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HYPERTENSION AND MYIOCADIAL INFARCTION: A STUDY IN KASHMIR INSTITUTE OF CARDIOLOGY MIRPUR, KASHMIR PAKISTAN.

KHAN KS[1], MAHMOOD R[*2], ANJUM J[3], SHOUKAT Z[4], ALAM S[5] AND IQBAL W[6]

1: Dr. Khuram Shahzad Khan (MD, MPhil) Assistant Professor Department of Physiology, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, Kashmir Pakistan

2: Dr. Rashad Mahmood (MD, MPhil, PhD) Assistant Professor Department of Physiology, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, Kashmir Pakistan

3: Dr. Jahngir Anjum (MBBS, FCPS), Assistant Professor Department of Medicine, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, Kashmir Pakistan

4: Dr Zara shoukat (MBBS) Post Graduate Trainee in Physiology, Foundation University Islamabad Campus

5: Dr. Saeed Alam (MBBS, FCPS) Assistant Professor Department of Cardiology, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, Kashmir Pakistan

6: Dr. Waheed Iqbal (MBBS, FCPS), Associate Professor Department of Medicine, Mohtarma Benazir Bhutto Shaheed Medical College, Mirpur, Kashmir Pakistan

***Corresponding Author: Dr. Rashad Mahmood: E Mail: rashadmahmood74@yahoo.com**

Cell Phone 0092-335-1662233; Fax 0092-5827-920501

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ABSTRACT

Objective: The present study was conducted to observe the behavior of the MI evaluating various cardiac biomarkers for the detection of MI in relation with Risk factors of hypertension in both genders, with or without Myocardial Infarction.

Study Design: This case control study was conducted over indoor patients in Kashmir Institute of Cardiology Mirpur, Azad Jammu and Kashmir Pakistan.

Materials and Methods: Study was conducted in Kashmir Institute of Cardiology Mirpur, Azad Jammu and Kashmir. Total 240 patients were recruited in the study. 120 admitted patients of Acute Myocardial Infarction (AMI) in Kashmir Institute of Cardiology were registered. The span of study was from June 2013 to July 2014. 120 age and sex matched controls were included in the study. Informed written consent was obtained by the participants of study. Detailed medical/surgical history was obtained and recorded.

Results: The mean concentration of cardiac biomarkers, CK-NAC, CK-MB and LDH enzymes was analyzed in MI affected hypertensive and normotensive group of population.

Conclusion: According to our findings, there was significant increase in cardiac enzymes CK-NAC, CK-MB and LDH in MI patients from both genders but there was an insignificant difference in non MI patients with hypertension. There is no evidence to support the later findings as reported earlier. Further analysis and study is needed to find the reasons for above-mentioned results in non-MI patients.

Keywords: CK-NAC, LDH, Cardiac Enzymes in hypertensive, Myocardial infarction in hypertensive

INTRODUCTION

Hypertension is credited as the leading cause of cardiovascular mortality by WHO. Nowadays HTN is defined as systolic blood pressure of more than 140 mm Hg and diastolic blood pressure of more than 90 mm Hg. It has been foretold that in 2025 there will be 60% to 1.56 billion increase in the number of Adult HTN patients **[1]**. Out of control HTN could lead to Myocardial Infraction **[2]**.

HTN is major and independent risk factor for MI. It is a chief risk factor for atherosclerosis in coronary blood vessels, resulting in MI. HTN and MI are closely linked **[3]**. HTN is present in approximately69% of patients with a first myocardial infarction **[4]** and bears an independent continuous relationship with the incidence of several CV events **[5-7]**. Nevertheless, HTN is also a key risk factor for sudden cardiac death **[8]**. HTN is associated with changes in vasomotor tone and sodium and fluid imbalance, as they are the main controllers of blood pressure **[9]**. Many of the life style factors such as obesity, physical inactivity, and poor diet, including high intake of alcohol and salt act as risk factors for HTN because of their potentially weight-increasing effect. Excess body weight contributes to blood pressure levels from infancy and is the most important factor causing a predisposition to HTN. In addition, overweight and obesity rises the risk of insulin resistance **[10]**. On the other hand, insulin resistance is another risk factor for HTN **[11]**. High blood

pressure is related to CHD in both men and women, and the risk increases progressively with increasing blood pressure **[2, 12]**.

