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SHORT COMMUNICATION

ELEVATED B-TYPE NATRIURETIC PEPTIDE LEVEL EXPRESSION ASSOCIATED WITH ACUTE MYOCARDIAL INFARCTION PATIENTS IN JAMMU POPULATION (INDIA)

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ABSTRACT

B-type natriuretic peptide (BNP) is a highly sensitive and specific indicator of the size of myocardial infarction, which can help in assessing the degree of cardiovascular risk. Elevated BNP levels in patients hospitalized for acute myocardial infarction (AMI) are associated with heart failure and mortality, and the measurements of BNP in a short-term period could be helpful to predict the future events. The role of short-term follow-up BNP level has not been established in the patients with AMI. This retrospective study was conducted on the patients admitted to the Government Medical College, Jammu (India). The analysis of blood EDTA sample was analysed for BNP and this test was performed by using a fully automated random access immunoassay analyser whose principle is based on micro-particle enzyme immunoassay (MEIA). The reference range of BNP is 0-100 pg mL^{-1}. The study revealed a 90% BNP increase in AMI patients in comparison to the 10% increase in normal healthy ones. However, BNP showed elevated levels in healthy individuals suffering from renal insufficiency. The BNP was > 100 pg mL^{-1} in the majority of AMI patients while in controls BNP is <100 pg mL^{-1}.

Keywords: Acute myocardial infarction, B-type natriuretic peptide, enzyme immunoassay

INTRODUCTION

Elevated B-type natriuretic peptide (BNP) levels in patients hospitalized for acute myocardial infarction (AMI) are associated with heart failure and mortality. Kaplan-Meier survival curves and log-rank test have been used to compare the survival rates among the 4 different BNP groups according to all-cause mortality and MACE (Lee et al., 2019). A p-value <0.05 was considered statistically significant. Data analyses were performed with SAS 9.4 version (SAS Inc., Cary, NC, USA) and IBM SPSS Statistics for Windows, version 20.0. More than 26 million people all over the world are suffering from heart failure (HF) and cardiac dysfunction, which are currently serious global public health problems (Savarese and Lund, 2017). The global burden of HF and cardiac dysfunction is increasing rapidly and substantially with the aging of the population. Due to high morbidity and mortality, the diagnosis of HF and cardiac dysfunction is extremely important in both clinical and forensic medicine (Zhipeng *et al.*, 2019).

In acute inferior myocardial infarction (MI), initially increased BNP levels may be valuable in predicting the right ventricle involvement. Higher rates of hypotension, right ventricular dysfunction and increased left ventricle diameters have been observed in patients with BNP levels ≥ 400 pg mL^{-1}

(Yildirim *et al.*, 2018). The most important use of natriuretic peptides is to help in establishing the diagnosis of heart failure (HF) in a patient in an urgent care setting wherein the diagnosis is uncertain. The reference values of brain-type natriuretic peptide (BNP) and N-terminal (NT) proBNP are different to exclude or confirm a diagnosis of heart failure. These values also depend on the age and gender, and are higher in elderly persons and women (Mangla *et al.,* 2021). Natriuretic peptides are biomarkers of myocardial stress and are frequently elevated among patients with severe respiratory illnesses typically in the absence of elevated filling pressures or clinical heart failure. Much like troponin, the elevation of BNP or NT-proBNP is associated with unfavourable course among patients with acute respiratory distress syndrome (ARDS). Patients with COVID-19 often demonstrate significant elevation of BNP or NT-proBNP. In present study, we investigated the association of increased BNP expression with acute myocardial infarction in the Jammu region (India).

MATERIALS AND METHODS

A case-control retrospective study was conducted on the patients admitted to Government Medical College (GMC), Jammu (India) during the years 2011 to 2013. The work was approved by the Ethical Committee of GMC Jammu vide No. IEC/Pharma/Thesis/Research/Project/5B/2011/2060 dated 20/10/2011. The criteria for the selection of patients and normal subjects were defined as per the standard guidelines of AMI (Reddy *et al.,* 2015). The inclusion criteria for cases were: the patients admitted to GMC, Jammu suffering from AMI disease and showing TROP-T positive test and abnormal ECG. The inclusion criteria for controls were non-diabetic, non-smoker, non-alcoholic, blood pressure 120/80 (*www.bloodpressure.uk.org*), and lipid profile within normal range. The patients with any kind of disease or disorder were excluded. Eighty patients were chosen as AMI patients and 60 patients as controls. Patients were divided into two groups. Group 1 comprised the patients admitted to coronary cardiac unit (CCU) having confirmed coronary heart disease (CHD) and group 2 were the normal subjects having no history of CHD. Whenever the first time any patient visited the GMC, Jammu, the demographic details of the patients were collected as per a preset proforma. The details were reviewed and the cases chosen for inclusion or exclusion in the study.

