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DOES PRE-INFARCTION DIABETIC CONTROL AFFECT THE OUTCOME OF ACUTE MYOCARDIAL INFARCTION?

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All the authors contributed significantly to the research that resulted in the submitted manuscript.

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ABSTRACT

Objectives: The aim of this study was to see the effect of glycemic control on the outcome of acute myocardial infarction (AMI), in well controlled and poorly controlled diabetic patients by measuring fructosamine levels.

Methodology: This prospective observational study was done in Department of Cardiology, Lady Reading Hospital, Peshawar, from May 2008 to December 2008. Both diabetic and nondiabetic patients having first AMI were included. Patients having stroke, advanced renal failure or COPD were excluded. Diabetic control was assessed on the basis of serum fructosamine level. Patients having fructosamine level <285 micro mol/l were considered to have good control of diabetes. All patients had standard medical treatment during their stay in hospital. One month later patients were evaluated for effort tolerance on treadmill.

Results: A total of 230 patients were studied. More diabetics were obese (36% vs. 14%, p= 0.001), hypertensive (34% vs. 14%, p=0.001) and had evidence of heart failure i.e. Killip class II & III (62% vs. 24%, p=0.001), IV (11% vs. 8%, p=0.04). Diabetic patients also had higher serum fructosamine level (475 ± 115 vs. 230 ± 50 micro mol/l, p =0.002), triglyceride level (232 ± 19 vs. 160 ± 25mg%, p=0.001) and had slightly higher mortality (14% vs. 6%, p=0.19). Diabetes was well controlled in 30 patients with fructosamine (248 ± 26 vs. 470 ± 152micro mol/l, p=0.001). Heart failure was more common in patients with poorly controlled diabetes (85% vs. 47%, p=0.001).

Conclusion: Poor Diabetic status is associated with higher morbidity following acute myocardial infarction.

Key Words: Diabetes Mellitus, Myocardial infarction, Outcome, fructosamine.

INTRODUCTION

Diabetes mellitus has long been known to be causally related to coronary artery disease (CAD) with higher incidence of Acute Myocardial infarction (AMI)[1,2]and at least twice the fatality rate as compared to non-diabetics. [3-6]

Patients are generally unaware of their diabetes especially in the developing world where it is incidentally diagnosed or when the patient present with some complication e.g acute myocardial infarction (AMI), stroke etc. Ashur[7] and Akhtar[8] reported quite a good percentage of patients who were diagnosed to have diabetes when they were investigated after developing CAD.

Despite the association between diabetes and cardiac disease the effect of acute and chronic blood glucose metabolism on cardiac function in diabetic patients are not well defined. Some studies[9,10] suggest that chronically raised blood glucose level is associated with poor prognosis following AMI independent of other factors. There is excess accumulation of glycoprotein in the myocardium of chronically uncontrolled diabetics with altered left ventricular compliance and systolic function, termed diabetic cardiomyopathy.[11,12] Furthermore, diabetic patients have also been known to have severe and distal CAD leading to poorer cardiovascular profile before AMI and more severe damage thereafter, than non-diabetic patients.[13]

Conventional monitoring of diabetes by urine testing, random and fasting blood glucose give poor index of average glycemic status.[14] Serum fructosamine[15,16] and glycosylated hemoglobin[17] have been found to be extremely useful as an objective index of past medium to long-term glycemic status, the former indicative of past one to two week and latter of four to eight weeks of mean glucose level.

The aim of this study was to see the effect of glycemic control by measuring fructosamine levels, on the outcome of acute myocardial infarction, in well controlled and poorly controlled diabetic patients.