MATERIAL & METHODS

STUDY DESIGN

Case control study

SETTING

Study was conducted at indoor patient department Kashmir Institute of Cardiology Mirpur, Azad Jammu and Kashmir.

DURATION

Study was completed in 12 months.

SAMPLING TECHNIQUE

Non-probability purposive sampling technique was used.

POPULATION SELECTION AND SAMPLE SIZE

Total 240 patients were recruited in the study. 120 admitted patients of Acute Myocardial Infarction (AMI) in Kashmir Institute of Cardiology were registered as cases. The span of study was from June 2013 to July 2014. 120 age and sex matched controls were included in the study. Informed written consent was obtained by the participants of study. Detailed medical/surgical history was obtained and recorded.

SAMPLE SELECTION

Inclusion criteria

- Patients with chest pain suggestive of myocardial ischemia within 12 hours after the onset of symptoms on the basis of ECG changes.
- Persons presenting with non-infracted states of ischemia, routine, general health check-up were taken as controls.

Exclusion criteria

- Severe skeletal muscle damage or trauma as CK is deranged in skeletal muscle damage.
- Cardiac resuscitation
- Patients undergone cardiac surgery
- Patients suffering from re-infarction

DATA COLLECTION PROCEDURE

Serum samples were drawn from one of peripheral vein of arm, and serum was analyzed. Age and sex matched individuals presenting for a routine, general health check-up and diseases like hypertension, diabetes mellitus with ECG not suggestive of myocardial infarction were taken as the control group. Blood specimen were collected from each participant after admission suffering from acute symptoms. Serum levels of CK-NAC, CKMB and LDH was analyzed using chemistry analyzer Microlab.

Cardiac Enzymes Analyses

A) Creatine Kinase-MB

Principle:

Immunoinhibition Assay: An antibody is incorporated in the CK reagent. This antibody would bind to and inhibit the activity of the M subunit of CK-MB. This

means that only the activity of the B subunit in serum was measured. If the activity was multiplied by a factor 2, it would give the activity of CK-MB in serum.

Procedure:

20 µl of standard, specimens, and controls were dispensed into appropriate wells.200 µl of Enzyme Conjugate Reagent was added to each well and thoroughly mixed for 30 seconds. Complete mixing was ensured. Specimen was incubated at room temperature (18-25°C) for 60 minutes. Mixture was emptied and washed repeatedly by distilled water, and removed residual water droplets. 100 µl of TMB reagent was put into each well and gently mixed for 5 seconds, and incubated at room temperature for 20 minutes; reaction was stopped by adding 100 µl of solution to each well and gently mixed for 30 seconds. The color changes were assured. (Blue color changed to yellow color). Optical density was read at 450 nm with a microtiter plate reader within 15 minutes.

B) Lactate Dehydrogenase

Principle:

It utilizes the principle of spectrophotometry carried out at 340 nm. In the reaction, the LD catalyzed the reversible oxidation of L-Lactate to Pyruvate with the concurrent reduction of ß-Nicotinamide Adenine Dinucleotide (NAD) to ß-Nicotinamide Adenine Dinucleotide (reduced form) (NADH). The system monitored the rate of change in absorbance at 340 nm over a fixed-time interval. The rate of change in absorbance was directly proportional to the activity of LD in the sample.

