

Estimation of Brain Natriuretic Peptide (BNP) in Cardiac Failure Patients and its Association with Left Ventricular Ejection Fraction (LVEF)

Aamir Hussain, Yar Mohammad Nizamani, Asmat Kamal Ansari

ABSTRACT

OBJECTIVES: The present study was conducted to estimate brain natriuretic peptide (BNP) in heart failure patients and its association with left ventricular ejection fraction (LVEF).

STUDY DESIGN: Case control study.

PLACE & DURATION: Department of Medicine, Cardiology and Physiology, Isra University, Hyderabad from July 2014- Dec 2014

SUBJECTS AND METHODS: A sample of 60 subjects comprising of 30 normal controls (group I) and 30 diagnosed cases of heart failure (group II) were selected through non-probability purposive sampling as per inclusion and exclusion criteria. Blood samples were collected for the estimation of BNP. Left ventricular function was assessed by echocardiography. Data were analyzed on SPSS 21.0, Student's t-test and chi-square test were used for continuous and categorical variables respectively. Pearson's correlation was used for association of BNP and LVEF. P value ≤ 0.05 was taken significant.

RESULT: Mean age (\pm SD) of controls and cases were 51.5 ± 5.56 and 50.6 ± 5.25 years respectively ($p=0.91$). Of 60 subjects; 46 (76.6%) were male and 14 (23.3%) were female. BNP in controls and cases was noted as 77.06 ± 24.02 pg/ml and 17506.3 ± 13348 pg/ml respectively. BNP was significantly increased in heart failure patients and it showed inverse correlation with ejection fraction ($r = -0.76$, $p=0.0001$),

CONCLUSION: It is concluded that the BNP may be used an indicator of left ventricular function in settings where echocardiography facility is not available.

KEYWORDS: Brain natriuretic peptide, Heart failure, Left ventricular function.

This article may be cited as: Hussain A, Nizamani YM, Ansari AK. Estimation of Brain Natriuretic Peptide (BNP) in Cardiac Failure Patients and its Association with Left Ventricular Ejection Fraction (LVEF). J Liaquat Uni Med Health Sci. 2016;15(01):01-4.

INTRODUCTION

The Brain natriuretic peptide (BNP) was discovered in the late 1980s by Sudoh and co-workers. It is similar to atrial natriuretic peptide from the porcine brain. In human beings, BNP is synthesized and secreted primarily from left ventricular cardiomyocytes in response to increasing wall stretch, particularly during diastole.¹⁻³

The BNP is secreted in the Pro BNP form which is enzymatically cleaved into N-T Pro BNP (in active) and BNP (biologically active) which are secreted in a 1:1 ratio in circulation. The BNP concentration in plasma in healthy subjects is very low; approximately 1 fmol/ml (3.5 pg/ml).^{2,4-6}

Many previous studies had reported elevated BNP in cardiac failure patients. The congestive cardiac failure (CCF) is a clinical condition characterized by reduced cardiac output primarily because of reduced left ventricular functioning. Approximately 1-2% of the United States of America population suffers from heart fail-

ure, and an incidence of 400,000 new cases annually.³ Data is not available for the Pakistani population at national level. Heart failure is a progressive disease with a poor prognosis, with 60-70% of patients dying within 6 years of first diagnosis.⁷⁻⁹

It is reported that the BNP increases as the left ventricular (LV) pressure falls and reflects the severity of LV dysfunction. BNP is reported to be inversely associated with ejection fraction of LV and correlates positively with increasing LV mass and indices of LV filling pressure.¹⁰⁻¹²

However, a search of national data reveals no study ever conducted to analyze the BNP levels with special reference to left ventricular ejection fraction (LVEF) as detected by echocardiography; hence it is worthy to analyze the relationship of BNP and LVEF. The present study was conducted to analyze the BNP in heart failure patients and analyze its association with left ventricular functioning as measured by echocardiography.