METHODOLOGY

This is a prospective observational short-term study, carried out from May to December 2008, at Cardiology Department, Lady Reading Hospital, Peshawar. During this period, a total of 230 patients with first AMI were enrolled after their informed written consent. Obesity was defined as Body Mass Index (BMI) $\geqslant$ 30kg/m^2, hypertension was defined as history of hypertension or blood pressure of $\geqslant$ 140/90 mmHg and ST elevation myocardial infarction (STEMI) was defined as ST segment elevation was measured in millimeters at 80msec beyond the J-point, ST elevation of at least 2 mm in 2 or more contiguous leads ECG. Killip Class was defined as I; Basilar rales in both the lungs, II; Rales present upto the mid of the chest, III; Rales present in more than mid of the chest and IV; Chest full of rales with cold peripheries and unrecordable blood pressure, sinus tachcardia as sinus rythym with heart rate of more than 100 beats per minute, while left ventricular end diastolic volume was upto 57mm was considered normal by Cube Method.

Patients of either gender, diabetic and non-diabetics having first myocardial infarction and age less than 70 years were included in the study. Patients with life threatening co-morbidity like stroke, advanced COPD or renal failure were excluded from the study.

Diabetes was considered present if the patient had been given the diagnosis and was receiving treatment i.e. diet, oral hypoglycemic agents and/or insulin. Patients with no previous history of diabetes but a fasting glucose of more than 126mg/dl or random blood glucose more than 200mg/dl on two occasions were labeled as diabetics. Patients average glycemic status was evaluated by checking their serum fructosamine levels (Glucoprotein by LXN Corporation, San Diego). Diabetes was considered adequately controlled if serum fructosamine was less than 285 micro mol/l.

Patients were kept in CCU for 48 hours and closely monitored for hemodynamic status and arrhythmias and managed accordingly. All patients received standard medical therapy. At one month follow-up, all patients had exercise tolerance test (ETT) by Modified Bruce Protocol.

Data was analyzed using SPSS version 12. All categorical variables were described as percentages and continuous variables as mean $\pm$ standard deviation. Differences between categorical variable were tested by chi square test. Continuous variables were compared by student t-test. Statistical significance was defined as $P<0.05$.

RESULTS

From May to December 2008, a total of 230 patients with first AMI, 110 (47.9%) in diabetic and 120 (52.1%) in nondiabetic group were studied. The two groups were well matched regarding age, sex, smoking habits, presenting complaints and site of infarct. More patients in diabetic group were obese (36% vs. 14%, $p=0.001$), hypertensive (34% vs. 13%, $p=0.001$), and had evidence of heart failure i,e Killip class II & III(62% vs. 24%, $p=0.001$) Killip class IV(11% vs. 8%, $p=0.04$).Serum fructosamine was high in diabetic group (475$\pm$115 vs 230$\pm$50 micro mol/l, $p=0.001$) indicating higher glycemic status. Triglyceride level was also high (230 $\pm$ 19 vs. 160 $\pm$ 25mg, $p=0.001$) indicating higher lipemic status (Table 1). Diabetic patients were more likely to have sinus tachycardia on ECG (39% vs. 12%) and also had enlargement of left ventricular end diastolic volume (LVEDV) on echocardiography (38% vs. 19%, $p=0.19$). Post discharge exercise testing revealed that diabetic patients had poor effort tolerance with lesser

Table 1: Baseline Characteristics of Non-diabetic & Diabetic Patients

Variables	Non-Diabetic (n=120)	Diabetic (n=110)	P-value
Age	56±6	52±7	0.17
Sex			
Male	85 (71%)	82 (74%)	0.25
Female	35 (29%)	28 (26%)	0.15
Hypertension	15 (13%)	38 (34%)	0.001
Obesity	17 (14%)	40 (36%)	0.001
Smokers	26 (22%)	25 (23%)	0.27
Presenting Symptoms			
Chest Pain	108 (90%)	86 (78%)	0.24
Dyspnea	9 (8%)	35 (32%)	0.18
Syncope	2 (1.7%)	4 (3.6%)	0.23
Thrombolytic Therapy	73 (60%)	70 (63%)	0.11
Killip Class			
I	82 (68%)	30 (27%)	0.001
II & III	29 (24%)	68 (62%)	0.001
IV	9 (8%)	12 (11%)	0.04
Metabolic Status			
Fasting Glucose (mg/dl)	92±13	146±28	0.001
Fructosamine (micro mol/l)	230±50	475±115	0.002
Cholesterol (mg/dl)	190±19	195±21	0.04
Triglyceride (mg/dl)	160±25	232±19	0.001
Mortality	6(5%)	14(13%)	0.19