Pyruvate + NADH + H → L- lactate + NAD

Procedure:

0.05ml of Sample of serum was obtained and was mixed with 3 ml of reagent (phosphate buffer, pyruvate and reconstituted NADH). Both were mixed and initial absorbance at 340nm was obtained after 0.5min. Timer was started simultaneously and reading was obtained after 1, 2 and 3 minutes. Decrease in absorbance per minute ΔA/min. was recorded from the linear path of the assay with greater slope. ΔA/min. was multiplied by the Factor 9683 to calculate U/L of LDH.

DATA ANALYSIS

Data entry and analysis was done by using SPSS 20. Quantitative variables were presented by using mean±SD. Study variables were analyzed by using frequency table and percentages. Participants were divided into 3 age groups: 21-39, 40-59 and 60 years and above for statistical analysis. Association between study variables in between the groups and within the groups was assessed by applying ANOVA to see

the level of CK-NAC, CK-MB and LDH. P<0.005 was taken as significant.

RESULTS

The cardiac enzymes used as biomarkers of myocardial infarction (MI) have been assayed in MI affected and compatible non-MI control subjects. The pertinent cardiac enzymes in relation to MI included CK-NAC, CK-MB and LDH. The responses of the cardiac enzymes have been analyzed in relation to hypertension and normotensive in both genders.

Cardiac Enzymes In Relation To Myocardial Infarction Status & Non-Infarction

Collectively, in all the subjects of study, mean cardiac enzyme concentrations were increased in MI patients as compared to non-MI subjects. CK-NAC was 54% higher(p= 0.000) in MI patients, with observed mean 364.48±39.11 as compared to observed mean 167.10±3.11 in non-MI subjects, CK-MB was 54% higher (p= 0.000) in MI patients, with observed mean 52.58±5.6 as compared to observed mean 23.85±0.5 in non-MI subjects. LDH was 28% higher (p= 0.000) in MI patients, with observed mean 482.96±27 as compared to observed mean 346.70±6.2 in non-MI subjects as shown in **Table 1 and Figure 1**.

Gender Wise Analysis Of Hypertension

Hypertensive Males In Myocardial Infarction

Creatinine Kinase – Myocardial Band:

The mean concentration of CK-MB in MI affected hypertensive males was 59±10, whereas 50.60±9 among non-hypertensives. 15% lower values were observed in normotensives as compared to hypertensives. However, the differences between hypertensive and normotensives were insignificant statistically.

Lactate Dehydrogenase:

The average concentration of LDH in MI affected hypertensive males was 504.17±41 and 465.13±48 U/L among normotensive MI affected males. 7.5 % less values of LDH were observed among normotensive as compared to hypertensive group in MI affected males **(Table 2)**.

Female Subjects With Hypertension In Myocardial Infarction

Creatinine Kinase –Myocardial Band:

The mean concentration of CK-MB in MI affected hypertensive females was 47±9 U/L whereas among normotensives, mean CK-MB concentration was 52±19 U/L. 9.5% lower values were observed in hypertensive as compared to normotensive females. However, the differences between hypertensive and non-hypertensive groups were insignificant statistically.

Lactate Dehydrogenase:

The average concentration of LDH in MI affected hypertensive females was 536±89 and 434±34 U/L among normotensive females. 18% less LDH concentration was observed among normotensives as

compared to hypertensive MI affected females **(Table 3, Figure 2)**.

Male Subjects With Hypertension In Non-Myocardial Infarction

Creatinine Kinase – Myocardial Band:

The mean concentration of CK-MB in non-MI hypertensive males was 24±0.7U/L. In normotensive males, the mean concentration was 21.47±0.6U/L.12.5% lower value was observed in normotensive as compared to hypertensive males. However, the differences between hypertensive and normotensive patients were insignificant statistically (0.064).

Lactate Dehydrogenase:

The average concentration of LDH in non-MI affected hypertensive males was 354±9 while it was 323±9U/L among non-MI affected normotensives. 9% less concentration of LDH was observed in hypertensives as compared to normotensive group. However, the differences between hypertensive and normotensive patients were insignificant statistically **(Table 4, Figure 3)**.

