disease. Atheromatous coronary artery disease is the common cause of myocardial infarction. Arteriosclerosis is a gradual process by which plaques of cholesterol are deposited in the walls of arteries. Cholesterol plaques cause hardening of the arterial walls and narrowing of the lumen of artery. Arteries that are narrowed by arteriosclerosis cannot deliver enough blood to maintain normal function of the parts of the body they supply [Tierney *et al.* 2002]. In many people, arteriosclerosis can remain silent (causing no symptoms or health problems) for years or decades. Although chest pain or pressure is the most common symptom of MI, the victims may experience a variety of symptoms like painful and/or squeezing sensation of the chest, Jaw pain, toothache, headache, Shortness of breath, nausea, vomiting, and/or general epigastria (upper middle abdomen) discomfort and sweating [Topol and Yadav 2000].

The following are reported independent risk factors for MI, in the order of decreasing importance: hypercholesterolemia (i.e. high serum LDL concentrations), hypertension (high diastolic pressure), smoking, hyperglycemia (e.g. diabetes mellitus), family history, lack of exercise, stress, diet rich in saturated fats, diet low in antioxidants, obesity and age [Irene *et al.* 2003].

The presence or absence and the amount of myocardial damage can be assessed by a number of different means like pathologic examination, ECG recordings, measurement of cardiac enzymes in the blood, echocardiography and cardiac catheterization [Chou and Knilans 1996].

Cardiac enzymes are found in heart tissue, and they serve as catalysts for the heart's biochemical reactions. Key cardiac enzymes are Troponin and Creatine Phosphokinase (CPK). Troponin-T is a part of the troponin complex and binds to tropomyosin, interlocking them to form a troponin-tropomyosin complex. Cardiac Troponin regulates the cardiac muscle contraction in response to changes in calcium concentration [Ogawa *et al.* 2000]. Creatinine Kinase (CPK) is increased in over 90% of myocardial infarctions. However, it can be increased in muscle trauma, physical exertion, postoperatively, convulsions, delirium tremens and other conditions [Smith *et al.* 1976]. Aspartate transferase (AST) and lactic dehydrogenase (LDH) are also biochemical markers for the diagnosis of acute myocardial infarction [Edgair and Gonzalez 2006].

This study was conducted to observe which age group of the patients is mostly affected from the MI in Ch. Pervaiz Elahi Institute of Cardiology (CPEIC), Multan, Pakistan (Southern Punjab, Pakistan) evaluating various cardiac biomarkers (Troponin-T, CPK, CKMB, AST and LDH enzymes) for the detection of MI and the role of risk factors especially hypertension, age factor and diabetes.

PATIENTS AND METHODS

MATERIALS AND INSTRUMENTATION

Troponin-T Kit (ROCHE, Pakistan) was used to detect the value of enzyme Troponin-T in the blood sample, based on ICT (Immune Chromatography) principle. All other cardiac enzymes like LDH (Lactic Dehydrogenase), CPK (Creatine Phosphokinase), CKMB (Iso-enzyme of CK) and SGOT (serum glutamate oxytransferase)/AST (Aspartate transferase) enzymes were determined using Hitachi 902 Chemistry analyzer by the photometric method and reagents provided by ROCHE. Blood Pressure Monitoring was made using Mercurial Sphygmomanometer and stethoscope (Yamash, Japan). ECG (electrocardiogram) was recorded using Fukuda M.E Cardiosun C120, Japan.

STUDY SUBJECTS AND STUDY DESIGN

For this study, One hundred (100) patients (age range 20-90 years) of either sex with severe chest pain were selected randomly in the Emergency Department, CPEIC Multan (One year study period). All the patients were related to southern Punjab region of Pakistan. The patients were divided into four groups to observe which age group was most affected with the MI. The Performance of basic data as experimental tool was maintained in columns of age, sex, family history, weight, blood pressure and pulse rate for observations. The blood sample of in-patients were taken and tested in the Main Laboratory, CPEIC Multan for the evaluation of all the cardiac enzymes and other related clinical parameters. Secondly, comparison of all the four cardiac enzymes was studied to examine the affectivity of Troponin-T. Thirty patients of either sex and all ages were randomly selected as the control (Table 3) for the comparison of all enzymes of infarcted and healthy (non-infarcted) patients.

