EFFECT OF GLYCEMIC CONTROL ON KILLIP GRADING AND BNP LEVELS IN TYPE 2 DIABETES MELLITUS PATIENTS AFTER ACUTE MYOCARDIAL INFARCTION

Soheb Rehman, Mehwish Durrani, Shamim Bibi

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Author Information

From: Department of Biochemistry, Rehman Medical College, Peshawar, Khyber Pakhtunkhwa, Pakistan.

Dr. Soheb Rehman, Assistant Professor.
(Corresponding Author)
Email: soheb.rehman@rmi.edu.pk

Dr. Mehwish Durrani, Assistant Professor.

Dr. Shamim Bibi, Medical Officer, Acute Stroke Unit, Northwest General Hospital and Research Center, Peshawar.

ABSTRACT

Introduction: Despite prompt management of acute myocardial infarction in diabetics, complications do occur. The objective of the present study was to assess level of stress on the post-infarction left ventricular myocardium and its association with glycemic control.

Materials & Methods: This descriptive study was conducted in Lady Reading Hospital (LRH) and Rehman Medical Institute (RMI) Peshawar from November 2014 to March 2015 on 196 known type 2 diabetics who received thrombolytic treatment inside first 12 hours of Myocardial Infarction (MI); demographic data, Killip Scale grading, and echocardiography were recorded and blood samples analyzed for HbA1c and BNP after informed consent and convenience sampling. Post-MI risk assessment and stratification were done by Killip Scale and plasma BNP levels. Based on glycemic control, there were: optimal glycemic control group (mean HbA1c ≤7%) and suboptimal glycemic control group (mean HbA1c >7%). Based on ejection fraction (EF), there were: Group 1 (severe LV dysfunction, EF<30%), Group 2 (moderate LV dysfunction, EF=30-44%), Group 3 (mild LV dysfunction, EF=45-54%) and Group 4 (preserved LV function, EF≥55%). Data were analyzed for descriptive statistics by SPSS 16.0.

Results: Significant differences of BNP values were found between optimal and suboptimal groups in EF group 1 (p=0.01), EF group 2 (p<0.001) and EF group 3 (p<0.001), but not in EF group 4 (p=0.50). Significant negative correlation was found between plasma BNP and EF (optimal control group: r=-0.8, p<0.001; suboptimal control group: r=-0.7, p<0.001).

Conclusion: Plasma BNP levels were elevated in suboptimal control group compared to optimal group and its rise was proportional to decrease of EF in both groups, accentuating the significance of BNP in post-MI patients.

Keywords: Diabetes Mellitus, Type 2; Myocardial Infarction; Heart Failure; Echocardiography; Natriuretic Peptide, Brain.

The authors declared no conflict of interest. All authors contributed substantially to the planning of research (SR, MD, SB), data collection (SR, MD, SB), data analysis (SR) and write-up of the article (SR, MD, SB), and agreed to be accountable for all aspects of the work.

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INTRODUCTION

Cardiovascular disease (CVD) remains one of the foremost fears of medical professionals. Though CVD is the leading cause of death globally, 80% of these premature deaths occur in developing, low-income nations especially in Pak-Indo populations of subcontinent and African countries.[1,2] In India, approximately 25 percent of all deaths occur due to CVD and it is estimated that by 2030 CVD will contribute to approximately 50 percent of all deaths.[3] In Pakistan, CVD causes 35-40% of all deaths.

Among CVD, acute myocardial infarction (AMI) is the most common one. In Pakistan, 5.09 million people are suffering from AMI.[2] Approximately 300 different risk factors of AMI have been identified by Framingham study, the MONICA project and the INTERHEART study. Among those risk factors of AMI, diabetes mellitus (DM) is a global problem.[4,5] Diabetes mellitus (DM) is an established and independent risk factor for myocardial infarction and it magnifies the risk of AMI about 5-fold.[6] Pathophysiology of AMI in diabetic patients is complex and multifactorial.

Oxidative stress, imbalance in thrombosis or fibrinolysis and dyslipidemias render the cardiac myocardium in diabetics more prone to ischemic injury and heart failure.[7,8]

Despite prompt management of AMI, complications do occur.[9] Many epidemiological surveys indicate that approximately 25% patients of AMI develop heart failure. The probability of developing heart failure and mortality after AMI in diabetics is 2-4 fold higher than those without diabetes due to decreased tolerance of myocardium to ischemic injury in diabetics.[6,10] After acute myocardial infarction, plasma Brain Natriuretic Peptide (BNP) levels also increase rapidly for the first 24 hours due to ischemia and necrosis of myocardium and then tends to stabilize.[11] Plasma BNP levels are considered an important biochemical marker in the diagnosis, grading and management of heart failure patients.

The objective of the present study was to assess the level of stress on the left ventricular (LV) myocardium wall due to infarction and to find its association with glycemic control.