For the measurement of various parameters, 2 mL EDTA (purple top vacutainer) and 3 mL plain samples (red top vacutainer) were drawn from ante-cubital vein of controls and AMI patients (cases). Blood samples for controls were collected in sample collection room of the laboratory; and the samples for AMI patients was collected in CCU. All the samples were sent to diagnostic laboratory after proper labelling. The samples in red top tubes were as such kept for 30 min and allowed to clot. Then the samples were centrifuged at 3000 rpm for 10 min at a fixed angle. The serum was separated. The EDTA samples were centrifuged at 3000 rpm for 10 min and plasma was obtained. The samples from both the groups were then preserved at -20°C in a deep freezer (Thermofisher Scientific) until assays were run on a fully automated random access immunoassay analyzer (Abbott AxSYM) based on the micro-particle enzyme immunoassay principle (Fiore *et al.,* 1988). Statistical analysis of the data was done by using SPSS 20.0 version and $P < 0.05$ was considered significant.

RESULTS AND DISCUSSION

The demographic details on gender and district-wise distribution of cases and controls are given in Table 1 and 2. The average age of cases and controls was found to be 39.8 ± 8.6 and 37.67 ± 9.8 years, respectively. BNP, the most recommended test for AMI patients, was evaluated and inferred graphically in both the control and AMI population (Fig. 1). BNP was measured on AxSYM among

Table 1: Distribution of males and females among control and AMI population (cases) of Jammu

Gender	Control (non-AMI cases) population (60)	AMI (cases) population (80)
Male	33 (55%)	64 (80%)
Female	27 (45%)	16 (20%)

Table 2: Distribution of controls and cases in various districts of Jammu (India)

Districts	Control (non-AMI cases) [60]	AMI cases [80]
Jammu	54 (90%)	50 (62.5%)
Udhampur	0	6 (7.5%)
Kishtwar	0	0
Samba	1 (1.7%)	4 (5.0%)
Rajouri	1 (1.7%)	4 (5.0%)
Doda	0	4 (5.0%)
Kathua	0	3 (3.8%)
Poonch	0	6 (7.5%)
Ramban	0	2 (2.5%)
Reasi	4	1 (1.2%)

control and cases and then BNP level was calculated. BNP > 100 pg mL^{-1} is considered as risk factor for AMI disease. The study revealed that 78.4% normal control cases had BNP < 100 pg mL^{-1}; while in 21.6% cases BNP was > 100 pg mL^{-1} (Table 3). Among the 33 cases of male sex, 27 cases (81.8%) had BNP level < 100 pg mL^{-1} and the rest had BNP level > 100 pg mL^{-1}. In majority cases of females (N, 20; 74.1%) had BNP < 100 pg mL^{-1} and only 7 cases had BNP > 100 pg mL^{-1} indicating that in normal people the BNP level is mostly < 100 pg mL^{-1}. In AMI patients, 10% cases (N 8) had BNP level < 100 pg mL^{-1}; while 90% (N, 72) had BNP > 100 pg mL^{-1}. Out of 64 AMI male patients 5 (7.94%) had BNP < 100 pg mL^{-1} and 59 (92.18%) had BNP > 100 pg mL^{-1}. In female AMI patients 3 patients had BNP < 100 pg mL^{-1} while 13 had BNP >100 pg mL^{-1}. It is evident from the data that BNP level was > 100 pg mL^{-1} in the majority of AMI patients; while in most control cases BNP level was <100 pg mL^{-1} and the results were found to be significantly associated. BNP is a neuro-hormone released from the cardiac cells. The elevated BNP is a predictive marker of death and heart failure (Morrow *et al*., 2003). However, they are not useful for the diagnosis of AMI. Khan *et al.* (2008) have reported that circulating natriuretic peptide provides prognostic information better than that given by the thrombolysis in myocardial infarction (TIMI) risk score in patients with acute myocardial infarction. The addition of BNP in standard blood testing for patients with acute myocardial infarction may improve diagnostic sensitivity and provide more prognostic information. BNP 150 ng mL^{-1} in addition to myoglobin, CKMB, and troponin I improve the sensitivity for the diagnosis of NSTEMI in the emergency department (Reesukumal *et al.*, 2009).