Hypertensive Females In Non-Myocardial Infarction

Creatinine Kinase – Myocardial Band:

The mean concentration of CK-MB in non-MI affected hypertensive females was 22.80±0.5, and normotensive females was 31.50±0.9.The enzyme concentration was 29% higher in normotensives as compared to hypertensives. However, the difference between hypertensive and normotensive females was significant statistically (0.000).

Lactate Dehydrogenase:

The average concentration of LDH in non-MI affected hypertensive females and non-MI affected normotensive females was 331±11 and 397.00±34 U/L respectively. It was 16.5% less among hypertensives as compared to non-hypertensives in non-MI affected females. The difference between hypertensives and normotensives was significant statistically (0.027) **(Table 5, Figure 4, 5)**.

Table 1: Cardiac Enzymes in Cardiovascular Diseases In Relation To MI & non-MI

	CK-NAC	P	CK-MB	P	LDH	p
MI	364.48±39.1	0.000	52.58±5.6	0.000	482.96±26.7	0.000
Non – MI	167.10±3.11		23.85±0.5		346.70±6.2	
% difference	54		54		28	

*** Significant p value< 0.05**

Table 2: Cardiac enzymes in males following MI with and without hypertension

Enzymes	Concentration in hypertensives	Concentration in normotensives	F	P(<0.05)
CK-MB	59.02±10.4	50.6±9.1	0.367	0.547
LDH	504.17±41.7	465.13±48.2	0.347	0.558

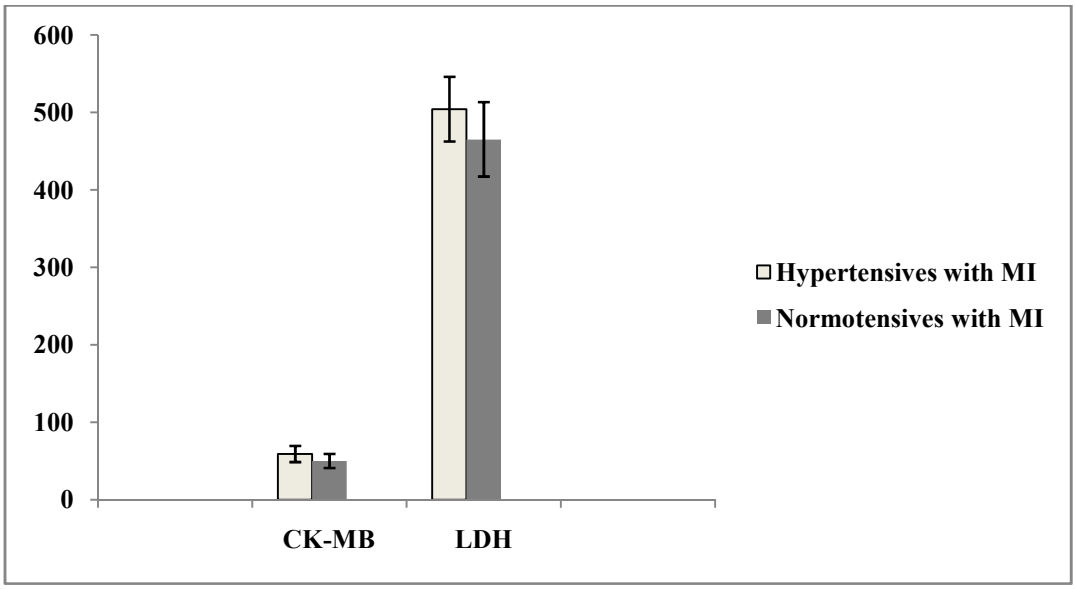

Figure 1: Cardiac enzymes in Hypertensive and Normotensive Males with Myocardial Infarction (MI). CK-MB: Creatine Kinase Myocardial Band; LDH: Lactate Dehydrogenase. *(P < 0.05): Statistically insignificant.