MATERIALS & METHODS

In this descriptive study, conducted from November 2014 to March 2015, 196 patients who were known type 2 diabetics and admitted for AMI treatment in department of cardiology, Lady Reading Hospital (LRH) and Rehman Medical Institute (RMI), Peshawar were included. Data and blood samples were collected after obtaining ethical approval from Khyber Medical University (KMU) Ethics Board and consent from department in-charges. Only those patients were included in this study who had received thrombolytic treatment inside first 12 hours of onset of symptoms of MI. DM was defined according to American Diabetes Association (ADA) guidelines.[12] The Guidelines by Third Global MI Task Forces were used for the diagnosis of AMI.[13]

Data were collected on specifically designed Performa. Patients' demographic data, clinical examination and Killip Scale grading were included in the Performa. Blood samples were taken and analyzed for HbA1c using Glycohemoglobin HbA_1 Human kit and BNP assay using ARCHITECT BNP Kits. Transthoracic echocardiography was done on all subjects included in the study by qualified sonographer and the values of ejection fraction (EF) were obtained. Post-MI risk assessment and stratification was done clinically using Killip Scale as well as biochemically by measuring plasma BNP levels. The level of post-MI heart failure was graded according to the Killip scale.[14]

Patients were divided into two groups on the basis of HbA1c level. Optimal glycemic control group was taken as patients with mean HbA1c ≤ 7% and suboptimal glycemic control group was taken as patients with mean HbA1c > 7%. These values are in accordance with the current definition by American Diabetes Association guidelines.[12]

Data were entered on regular basis and analyzed by SPSS 16 for descriptive statistics.

RESULTS

Out of 196 patients from both sexes included in this study, 59.2% were male and 40.8% were female; the mean age was 59±7.58 years.

Table 1 shows that 35(17.86%) patients had HbA1c ≤7% (optimal control group) with mean HbA1c of 6.67±0.18 and 161(82.14%) patients had HbA1c >7% (suboptimal control group) with mean HbA1c of 8.65±0.98 (p<0.001).

Table 1: Study Groups Based on HbA1c Levels

HbA1c Control Groups	No. of Patients *n* (%)	HbA1c (Mean±SD)	p value
Optimal (HbA1c ≤ 7)	35 (17.86)	6.67±0.18	<0.001
Suboptimal (HbA1c > 7)	161 (82.14)	8.65±0.98	

Table 2 shows that In optimal control group, 15(42.9%) patients had heart failure while 20(57.1%) patients did not have heart failure. In suboptimal control group (HbA1c >7, *n*=161), 69(42.9%) patients had heart failure while 92(57.1%) patients did not have heart failure (p>0.05).

Table 2: Killip Scale Distribution of the Study Groups Based on HbA1c Levels. Data are expressed as *n* (%).

Killip Class	HbA1c ≤ 7% (*n* = 35)	HbA1c > 7% (*n* = 161)	*p*-value
I	20 (57.1)	92 (57.1)	1.00
II	8 (22.9)	22(13.7)	0.28
III	4 (11.4)	32 (19.9)	0.34
IV	3 (8.5)	15 (9.3)	0.90

Subjects in both groups were divided into subgroups according to their ejection fraction (EF); There was significant difference between optimal and suboptimal control groups in all four groups (Group 1: 5.71% vs 7.51%, *p*=0.02; Group 2: 14.28% vs 32.29%, *p*<0.001; Group 3: 31.42% vs 49.06%, *p*<0.001 and Group 4: 48.57% vs 11.18%, *p*<0.001) as shown in Table 3.

Table 3: Ejection Fraction Distribution of the Study Groups Based on HbA1c Levels.

Group	Ejection Fraction (%)	HbA1c ≤ 7% (*n* = 35)	HbA1c > 7% (*n* = 161)	p value
1	< 30	2 (5.71)	12 (7.45)	0.02
2	30-44	5 (14.28)	52 (32.29)	<0.00
3	45-54	11 (31.42)	79 (49.06)	<0.00
4	≥ 55	17 (48.57)	18 (11.18)	<0.00

As shown in Table 4, subjects in group-1 with severe LV dysfunction (EF <30%) had the highest level of plasma BNP as compared to the subjects in group-4 (EF ≥ 55%) with the preserved LV function who had the lowest levels of plasma BNP**.** There was statistically significant difference between optimal and suboptimal groups in group 1**(***p*=0.01), group 2(*p*<0.001) and group 3 (*p*<0.001**)**, whereas there was no significant difference in group 4 (*p*=0.50).

Table 4: Comparison of BNP Levels and Ejection Fraction of the Study Groups Based on HbA1c Levels.

