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DIABETES MELLITUS AS RISK FACTORS FOR MYOCARDIAL INFARCTION WITH EMPHASIS ON CARDIAC BIOMARKERS AND ITS SEVERITY IN DIABETIC PATIENTSADMITTED IN KSHMIR INSTITUTE OF CARDIOLOGU MIRPUR KASHMIR, PAKISTAN

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ABSTRACT

Objective: The objective of following coherent population-based study was to elucidate diabetes mellitus as risk factors for myocardial infarction with emphasis on cardiac biomarkers and its severity in diabetic patients.

Study Design: Study was done at indoor patients of Department of Kashmir Institute of Cardiology Mirpur, Azad Jammu and Kashmir and time period was 12 months.

Materials and Methods: Total 240 patients were used in this study and 140 were indoor patients of Acute Myocardial Infarction (AMI) in Kashmir Institute of Cardiology and 120 subjects were used as a control for the accuracy of results. Complete record of their medical history was maintained and their agreement was taken.

Conclusion: It is concluded that concentration of cardiac biomarkers CK-NAC, CK-MB and LDH is significantly high in diabetic patients having MI than non diabetic patients with MI.

Keywords: CK-NAC, LDH, Cardiac Enzymes, Myocardial infarction, Diabetes Mellitus

INTRODUCTION

Diabetes Mellitus is appeared as one of the most threatening health issue of 21st century and it has been affected 366 million of people throughout the world **[1]**. According to World Health Organization, 2011, over 5.2 million diabetic patients were reported in Pakistan during 2003 and researchers are estimating that figure can be 13.9 million in 2030.There are up to 80% diabetic patients in developing and low income countries **[2]**.

Diabetes badly affects many other systems of the body and it is affecting vascular system so is a risk factor for cardio vascular disease. Hyperglycemia due to diabetes affects myocardial damage so cause ischemic attacks **[3]**.Many pathways are involved in increasing of atherosclerosis due to high blood glucose levels **[4]**.

High blood sugar level is indirectly involved in worsening increase of low lipoprotein (LDL) levels reduced high density lipoprotein (HDL) levels and increased levels of TG levels. Hyperglycemia leads increased atherosclerotic process and develop endothelial dysfunction that promotes vasoconstrictive, prothrombotic and proinflammatory process which is involved in the formation of plaque and rupture **[5]**.

During the developing stage of diabetes, atherogenic dyslipidemia and impaired endothelial function and high level of fatty acids and subclinical inflammation contributes for CVD **[6]**.

The following population bases study of people of Mirpur Azad Kashmir is conducted to test MI evaluating in different cardiac biomarkers for the detection of MI in relation to the diabetes mellitus and severity of MI in diabetic patients.

MATERIAL & METHODS

STUDY DESIGN

Following case study was held at Kashmir Institute of Cardiology Mirpur, AJK and sample subjects were patients at indoor patient department in following time duration from June 2013 to July 2014.

SAMPLE COLLECTION

Total no of patients was taken 240 from which 120 subjects were registered patients of MI at Kashmir Institute of Cardiology and 120 subjects were included in study as a control after their written agreement. Sampling technique was non-probability purposive. Detailed medical history was obtained with their health certificates and recorded.

Inclusion criteria were for the patients of chest pain suggestive of MI during early 12 hours of onset of symptoms. Exclusion criteria was for patients who has been undergone cardiac surgery or suffering from re-infarction.

DATA COLLECTION PROCEDURE

Blood sampling was done from were drawn from one peripheral vein of arm, and serum was taken through centrifugation then it analyzed. Control group subjects were those persons who were presented for routine checkup for hypertension and diabetes mellitus. Serum levels of CK-NAC, CKMB and LDH was examined through chemistry analyzer Microlab.

ANALYSES OF CARDIAC ENZYMES

1) CREATINE KINASE –NAC

Assay method was performed which is ATP formation with enzymes hexokinase and glucose-6-phosphate dehydrogenase as coupling enzymes. This enzyme performs following catalytic activity.

$$\text{Creatine phosphate} + \text{ADP} \xrightarrow{\text{CK}} \text{Creatine} + \text{ATP}$$

$$\text{Glucose} + \text{ATP} \xrightarrow{\text{HK}} \text{Glucose-6-P} + \text{ADP}$$

$$\text{Glucose-6-P} + \text{NADP} \xrightarrow{\text{G-6-PDH}} \text{Glucose-6-P} + \text{NADPH} + \text{H}$$

Procedure:

Substrate reagent was taken in 1ml cuvette and incubation was done at 37 C for 3 minutes with wavelength at 340nm. 0. 50 µL of sample was used to mix in it and after color change at different time intervals absorbance was recorded and mean change in absorbance was taken from readings as ΔA/min and multiplied by the Factor 3376 to calculate U/L of CK.