Table 3: Cardiac enzymes in females following MI with and without hypertension

Enzymes	Concentration in hypertensives	Concentration in normotensives	F	p
CK-MB	48±9.2	52.08±19	0.038	0.846
LDH	536.42±89.8	434.53±34.5	1.121	0.297

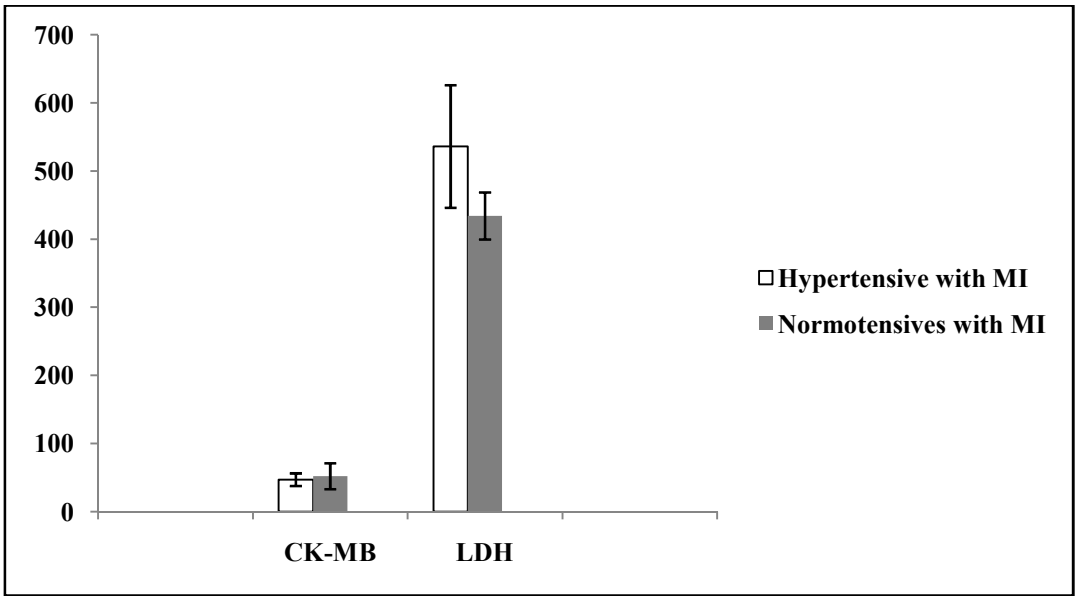

Figure 2: Cardiac enzymes in Hypertensive and Normotensive Females with Myocardial Infarction (MI). CK-MB: Creatine Kinase Myocardial Band; LDH: Lactate Dehydrogenase. *P< 0.05: Insignificant statistically

Table 4: Cardiac enzymes in non-MI males with and without HTN

Enzymes	Concentration in hypertensives	Concentration in normotensives	F	P(<0.05)
CK-MB	24.13±0.7	21.47±0.6	3.495	0.065
LDH	354.38±9	323.64±9.1	3.529	0.064