Table 3: Distribution of BNP in control and AMI population (cases) of Jammu (India)

Subjects	Non-AMI (control) cases (N = 60)		AMI cases (N = 80)		*P*-value
	BNP <100 pg mL^{-1} N (%)	BNP >100 pg mL^{-1} N (%)	BNP <100 pg mL^{-1} N (%)	BNP >100 pg mL^{-1} N (%)	
Males	27 (81.8)	6 (18.2)	5 (7.8)	59 (92.2)	0.041
Females	20 (74.1)	7 (25.9)	3 (18.7)	13 (81.3)	0.035
Total	47 (78.4)	13 (21.6)	8 (10.0)	72 (90.0)	

Brain natriuretic peptide (BNP) is released from ventricular myocytes due to their stretching and volume overload. In heart failure, there is BNP release. In this study, the BNP in 80 patients with AMI, control group (n = 60) was similar by age and gender to AMI group (Table I). Nalbantic *et al* (2012) found statistically significant elevation of BNP as compared to the control (462.875 pg mL^{-1} vs 35.356 pg mL^{-1}, $p < 0.001$). The patients with severe systolic dysfunction had highest BNP levels. BNP is elevated in AMI and is a quantitative biochemical marker related to the extent of infarction and the left ventricle systolic dysfunction. Besides echocardiography calculation, elevation of BNP could be used for quick and easy determination of the left ventricle systolic dysfunction. Since last

ten years, myoglobin along with CK-MB, the BNP level is analyzed by point of care testing machine manufactured by many reputed companies like Allere and Roche Diagnostics. In these machines electrochemical detection of redox active cardiac marker myoglobin, using aptamer functionalized black phosphorus nanostructured electrodes is done by measuring direct electron transfer (Kumar *et al.*, 2016). In 2019, researchers studied that the biological features, the research and application status, and the future research prospects of BNP and NT-proBNP in both clinical medicine and forensic medicine, thereby providing valuable assistance for clinicians and forensic pathologists (Zhipeng *et al.*, 2019).

The patients with baseline BNP > 100 pg mL^{-1} had substantially higher mortality and composite events (20.9 and 32.2%) than those with BNP ≤ 100 pg mL^{-1} (5.6 and 15.5%). BNP improved both classification and discrimination of outcomes ($p \leq 0.003$), regardless of left ventricular systolic function (Kotecha *et al.,* 2019). The increase in BNP secretion was effective for palliation of coronary vasoconstriction. However, the level of BNP secretion induced by ischaemia was still inadequate for full coronary dilatation (Itakura *et al.,* 2020). The significance of this finding is uncertain and should not necessarily trigger an evaluation or treatment for heart failure unless there is clear clinical evidence for diagnosis (Januzzi *et al.*, 2020).

Conclusion: In this study, BNP level in AMI patients (n = 80) and control group (n = 60) was similar by age and gender to the AMI group. This study found that BNP level was > 100 pg mL^{-1} in majority of AMI patients, while in most control cases the BNP level was < 100 pg mL^{-1}. The study revealed that BNP is an effective method for detecting heart failure.

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Ethical statement: The study was undertaken in accordance with the ethical standards of the Institutional Ethics Committee of GMC Jammu which was constituted as per the guidelines formulated by the Indian Council of Medical Research (ICMR).

REFERENCES

Cao, Z., Jia, Y. and Zhu, B. 2019. BNP and NT-proBNP as diagnostic biomarkers for cardiac dysfunction in both clinical and forensic medicine. *International Journal of Molecular Sciences*, **20**: 1820. [*https://doi.org/10.3390/ijms20081820*].

Durak-Nalbantić, A., Džubur, A., Dilić, M., Pozderac, Ž., Mujanović-Narančić, A., Kulić, M., Hodžić, E., Resić, N., Brdjanović, S. and Zvizdić, F. 2012. Brain natriuretic peptide release in acute myocardial infarction. *Bosnian Journal of Basic Medical Sciences*, **12**(3): 164-168.