Group	Ejection Fraction (%)	BNP Levels (pg/ml) Optimal Group (Mean±SD)	BNP Levels (pg/ml) Suboptimal Group (Mean±SD)	*p* value
1	< 30	1185.73±728.32	1580.92±798.29	0.01
2	30-44	508.00±123.77	752.14±366.04	<0.001
3	45-54	243.64±91.26	411.67±266.00	<0.001
4	≥ 55	229.00±118.32	240.78±78.37	0.50

Figure 1 shows a statistically significant strong negative correlation in optimal control group between plasma BNP levels and EF (*r*=-0.8, *p*<0.001).

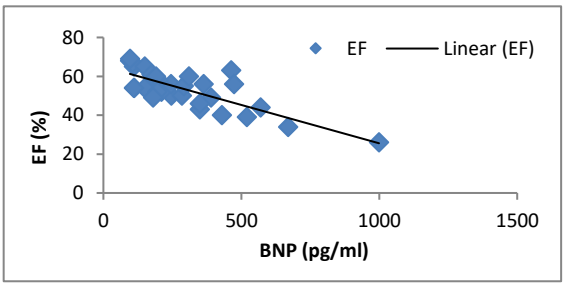

Figure 1: Correlation of BNP levels and Ejection Fraction (EF) in Optimal Control Group (*r* = -0.8, *p*<0.001)

Figure No. 2 depicts significant moderate negative correlation in suboptimal control group between plasma BNP levels and EF (r = -0.7, p = <0.00).

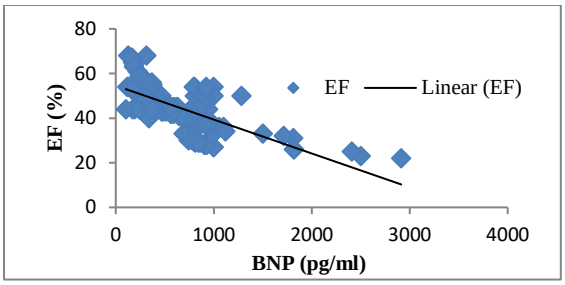

Figure 2: Correlation of BNP levels and Ejection Fraction (EF) in Suboptimal Control Group (r = -0.7, p<0.001)

DISCUSSION

When heart failure frequency was determined by Killip Scale grading criteria, present study found out that 57.14% subjects did not develop heart failure whereas 42.86% subjects were in heart failure (Table 2). Similar results were obtained by Khan et al.[17] in which 39.5% diabetic patients developed heart failure after AMI. This might be due to almost similar sample size (182 in Khan MA et al., and 196 in this study). The findings are slightly different from the results of Khan Set al.[18] in which 63% post-AMI patients did not develop heart failure, and 37% develop heart failure. Among those who developed heart failure, 9.18% were in Killip Class IV (Table 2). Mak et al.[19] showed that only 1-2% subjects were in Killip Class IV. In the current research, no association was found between glycemic control and Killip scale grading. Although both Killip Scale and plasma BNP levels were used to assess heart failure but the results in terms of association with HbA1c came out to be non-significant from each other contrary to expectations. This conflict might be due to differences in the interpretation of clinical assessment of sign and symptoms and other features of Killip Scale grading by different examining individuals.

Another piece of information generated by this work is highly significant correlation between plasma BNP levels and EF in post-AMI diabetic patients. Subjects with severe LV dysfunction (EF <30%) had the highest level of BNP as compared to the subjects with preserved LV function (EF ≥ 55%) who had the lowest levels of BNP (Table 4). This outcome is in harmony with most of researchers (Nalbantic et al; van Veldhuisen et al).[20,21] Moreover there was significant strong negative correlation in optimal control group and moderate negative correlation in suboptimal control group between plasma BNP levels and EF (Figures 1 & 2**).** A study conducted by Dilic et al also showed negative correlation between plasma BNP levels and EF.[22] Similarly, Karakilic et al[23] reported inverse association between plasma BNP levels and EF. However, this does not mean BNP should be routinely used after AMI and exclude the routine use of echocardiography for the assessment of LV functions.

Limitations of this research work were its study design and sampling technique which resulted in selection bias because only previously diagnosed diabetic patients were included. Also, sample size was relatively small; therefore, we should be cautious in generalizing the results and conclusions of this study to general population of patients with AMI.

CONCLUSION

Plasma BNP levels were elevated in suboptimal control group compared to optimal group and the rise of BNP levels was proportional to decrease of EF in both groups. This accentuates the significance of BNP in post-MI patients.