SUBJECTS & METHODS

A comparative case control study was conducted at the Department of Medicine, Cardiology unit and Department of Physiology, Isra University, Hyderabad from July 2014 to December 2014. A sample of 60 subjects comprising of 30 normal controls (group I) and 30 diagnosed cases of heart failure (group II) were selected through non-probability purposive sampling as per inclusion and exclusion criteria. Diagnosed cases of cardiac failure of age ≥ 40 years but <60 years were selected. Volunteer subjects who gave a written informed consent were included. Cardiac failure patients with unstable ischemic heart disease, acute myocardial infarction, valvular heart disease, renal failure, pulmonary hypertension, diabetes mellitus and vitamin biotin intake were excluded. A thorough clinical examination was performed. Blood sample was collected from antecubital vein after sterilized alcohol gauze was applied to the area. 10ml of blood sample was collected in EDTA tubes. Brain natriuretic peptide was measured by a test termed as “Triage BNP test”.¹³ The Triage BNP test is an electrochemi luminescence immunoassay (ECLIA) for the quantitative determination of BNP in whole-blood and plasma specimens. The blood specimen was centrifuged in Thermo scientific, labofuge 400 haereus centrifuge machine for 5 minutes with a speed of 3500rpm. After 5 minutes sera were separated and placed into the automatic analyzer. BNP test was selected on machine which gave option of “START”. Button was pushed, after 18 minutes the result of BNP was shown on the screen of automatic analyzer machine.

Echocardiography was performed by cardiologist for the diagnosis and detection of left ventricular parameters. Findings were discussed and interpreted with senior cardiologist. The data was analyzed on SPSS 21.0 (IBM, incorporation, USA) software. Student’s t-test and chi-square test were used for continuous and categorical variables respectively. Pearson’s correlation was used to identify association of BNP and LVEF. P value ≤0.05 was taken significant.

RESULTS

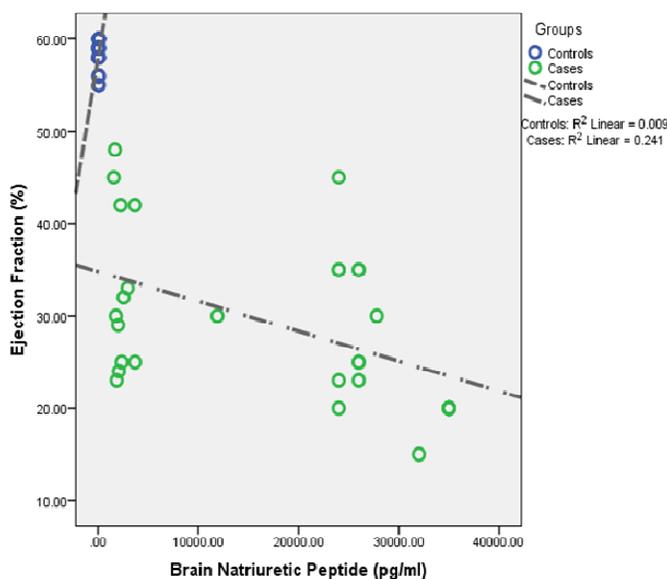
Out of 60 subjects; 30 were normal subjects taken as controls (group I) and 30 (group II) were diagnosed cases of heart failure. Study subjects characteristics are shown in table I. Mean (±SD) age of controls and cases were 51.5±5.56 and 50.6±5.25 years respectively (p=0.91) with a range of 44-60 and 45-60 years respectively. The gender distribution in the groups is shown in table I. The male population dominated over the female in present study. Of 60 subjects; 46 (76.6%) were male and 14 (23.3%) were female, however controls and cases were gender matched, as

shown in table I. Mean± SD of BMI in both groups was noted as 26.5±3.90 and 25.6 ±3.66kg/m² respectively (p=0.90). The ejection fraction (EF%) in controls was within normal range (55-60) with mean ± SD (58.4±1.67). However, the heart failure cases were having very low EF. Mean ± SD of EF in cases was noted as 29.13±8.83 (range 14-48%)(p=0.0001). BNP in controls and cases was noted as 77.06±24.02pg/ml (range 55-99 pg/ml) and 17506.3 ±13348 pg/ml (range 1570-35000 pg/ml) respectively (p=0.0001). The BNP values in heart failure subjects as higher as 35000 pg/ml were noted (p=0.0001).