2) CREATINE KINASE-MB

Immunoinhibition Assay was done for CK-MB in which an antibody is incorporated in the CK reagent and it can bind to inhibit the activity of the M subunit of CK-MB. So only activity of B subunit in serum was measured.

Procedure:

20 µl of standard, specimens, and controls were taken and in200 µl of enzyme conjugate reagent was added in it and mixed for 30 seconds. Incubation was done at room temperature (18-25°C) for 60 minutes. 100 µl of TMB reagent was added into each well contain reagents and mixing was done for 5 seconds. After the

change of color, OD was measured at 450 nm in microtiter plate reader.

DATA ANALYSIS

Data analysis was done by using SPSS 20 system. Quantitative variables have used mean± SD. For statistical analysis, study subjects were divided into 3 different age groups from 21-39, 40-59 and 60 years age. Association of study variables was measured by applying ANOVA to see the values of CK-NAC, CK-MB and LDH. P<0.005 was taken as significant value.

RESULTS

The cardiac enzymes were used as biomarkers of MI have been assayed in MI affected diabetic and nondiabetic subjects.

ANALYSIS OF MI WITH DIABETES

DIABETIC AND NON- DIABETIC MALE PATIENTS WITH MI

CREATININE KINASE-NAC:

The mean CK-NAC was 226.70±41U/L in male diabetic patients with MI and it was 429.51 ± 60 in MI affected non-diabetic patients. This showed the value of CK-NAC was 47% lower in diabetics as compared to non-diabetics. Difference is compared in table no 1.However differences were insignificant statistically (**Table 1, Figure 1**).

CREATININE KINASE–MYOCARDIAL BAND:

The mean CK-MB value in MI affected male diabetics was 59.15±26 and in non-diabetics, it was 53.55±10. The value was 10% lower in non-diabetics than diabetic patients with MI. However, the difference was insignificant statistically.

DIABETIC AND NON-DIABETIC FEMALE PATIENTS OFMI

CREATININE KINASE-NAC:

The CK-NAC concentration was 365.31±80 U/L in female diabetic patients with MI and it was 239.±51 in MI affected non-diabetic females. The difference was insignificant statistically (P=.0.111). The value of CK-NAC in MI affected diabetic females was 34% greater than non-diabetic females (**Table 2, Figure 2**).

CREATININE KINASE MYOCARDIAL BAND:

The mean CK-MB in female diabetics with MI was 82.88±28U/L and it was 32±2.8 in non-diabetics females. It was 60% lower in non-diabetics as compared to diabetic patients with MI. The difference was significant statistically (p=0.017).

MALE DIABETIC/NON-DIABETIC PERSONS WITHOUT MI

CREATININE KINASE-NAC:

The mean CK-NAC was 198.31±15.5 U/L in diabetic male patients without MI and it was 159.73±2.7 in non-diabetic male subjects without MI. 19%lower value of enzyme in non-diabetics subjects as compared to diabetics. The difference was significant statistically (**Table 3, Figure 3**).

CREATININE KINASE – MYOCARDIAL BAND:

The mean CK-MB in diabetic male subjects without MI was 25.78±5 and it was 22.92±0.7 in non diabetics without MI. So, 12% lower value in non-diabetics as compared to the diabetics. The differences between diabetics and non-diabetics were not significant statistically.

FEMALE DIABETIC/NON-DIABETIC SUBJECTS WITHOUT MI

CREATININE KINASE-NAC:

The mean CK-NAC was 153.00±11.7 U/L in diabetic females without MI and it was 175.55±2.6 in non-diabetic females without MI. 12.5% lower value were in diabetic females as compared to non-diabetics. The difference was significant statistically (P=.0.022) (**Table 4, Figure 4**).