*** Significant p value<0.05**

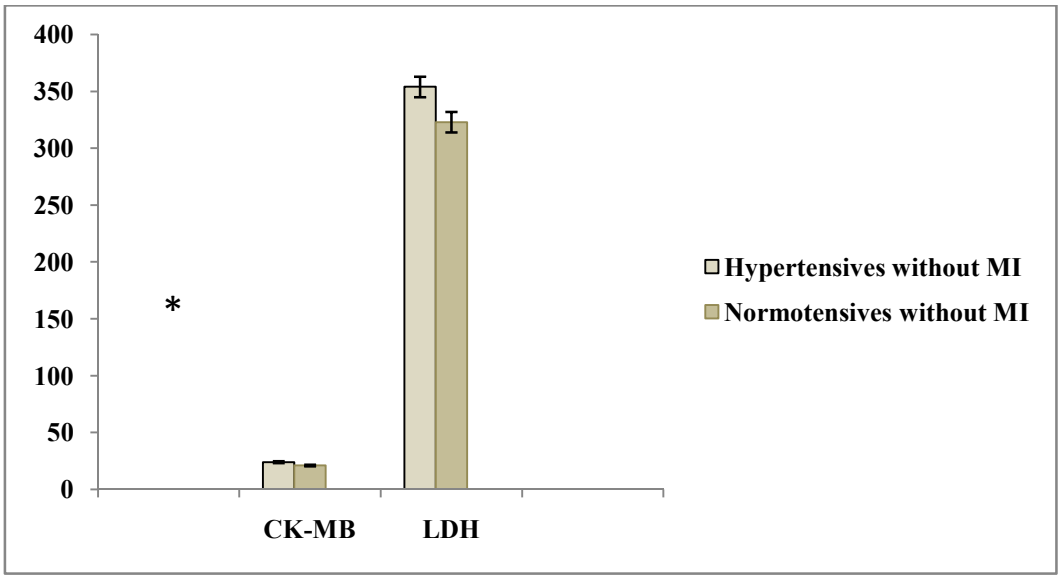

Figure 3: Cardiac enzymes in Hypertensive and Normotensive Males without Myocardial Infarction (non-MI). CK-MB: Creatine Kinase Myocardial Band; LDH: Lactate Dehydrogenase. *P < 0.05: Significant statistically

Table 5: Cardiac enzymes in non-MI females with and without hypertension

Enzymes	Concentration in hypertensives	Concentration in normotensives	F	P(<0.05)
CK-MB	22.8±0.5	31.5±0.9	62.091	0.000
LDH	331.85±11.6	397±34.3	5.381	0.027

***Significant p value<0.05**

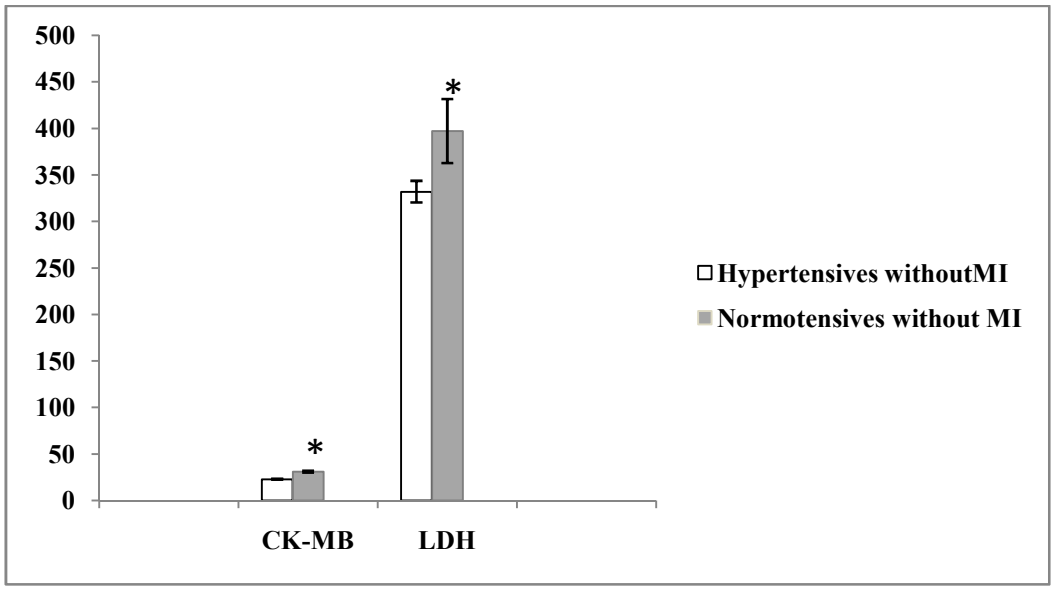

Figure 4: Cardiac enzymes in Hypertensive and Normotensive Females without Myocardial Infarction (non-MI). CK-MB: Creatine Kinase Myocardial Band; LDH: Lactate Dehydrogenase. *P< 0.05: Significant statistically