REFERENCES

1. Mensah GA. Ischaemic heart disease in Africa. Heart. 2008;94(7):836-43.
2. Abbas S, Kitchlew AR, Abbas, S. Disease Burden of Ischemic Heart Disease in Pakistan and its Risk Factors. Ann Pak Inst Med Sci. 2009;5(3):145-50.
3. Gupta R, Joshi P, Mohan V, Reddy KS, Yusuf S. Epidemiology and causation of coronary heart disease and stroke in India. Heart. 2008;94(1):16-26.
4. Mackay J, Mensah G. Geneva: World Health Organization in collaboration with Centers for Disease Control and Prevention. Atlas of heart disease and stroke 2004.
5. European Society of Cardiology. World Heart Day: New European statistics released on heart disease and stroke 2012. [Online] Available at: http://www.escardio.org/The-ESC/Press-Office/Press-releases/Last-5years/World-Heart-Day-New-European-statistics-released-on-heart-disease-and stroke [Accessed 22 May, 2016].
6. Chaudhary MA. Cardiovascular diseases claim 200,000 lives annually in Pakistan. *The News*. [Online] 29th September 2012. Available from: http://www.thenews.com.pk/Todays-News-6-134656-Cardiovasculardiseases-claim-200,000-lives-annually-in-Pakistan.
7. Farbstein D, Levy AP. HDL dysfunction in diabetes: causes and possible treatments. Expert Rev Cardiovasc Ther. 2012;10 (3):353-61.
8. Ansley DM, Wang B. Oxidative stress and myocardial injury in the diabetic heart. J Pathol. 2013;229(2):232-41.
9. Otter W, Kleybrink S, Doering W, Standl E, Schnell O. Hospital outcome of acute myocardial infarction in patients with and without diabetes mellitus. Diabet Med. 2004:21(2):183-87.
10. Norhammar A, Malmberg K, Diderholm E, Lagergvist B, Lindahl B, Ryden L, et al. Diabetes mellitus: the major risk factor in unstable coronary artery disease even after consideration of the extent of coronary artery disease and benefits of revascularization. J Am Coll Cardiol. 2004;43(4):585-91.
11. Nonogi H. Complications of Acute Myocardial Infarction. Japan Med Assoc J. 2002;45(4):149-54.
12. Brown JR, Edwards FH, O'Connor GT, Ross CS, Furnary AP. The diabetic disadvantage: historical outcomes measures in diabetic patients undergoing cardiac surgery – the pre-intravenous insulin era. Semin Thorac Cardiovasc Surg. 2006;18(4):281-88.
13. de-Lemos JA, Morrow DA. Brain Natriuretic Peptide Measurement in Acute Coronary Syndromes Ready for Clinical Application? Circulation. 2002;106:2868-70.
14. American Diabetes Association (ADA). Standards of Medical Care in Diabetes-2015. Diabetes Care. 2015;38(1):33-40.
15. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD on behalf of the Joint ESC/ACCF/AHA/WHF Task Force for the Redefinition of Myocardial Infarction. Universal definition of myocardial infarction. J Am Coll Cardiol. 2012:60(16):1581-98.
16. El-Menyar A, Zubaid M, AlMahmeed W, Sulaiman K, AlNabti AR, Singh R, et al. Killip classification in patients with acute coronary syndrome: insight from a multicenter registry. Am J Emerg Med. 2012;30(1):97-103.
17. Khan MA, Khawaja MN, Hakeem F. Predicting clinical outcome in diabetic vs non diabetics with Acute Myocardial Infarction after thrombolysis, using ECG as a tool. J Pak Med Assoc. 2011;61(10):1032-7.
18. Khan S, Matiullah, Adnan Y, Noor L, Ghaffar R, Awan ZA. Frequency of Heart Failure and its Clinical Outcome among Patients Presenting with Acute Myocardial Infarction. Pak J Physiol. 2012;8(2):37-9.
19. Mak K, Moliterno DJ, Granger CB, Miller DP, White HD, Wilcox RG, et al. Influence of Diabetes Mellitus on Clinical Outcome in the Thrombolytic Era of Acute Myocardial Infarction. J Am Coll Cardiol. 1997;30(1):171-9.
20. Durak-Nalbantic A, Dzubur A, Dilic M, Pozderac Z, Mujanovic-Narancic A, Kulic M. Brain natriuretic peptide release in acute myocardial

infarction. Bosn J Basic Med Sci. 2012;12(3):164-8.

21. vanVeldhuisen DJ, Linssen GC, Jaarsma T. B-type natriuretic peptide and prognosis in heart failure patients with preserved and reduced ejection fraction. J Am Coll Cardiol. 2013;14:1498–506.
22. Dilic M, Nalbantic DA, Arslanagic A, Huskic J, Brdjanovic S, Kulic M, et al. Biphasic and monophasic pattern of BNP release in acute myocardial infarction. Coll Antropol. 2011;35(1):155-9.
23. Karakilic E, Kepez A, Abali G, Coskun F, Kunt M, Tokgozoglu L. The relationship between B-type natriuretic peptide levels and echocardiographic parameters in patients with heart failure admitted to the emergency department. Anadolu Kardiyol Derg. 2010;10(2):143-9.