TABLE I: CHARACTERISTICS OF STUDY POPULATION (n=60)

	Controls (n=30)	Cases (n=30)	p-value
Age (years)	51.5±5.56	50.6±5.25	0.76
Male	23 (%)	23 (%)	0.99
Female	7 (%)	7 (%)	0.99
BMI (Kg/m ²)	26.5±3.90	27.6±3.66	0.63
Ejection Fraction (%)	58.4±1.67	29.13±8.83	0.0001
Brain Natriuretic Peptide (BNP)pg/ml	77.06±24.02	17506.3±13348	0.0001

GRAPH I: SCATTER GRAPHS SHOWING THE ASSOCIATION OF BNP AND EJECTION FRACTION IN CONTROLS AND CASES



DISCUSSION

The left ventricular hypertrophy (LVH) is one of the major complications of systemic hypertension. LVH is

regarded as independent risk factor of cardiac disease irrespective of other risk factors like hypertension, ischemia etc. Cardiac failure is the most common complications of LVH.¹³⁻¹⁶

The present study reports elevated BNP levels in cardiac failure patients. The BNP in controls and cases was noted as 77.06 ± 24.02 pg/ml (range 55-99 pg/ml) and 17506.3 ± 13348 pg/ml (range 1570-35000 pg/ml) respectively ($p=0.0001$). The BNP values in heart failure subjects as higher as 35000 pg/ml were noted ($p=0.0001$). BNP showed inverse correlation with left ventricular ejection fraction (LVEF) ($r = -0.76$, as shown in graph I).

The cardiac failure patients with LVH and left ventricular dysfunction release BNP in large quantities been reported previously.¹⁴⁻¹⁶ The BNP secretion by ventricles may rise 2-10 times higher than normal. The BNP levels have been reported directly proportional to ventricular dysfunction. In patients with systemic hypertension, left ventricular hypertrophy and dysfunction is inevitable, hence BNP is best clinical indicator. Estimation of BNP may be convenient than Echocardiography and can be performed at primary health care centers and in rural areas where health care facilities are not available. The findings of present study are consistent with above studies. Similar findings had been reported by other studies.¹⁷⁻¹⁸ Shaikh et al¹⁴ from Pakistan has reported the diagnostic utility of BNP in cardiac failure. It was reported that the BNP level correlate with left ventricular functioning. Similar are the findings of another previous study.¹⁹ Jaffry et al²⁰ conducted a study at the Aga Khan University Hospital Karachi, reported BNP values in 190 patients of cardiac failure with impaired renal function. The study reported elevated BNP levels in cardiac failure and 1.5 to 2.5 more increase in impaired renal function subjects. The finding of elevated BNP levels in cardiac failure patients is a supporting finding to our present study.

The study of Shaikh et al²¹ has reported Pro-BNP levels and association with LVEF and acute dyspnea in cardiac failure patients. One hundred patients were studied at Al-Tabba heart institute Karachi. This study has reported that the Pro-BNP was strongly negatively correlated with the LV dimensions and LVEF on echocardiography. In present study, similar observation has been made for BNP correlation with echocardiography findings. As the BNP and Pro-NT-BNP are secreted in equimolar concentrations and blood plasma levels are similar, hence the findings are comparable with aforementioned study. It may be concluded that the BNP may prove of help in halting the Left ventricular hypertrophy and cardiac failure in remote areas where echocardiography findings are lacking. However, further studies are recommended to set

a cut point value of BNP with ejection fraction to make it standardized.

CONCLUSION

The present study reports that the brain natriuretic peptide is raised in heart failure patients. BNP shows a significant negative correlation with left ventricular ejection fraction, hence may be used as an indicator of left ventricular function instead of echocardiography.

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AUTHOR AFFILIATION:

Dr. Aamir Hussain

Assistant Professor, Department of Physiology
Isra University Hyderabad, Sindh-Pakistan.

Dr. Yar Mohammad Nizamani

Assistant Professor, Department of Physiology
Isra University Hyderabad, Sindh-Pakistan.

Dr. Asmat Kamal Ansari (*Corresponding Author*)

Professor, Department of Physiology
Isra University Hyderabad, Sindh-Pakistan.
E-mail: asmatansari5@gmail.com