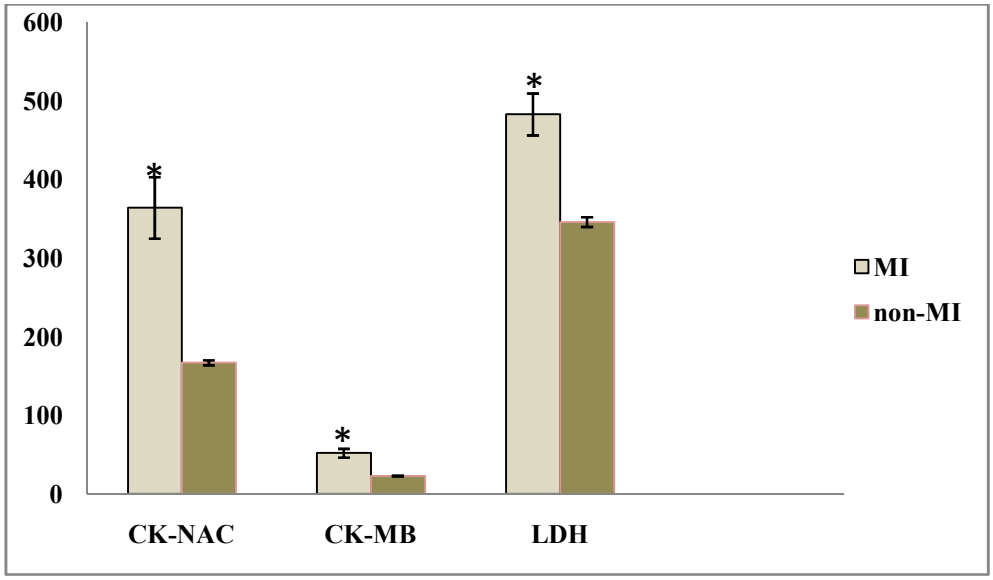

Figure 5: Cardiac enzymes in Cardiovascular Disease in relation to Myocardial Infarction (MI).& non-MI. CK-MB: Creatine Kinase Mycardial Band; LDH: Lactate dehydrogenase. *P < 0.05: Statistically significant

DISCUSSION

Coronary artery disease is considered as the leading cause of morbidity and mortality in myocardial infarction. Approximately about 25% of patients presenting with chest pain are diagnosed as suffering from MI **[13]**. Onset of coronary artery disease may proceed due to aging with the additional factors, of nutrition, inactivity, genetics etc. It develops without significant indicators for it and if there appear certain are mixed for multiple disorders. Generally, it appears with the episode of MI that has been characterized with the specific responses of cardiac enzymes. Although cardiac enzymes have been assessed for, diagnostic purposes otherwise the cardiac enzymes may have specific patterns varying in the different states of subject inflicted with MI. Thus, the present study had been conducted in the population of Mirpur, AJK in order to analyze the age and gender related changes in cardiac enzymes in subjects with and without MI presenting to Kashmir Institute of Cardiology with the history of chest pain from June 2013 to May 2014.

Cardiac enzymes used as biomarkers of MI. In the current study, significant differences ($p<0.05$) in serum concentrations of cardiac enzymes, CK, CK-MB and LDH were observed in MI subjects as compared to non-MI subjects. This finding is consistent with the finding of **[14]** who also reported significant increased levels of CK and CK-MB for both sexes with and without MI. **[15]** reported significant higher levels of LDH in patients of MI as compared to controls. **[15]** also reported increased CK levels in their study but could not reach significant level as compared to current study.

Hypertension has been regarded as the major risk factors for MI. In the present study, it was observed that insignificant

differences existed in CK-NAC,CK-MB and LDH levels in hypertensive and normotensives in both genders with MI($p>0.05$). These findings are inconsistent from researchers who reported significantly higher levels of CK-NAC and LDH in hypertensive patients with MI. Similarly, another study also reported significant higher levels of CK-NAC in hypertensive patients with MI **[15]**.