CREATININE KINASE – MYOCARDIAL BAND:

The mean CK-MB in diabetic females without MI was 24.77±0.7 and it was 24.89±1innon diabetics. 0.5% lower value was in diabetics as compared to the non-diabetics. The differences were insignificant statistically.

Table 1: Cardiac Biomarkers in diabetic and non-diabetic males with MI

Enzymes	Concentrations in diabetics (U/L)	Concentrations in non-diabetics(U/L)	F	P<0.05
CK-NAC	226±70	429.51±60	1.562	0.215
CK-MB	59.15±26.5	53.55±10	0.071	0.790

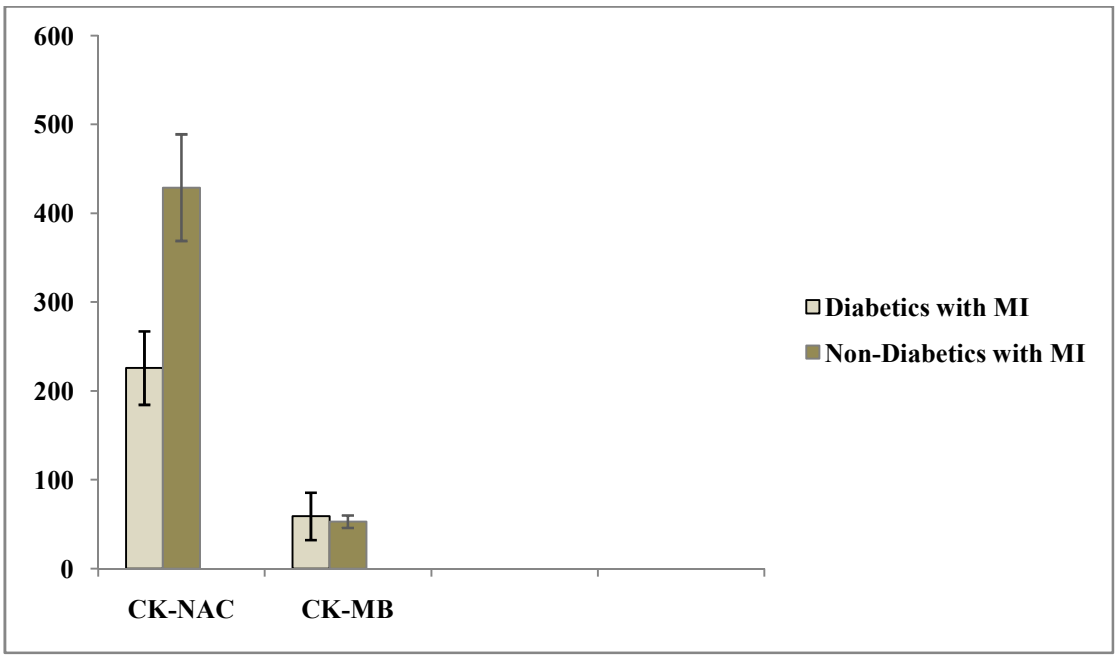

Figure 1: Levels of Cardiac enzymes in Diabetic and Non-Diabetic Male patients with MI. CK-NAC: Creatine Kinase N-acetylcholine; CK-MB: Creatine Kinase Myocardial Band. *P < 0.05: Insignificant statistically.

Table 2: Diabetic and Non-Diabetic Female patients with MI

Enzymes	Concentrations in diabetics (U/L)	Concentrations in non-diabetics (U/L)	F	P<0.05