Fiore, M., Mitchell, J., Doan, T., Nelson, R., Winter, G., Grandone, C., Zeng, K., Haraden, R., Smith, J. and Harris, K. 1988. The Abbott IMx automated benchtop immunochemistry analyzer system. *Clinical Chemistry*, **34**: 1726-1732.

Itakura, R., Inoue, Y., Ogawa, K., Nagoshi, T., Minai, K., Ogawa, T., Kawai, M. and Yoshimura, M. 2020. A highly-sensitized response of B-type natriuretic peptide to cardiac ischaemia quantified by intracoronary pressure measurements. *Scientific Reports*, **10**: 1-11.

Januzzi, J.L. 2020. Troponin and BNP use in COVID-19. *Cardiology Magazine*, 18 March, 2020. [*https://www.acc.org/latest-in-cardiology//articles/2020/03/18/25/troponin-and-bnp-use-in- covid19*].

Khan, S.Q., Dhillon, O., Kelly, D., Squire, I.B., Struck, J., Quinn, P., Morgenthaler, N.G., Bergmann, A., Davies, J.E. and Ng, L.L. 2008. Plasma N-terminal B-type natriuretic peptide as an indicator of long-term survival after acute myocardial infarction: Comparison with plasma midregional

pro-atrial natriuretic peptide: The LAMP (Leicester acute myocardial infarction peptide) study. *Journal of the American College of Cardiology*, **51**: 1857-1864.

Kotecha, D., Flather, M.D., Atar, D., Collins, P., Pepper, J., Jenkins, E., Reid, C.M. and Eccleston, D. 2019. B-type natriuretic peptide trumps other prognostic markers in patients assessed for coronary disease. *BMC Medicine*, **17**: 1-11.

Kumar, V., Brent, J.R., Shorie, M., Kaur, H., Chadha, G., Thomas, A.G., Lewis, E.A., Rooney, A.P., Nguyen, L., Zhong, X.L. and Burke, M.G. 2016. Nanostructured aptamer-functionalized black phosphorus sensing platform for label-free detection of myoglobin, a cardiovascular disease biomarker. *ACS Applied Materials & Interfaces*, **8**: 22860-22868.

Lee, J.W., Choi, E., Khanam, S.S., Son, J.W., Youn, Y.J., Ahn, M.S., Ahn, S.G., Kim, J.Y., Lee, S.H., Yoon, J. and Yoo, B.S. 2019. Prognostic value of short-term follow-up B-type natriuretic peptide levels after hospital discharge in patients with acute myocardial infarction. *International Journal of Cardiology*, **289**: 19-23.

Morrow, D.A., de Lemos, J.A., Sabatine, M.S., Murphy, S.A., Demopoulos, L.A., DiBattiste, P.M., McCabe, C.H., Gibson, C.M., Cannon, C.P. and Braunwald, E. 2003. Evaluation of B-type natriuretic peptide for risk assessment in unstable angina/non–ST-elevation myocardial infarction: B-type natriuretic peptide and prognosis in TACTICS-TIMI 18. *Journal of the American College of Cardiology*, **41**: 1264-1272.

Reddy, K., Khaliq, A. and Henning, R.J. 2015. Recent advances in the diagnosis and treatment of acute myocardial infarction. *World Journal of Cardiology*, **7**: 243-276.

Reesukumal, K., Pratumvinit, B., Maneesai, A., Tresukosol, D. and Opartkiattikul, N. 2009. An evaluation of B-type natriuretic peptide in addition to myoglobin, creatine kinase-MB, and troponin I on the emergency department patients with acute myocardial infarction. *Siriraj Medical Journal*, **61**: 126-129.

Savarese, G. and Lund, L.H. 2017. Global public health burden of heart failure. *Cardiac Failure Review*, **3**: 7-11.

Yildirim, T., Yildirim, S. E., Aktoz, M. And Altun, A. 2018. Brain natriuretic peptide levels in acute inferior myocardial infarction. *Journal of Clinical Medicine Research*, **10**: 254-259.

Zandijk, A.J., van Norel, M.R., Julius, F.E., Sepehrvand, N., Pannu, N., McAlister, F.A., Voors, A.A. and Ezekowitz, J.A. 2021. Chloride in heart failure: The neglected electrolyte. *Heart Failure*, **9**: 904-915.