STATISTICS

Mean and standard error of mean (\pm SEM) was calculated on MS Excel-2007. Student's t-test was applied and probability was determined at 5% level of significance.

RESULTS

The whole data obtained from MI affected patients was divided in the six groups (years 20-29, 30-39, 40-49, 50-59, 60-69 and 70 and above) on

the basis of the age (Table 1). The elevated cardiac biomarkers in different age groups among the infarcted patients have been observed (Fig. 1). The patient prevalence of Troponin-T was observed to be high for the age group of 40-49 (31 patients), 50-59 (29 patients), and 60-69 (17 patients) which was associated with underlying acute MI. The CPK, CKMB, SGOT, LDH levels were found to be highest in age group of 30-39 with a mean of 926.75U/L, 59.75 U/L, 77.375 U/L and 689.75 U/L and lowest in age group of 20-29 with a mean of 225.5 U/L, 25.5 U/L, 39.5 U/L and 457U/L, respectively. It is clear from the results that all the determinants for MI were observed to be elevated in patients who have been reported as MI patients in the CPEIC, Multan. All the enzymes levels were significantly ($p < 0.05$) higher in the MI patients (Table 2). Troponin-T (0.351 ± 0.52), CPK (499 ± 85.5), CK-MB (45 ± 4.78), AST (60.3 ± 7.5) and LDH (542 ± 292) were significantly ($p < 0.05$) higher than the control values (0.014 ± 0.005), (90.3 ± 26.2), (20.77 ± 3.6), (20.3 ± 6.19), (373.4 ± 56.6), respectively. The comparison of various biomarkers (Troponin-T, CPK, CKMB, SGOT and LDH) of infarcted patients with that of the control group is exhibited in Table 2. Students t-test application shows significant ($p < 0.05$) difference between each parameter of infarcted and healthy (non-infarcted) patients. The comparison of mean systolic and diastolic blood pressure and pulse rate of infarcted patients with that of the control group is exhibited in Table 3. Students t-test application shows significant ($p < 0.05$) difference between each parameter of infarcted and healthy (non-infarcted) patients.

Table 1: The patients affected with myocardial infarction with reference to age groups.

Age group	Infarcted patients
20-29	2
30-39	9
40-49	31
50-59	29
60-69	17
70 and above	12
Total	100

Table 2: Comparison of mean values (\pm S.D.) of different cardiac biomarkers (Troponin-T, CPK, CKMB, SGOT and LDH) among the acute myocardial infarction patients as compared to that of the control group.

Groups	Troponin-T	CPK	CK-MB	SGOT	LDH
Infarcted Patient	0.351 ± 0.521	499.2 ± 85.5	45.02 ± 4.78	60.3 ± 7.49	542.3 ± 29.2
Control Patients	0.014 ± 0.005	90.3 ± 26.2	20.77 ± 3.63	20.3 ± 6.19	373.4 ± 56.6

Note: t-test ($p < 0.05$) has shown a significant difference.

Table 3: Comparison of mean values (\pm S.D.) of blood pressure and pulse rate of infarcted patients with that of the control group.

Groups	Systolic B.P. (mmHg)	Diastolic B.P. (mmHg)	Pulse Rate/Min
Infarcted Patient (100)	129.2 \pm 21.4	83.9 \pm 11.4	84.8 \pm 16.7
Control Patients (30)	119.33 \pm 8.28	79.67 \pm 5.71	76.90 \pm 12.90

Note: t-test ($p < 0.05$) has shown a significant difference.