exercise time (7.5±3.2 vs. 10±1.5 min) however, there was no significant difference regarding angina and ischemic response (Table 2). Mortality was slightly higher in diabetics (13% vs. 5%, p=0.19) but it was statistically not significant. Patients with poorly controlled diabetes were more likely to be in heart failure than those who were well controlled (85% vs. 47%, p=0.29) (Table 3).

DISCUSSION

Since the discovery of insulin, not many diabetic patients succumb to premature death but at the cost of long-term microvascular, macrovascular and neurological complications.[4-6] UNICEF [18] expert report in 1994 and WHO[19] reports in 1997 had predicted that more than 100 million people would be affected by diabetes in near future particularly the Asia would lead in the incidence of diabetes. Shera[20] had also pointed out that diabetes would be the number one health hazard in Pakistan after the year 2000. It is imperative to diagnose diabetes in its initial stages to provide proper treatment in order to prevent its complications. Famous UKPD[21] study has shown beneficial effect of good control of diabetes in terms of prevention of AMI.

Diabetics develop CAD at a younger age with widespread coronary involvement. Mittenen et al,[22] reported higher in hospital mortality with first AMI and that 50% of them are dead by one year. A number of studies have confirmed that the syndrome of insulin resistance is prevalent in South East Asia, including Pakistan.[23,24]

Increased plasma glucose on admission to CCU has been ascribed to stress of myocardial infarction or neuroendocrine changes in early phase of AMI. Some

Table 2: Comparison of ECG, Echo and Stress Test between Non-Diabetic and Diabetics

Variables	Non-Diabetic (n=120)	Diabetic (n=110)	P-value
A) ECG Location of Infarct			
Anterior	56(47%0	45 (41%)	0.26
Inferior	49 (41%)	49 (45%)	0.14
Non "Q"	13 (12%)	16 (14%)	0.28
Arrhythmias			
Sinus Tachycardia	14 (12%)	43 (39%)	0.001
Brady Arrhythmia's	13 (11%)	16 (14%)	0.28
Tachy Arrhythmia's			
AF	6 (5%)	5 (4%)	0.22
VT/ VF	13 (11)%	10 (9%)	0.23
B) Echocardiography			
LV-EF	46±8%	39±5%	0.002
LV Enlargement	19%	38%	0.19
C) Stress Test			
Average Time (min)	10±1.5	7.5±3.2	0.15
Abnormal Results			
Ischemia (St Depression)	32%	45%	0.27
PVC's	18%	35%	0.19
Non Sustained VT	1	2	0.26
Reason For Discontinuing			
Target Heart Rate	30%	22%	0.11
Angina	25%	38%	0.24
Fatigue	30%	15%	0.29
Dysponea	15%	25%	0.17

LV EF = Left Ventriculer Ejection Fractrion

investigators relate this hyperglycemia to undiagnosed diabetes mellitus. We assessed random and fasting blood glucose level of our study population along with serum fructosamine. Serum fructosamine is a unique retrospective index of average blood glucose level in the past 1-2 weeks and is used as a tool to monitor glycemic control.[15] Serum fructosamine is a measurement of glycosylated serum proteins, which is based on a colorimetric determination utilizing the reducing properties of fructosamine at high pH. It has the advantage that it is simple, rapid, in-expensive and can be automated, thus reducing the amount of lab time required for assay. Fructosamine concentration correlates with HbAlc and other measures of glycemia and appeared more useful than HbA1c for monitoring short term evaluation of diabetes control.