CK-NAC	365.31±80	239.50±51	1.870	0.180
CK-MB	82.88±28	32.26±2.8	6.188	0.017

*p<0.05

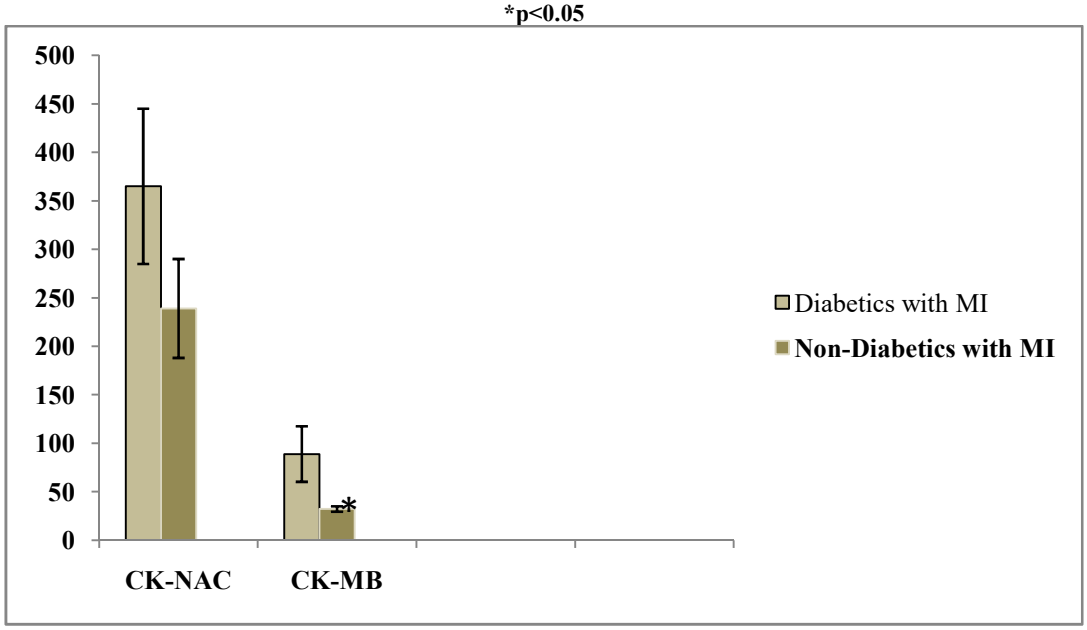

Figure 2: Cardiac enzymes in Diabetic and non-Diabetic Female patients with MI
CK-NAC: Creatine Kinase N-acetylcholine; CK-MB: Creatine Kinase Myocardial Band. *P < 0.05: Significant statistically

Table 3: Male Diabetic/Non-Diabetic Subjects Without MI

Enzymes	Concentrations in diabetics (U/L)	Concentrations in non-diabetics (U/L)	F	P<0.05
CK-NAC	198.31±15.5	159.73±2.7	17.361	0.000
CK-MB	25.78±1.2	22.92±0.7	3.199	0.077

*Significant p value<0.05

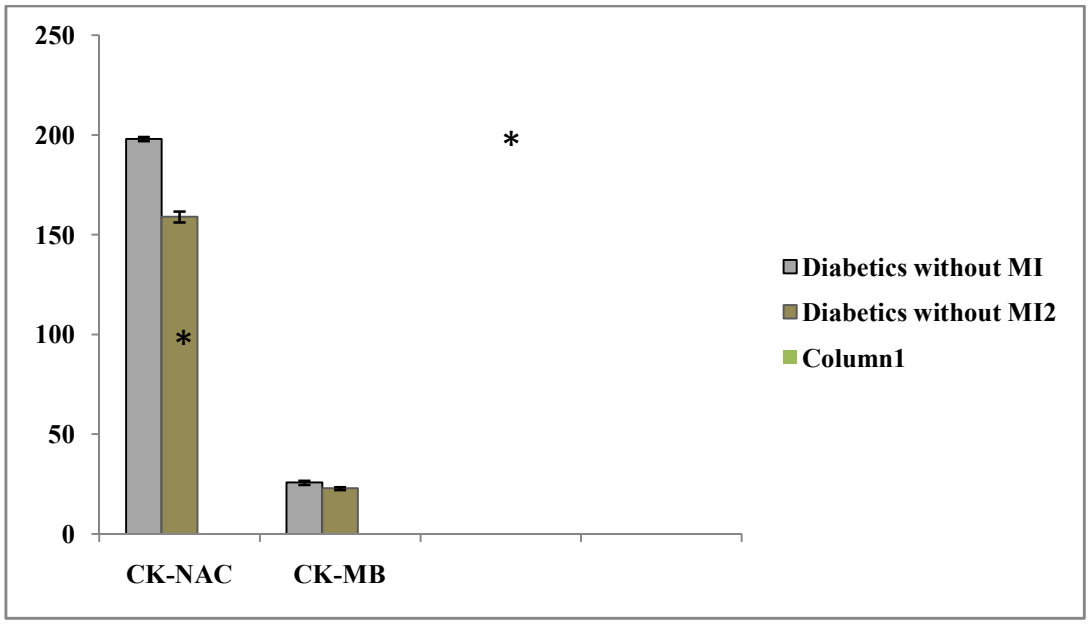

Figure 3: Cardiac enzymes in Diabetic and Non-Diabetic Males without MI
CK-NAC: Creatine Kinase N-acetylcholine; CK-MB: Creatine Kinase Myocardial Band.
***P < 0.05: Significant statistically**