CONCLUSION

Hypertension is associated to myocardial infarction as a risk factor, an atherogenic factor and a hemodynamic factor. It may also happen in the development of an acute myocardial infarction. Both these disorders have serious adverse cardiac effects and both have deep effects on morbidity and mortality **[16]**. According to our findings, there was significant increase in cardiac enzymes in MI patients from both genders but there was an insignificant difference in non-MI patients with hypertension. There is no evidence to support the later findings as reported earlier. Further analysis and study is needed to find the reasons for above-mentioned results in non-MI patients.

REFERENCES

[1] He J, Gu D, Chen J, *et al*. Premature deaths attributable to blood pressure in China: a prospective cohort study. *Lancet.* 2009; **374**(9703): 1765–72.

[2] Lawes CMM, Hoorn SV, Rodgers A. Global burden of blood-pressure related disease. *Lancet*. 2008; **371**: 1513–1518.

[3] Aronow WS, Fleg JL, Pepine CJ, Artinian NT *et al*. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus documents developed in collaboration with the American Academy of Neurology, American Geriatrics Society, American Society for Preventive Cardiology, American Society of Hypertension, American Society of Nephrology, Association of Black Cardiologists, and European Society of Hypertension. *J Am Coll Cardio*l. 2011; **57**: 2037-2114.

[4] Lloyd-Jones D, Adams R, Carnethon M *et al*. Heart disease and stroke statistics-2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circ.* 2009; **119**: 21-181.

[5] Britton KA, Gaziano JM, Djousse L. Normal systolic blood pressure and risk of heart failure in US male

physicians. *Eur J Heart Fail.* 2009; **11**: 1129–1134.

[6] Kalaitzidis RG, Bakris GL. Pre-hypertension: is it relevant for nephrologists? *Kidney Int.* 2010; **77**:194–200.

[7] Mancia G, Fagard R, Narkiewicz K. *et al*. ESH/ESC Guidelines for the management of arterial hypertension The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J*.2013; **34**: 2159–128.

[8] Bakris GL, Sica D, Weber M.*et al*. The comparative effects of azilsartan medoxomil and olmesartan on ambulatory and clinic blood pressure. *J Clin Hypertens*. 2011; 13(2): 81-88.

[9] Staessen JA, Wang J, Bianchi G.*et al*. Essential hypertension. *Lancet* 2003; **361**: 1629-41.

[10] Reaven GM. Insulin resistance: the link between obesity and cardiovascular disease. *Endocrinol. Metab. Clin N Am* 2008; **37**: 581-601.

[11] Reaven GM. Relationships among insulin resistance, type 2 diabetes, essential hypertension, and cardiovascular disease: Similarities and differences. *J Clin. Hypertens*. 2011; 238-43.

[12] Yusuf S, Hawken S, Ôunpuu S *et al*. Effect of potentially modifiable risk factors associated with myocardial infarction in 52countries case-control study. *Lancet* 2004; **364**: 937-52.

[13] Kumar A, Sivakanesan R and Gunasekera S. Ischemia modified albumin: A potent marker in acute myocardial infarction in normolipidemic. *Pak J Med Sci.* 2008; **24**(3): 364-67.

[14] Fethi Abed ALGani. Significance of Total Creatine Kinase and Creatine kinase-MB Levels in Patients with Acute Myocardial Infarction.*Int J Biol Med Res.* 2011; **2**(3): 762-765.

[15] Haseeb Ak, Abdullah SA, Samia HS. *et al*., Serum markers of tissue damage and oxidative stress in patients with acute myocardial infarction. *Biomed Res.* 2013; **24** (1): 15-20.

[16] Francis G. Dunn, Mb, Chb, Facc. Nell' Orleans. Louisiana. J AM cou, CARDIOl 1983.1(2). 528-32.