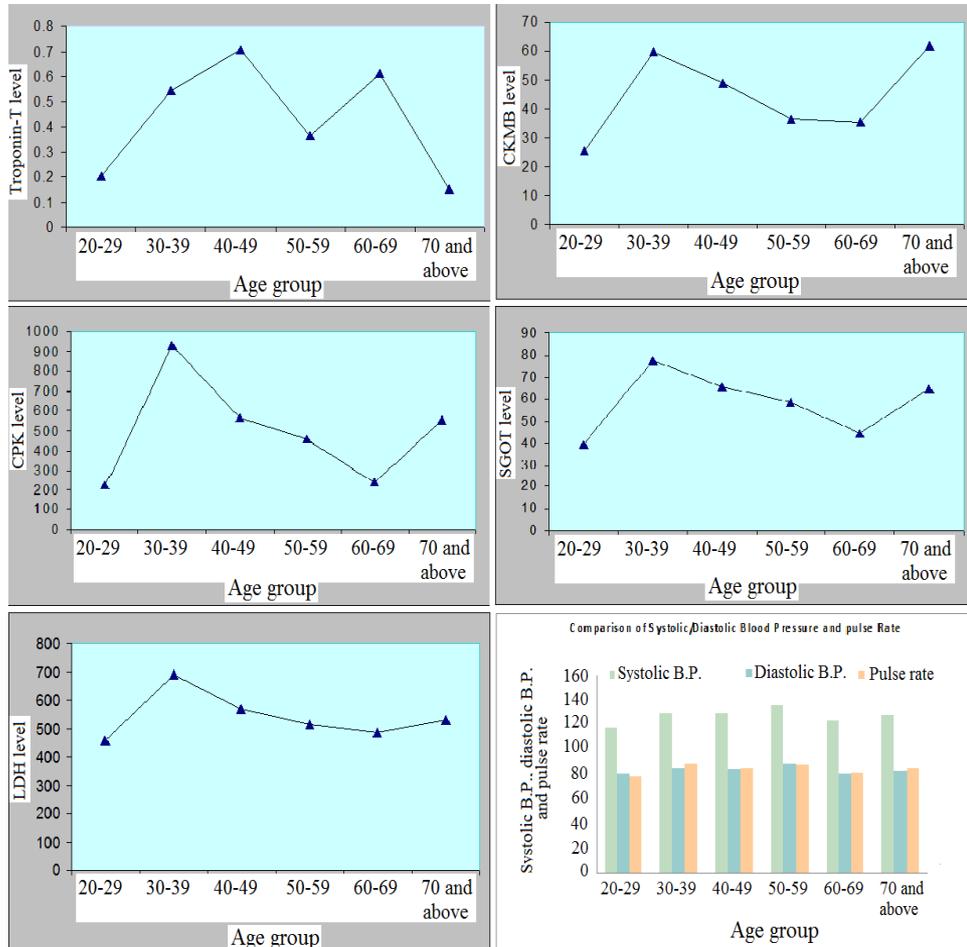


Fig. 1: The elevated cardiac biomarkers in different age groups among the infarcted patients.

DISCUSSION

The MI is the medical emergency in the whole world [Alpert *et al.* 2000] and patient suffering from MI should be admitted to the hospital. In the diagnosis of MI, ECG could not be evident and supportive in diagnosis during initial onset hours at all the times, whereas it is always crucial to diagnose MI earlier for timely therapeutic intrusion. Thus, during the acute

MI, various enzymes (as cardiac biomarkers) are released in the body namely Troponin-T, CPK, CKMB, LDH, and AST. When MI occurs these enzymes are released in abnormal form.

Positivity of Troponin-T always varies with the area of infarction and anterior infarction is maximum (85%) followed by anteroseptal and inferior MI whereas slightest positivity has been observed with right ventricular and/or posterior infarction [Luley 2000].

In this study, the elevated and/or abnormal release of these enzymes was determined during acute MI for its diagnosis. From the observed data, it is quite evident that serum Troponin-T, CPK, CKMB, SGOT, and LDH has a major role in the detection as well as management of acute MI as reported earlier [Hirschl *et al.* 2000]. The concentration of these cardiac biomarkers was found to be significantly ($p < 0.05$) high as compared to that of the control subjects. It is interesting that all the subjects with acute MI under this study were having an elevated level of the systolic blood pressure and pulse rate. The t-test analysis has shown a significant difference ($p < 0.05$) in blood pressure among patients with acute MI and without MI i.e. control group (Fig. 1). These results agree with the outcomes obtained from the previous study [Lindahl *et al.* 1996].

As the patients were divided into different age groups, the patient prevalence of Troponin-T was observed to be high for the age group of 40-49 (31 patients), 50-59 (29 patients), and 60-69 (17 patients) which was associated with underlying acute MI (Fig. 2). Previous studies have reported the prevalence of Troponin-T elevation among dialysis patients, patients visiting emergency departments with angina, patients presenting to outpatient clinics, and healthy volunteers [Ng *et al.* 2001, Apple *et al.* 2003].