Table 4: Female diabetic/non-diabetic subjects without MI

Enzymes	Concentrations in diabetics (U/L)	Concentrations in non-diabetics (U/L)	F	P<0.05

CK-NAC	153±11.7	175.55±2.6	5.842	0.022
CK-MB	24.77±0.7	24.89±1	0.005	0.942

*Significant p value<0.05

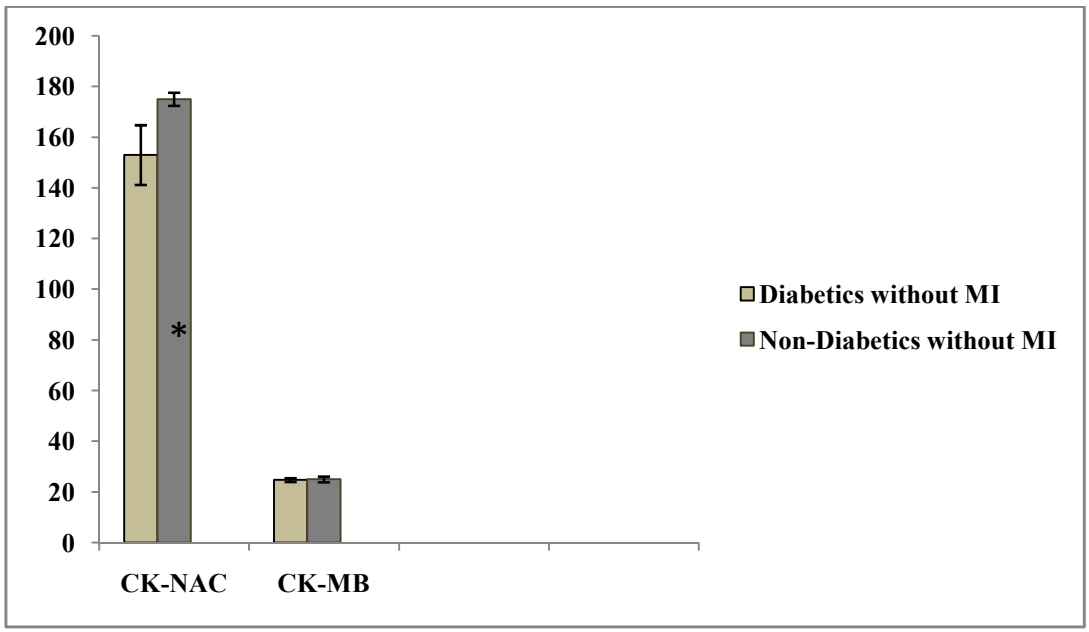

Figure 4: Cardiac enzymes in Diabetic and non-Diabetic Females without MI
CK-NAC: Creatine Kinase N-acetylcholine; CK-MB: Creatine Kinase Myocardial Band.
***P< 0.05: Significant statistically**

DISCUSSION

Diabetes mellitus is considered as a major risk factor of MI **[7]**. In this population based study, CK-NAC level (47%) was in greater concentration non diabetics but it was low in diabetic male patients with MI. But the concentration of LDH enzyme and CK-MB were higher in diabetic male patients of MI than non diabetic patients with MI.

These results are in accordance with Payal *et al*, 2014 that CK-MB levels were significantly high in diabetic patients with MI as compared to non-diabetics patients of MI. Higher levels of cardiac biomarkers CK-NAC and LDH were higher in diabetic patients with MI in comparison to non diabetic patients **[8]**.

CONCLUSION

The present study confirms that diabetes is a risk factor for MI and hyperglycemia directly or indirectly increases concentration of cardiac biomarkers. In conclusion, it has been observed that in male diabetic patients the concentration of cardiac enzymes and biomarkers of MI, CK-MB, CK-NAC and LDH are higher as compare to non diabetics and females. Diabetes is a risk factor of MI, other cardio vascular diseases and strokes. Future studies would elaborate the exact mechanism involved in fluctuation of concentration of cardiac biomarkers in diabetic MI and non diabetic MI patients.

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