In our study population proper glycemiccontrol was found to have favorable impact on the outcome of diabetic patients with AMI as evidenced by lower incidence of heart failure. Roth et al,[25] however, have showed no effect of diabetes control on the clinical course of AMI.

Diabetic patients have primary cardiomyopathy associated with both systolic and diastolic LV dysfunction that may be due to microangiopathy, increased extra cellular collagen deposition or abnormality of calcium transport, individually or in combination. Thus the diabetic patients have poorer

Table 3: Comparison of Controlled & Uncontrolled Diabetics

Variables	Controlled Diabetic (n=30)	Uncontrolled Diabetic (n=80)	P-value
Age	52 ± 9	50 ± 7	0.10
Sex (Male)	25 (83%)	57 (71%)	0.28
Hypertension	12 (40%)	30 (37%)	0.29
Obesity	9 (30%)	29 (36%)	0.30
Smokers	7 (23%)	18 (22%)	0.19
Anterior MI	11 (36%)	30 (37%)	0.28
Thrombolytic Therapy	25 (83%)	45 (56%)	0.29
Killip Class			
I	16 (53%)	12 (15%)	0.16
II& III	10 (34%)	58 (72%)	0.001
IV	04 (13%)	10 (13%)	0.29
Metabolic Status			
Fasting Glucose (mg/dl)	104 ± 14	170 ± 22	0.001
Fructosamine (micro mol/l)	248 ± 26	470 ± 152	0.001
Cholesterol (mg/dl)	195 ± 18	186 ± 25	0.26
Triglyceride (mg/dl)	230 ± 35	222 ± 29	0.35

cardiovascular profile before AMI and more severe damage thereafter, than non-diabetics. In our study, heart failure was more common in diabetics than non diabetics despite the fact that the two groups were well matched regarding age, sex, site of AMI, hypertension and thrombolytic therapy. Our figures are comparable with 67.3% reported by Parteman[26] and slightly higher than 50% reported by Forrester et al.[27]

Multivariate analysis has revealed that diabetics with AMI had higher mortality. This has been explained by the fact that these patients had lesser use of B-blocker, heparin, thrombolysis and acute revascularization which have shown equal benefits in diabetes and non-diabetics.[28,29] The patients with AMI and diabetes have impaired cardiopulmonary response to maximal and submaximal exercise testing and impaired chronotropic response to exercise even though their cardiac function at rest were similar to that of non-diabetic patients.[30]

Our diabetic patients had less effort tolerance than non-diabetics. The commonest reason for discontinuing the test was fatigue followed by angina. There was not much difference regarding ischemic response between the two groups. Our figure of 50% ischemic response in diabetic patients is higher than 32% reported by Smith et al,[31] and 40% by Sami et al.[32] This higher ischemic response was due to the fact that other studies used 60% heart rate limited protocol while our study was target heart rate limited.

Conventionally it is taught that diabetic patients with AMI present with atypical symptoms and frequently are admitted to hospital with painless infarction. In one series 42% of diabetic patients with AMI presented with no chest pain compared to 6% of non diabetic patients.[33] In another study 35% of patients were admitted to general wards, 27% without any pain and 8% with mild chest pain judged to be angina and not AMI. [4] We did not see this phenomenon in our population of patients i.e. majority of both diabetic and non diabetic patients complained of chest pain or pressure at the time of admission. Similar to our observation, Smith et al, [31] also reported chest pain in 96% of their diabetic patients. The reason for the considerable difference in chest pain as presenting symptom in earlier studies and our series is not clearly known.

CONCLUSION

Diabetes as such is associated with higher in hospital morbidity following acute myocardial infarction and poor effort tolerance thereafter especially in those who had poor diabetic control in the preinfarction period. Serum fructosamine is extremely useful as an objective index of recent glycemic status of one to two week.

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