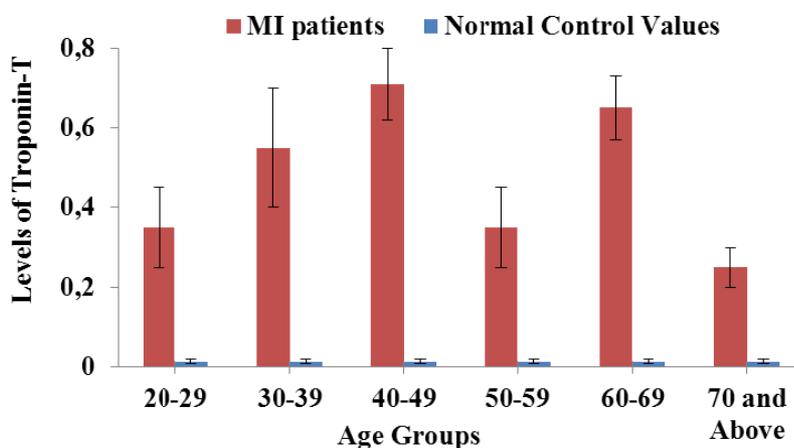


Fig. 2: The comparison of elevated Troponin-T in different age groups among the infarcted patients and control group.

In addition, LVH and CHF have previously been demonstrated to be associated with elevated Troponin-T levels in small patient populations or subgroups of patient [Dierkes *et al.* 2000, Hamm *et al.* 2002]. The CPK, CKMB, SGOT, LDH levels were found to be highest in age group of 30-39 with a mean of 926.75U/L, 59.75 U/L, 77.375 U/L and 689.75 U/L and lowest in age group of 20-29 with a mean of 225.5 U/L, 25.5 U/L, 39.5 U/L and 457U/L, respectively. It is clear that all the determinants for MI have been elevated in patients who have been reported as MI patients in the CPEIC, Multan. All the enzyme levels were significantly ($p < 0.05$) higher in the MI patients (Table 2). Troponin-T (0.351 ± 0.52), CPK (499 ± 85.5), CKMB (45 ± 4.78), AST (60.3 ± 7.5) and LDH (542 ± 292) were significantly ($p < 0.05$) higher from the control (0.014 ± 0.005), (90.3 ± 26.2), (20.77 ± 3.6), (20.3 ± 6.19) and (373.4 ± 56.6), respectively. This study was also in accordance with the previous studies done by Morrow 2001, which explained higher sensitivity for Troponin-T to diagnose MI. It is the investigation of choice that shows affectivity of other cardiac biomarkers (enzymes) which in some cases help in the diagnosis of MI [Lindahl *et al.* 2001]. The CKMB levels are also playing a significant role in the diagnosis of MI without ST-segment elevation on the basis of which the cardiac Troponin levels are comparable [Wu *et al.* 1999]. CKMB appears in blood earlier but its level/sensitivity is lower than Troponin-T during early hours of onset and Troponin-T is a better mean to detect MI earlier [Burton *et al.* 1976]. In comparison with other enzymes like CKMB and SGOT, the elevation level or sensitivity of Troponin-T in this study, was found to be higher (100%) which is comparable with already reported [Francis 1995]. Troponin-T cannot be elevated without myocardial injury but in some situation it is also important to detect the other cardiac biomarker where Troponin-T is negative as observed in our study but the patient is having chest pain (risk factor) which shows that patient is at risk and should be treated aggressively [Hamm *et al.* 2002]. It has also been reported in a previous study that high mortality in cases in which Troponin-T was positive occurred within 5 min of onset of MI [Luley 2000]. In conclusion, Troponin-T levels are potent, independent predictors of the short-term and long-term risk of MI and morbidity [Antman *et al.* 1996, Stubbs 1996].

CONCLUSIONS

Patients in the age group of 40-59 are mostly affected from the myocardial infarction. So the people in this age group having any positive sign or family history should be careful and the patients having high blood pressure are also at risk because in the results all infarcted patients have the tendency towards high blood pressure. All the cardiac biomarkers have their importance because in some cases the Troponin-T was negative but the patient was suffering from MI.

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