Significance of B-Type Natriuretic Peptide in Heart Failure: A Hospital Based Study

Tejal. S. Kakhandki[1], Kiran Aithal[2]

Author's Affiliation:

[1]Postgraduate, [2]Professor and HOD, Department of General Medicine, SDM College of Medical Sciences and Hospital, Dharwad, Karnataka 580009, India.

Corresponding Author:

Kiran Aithal, Professor and HOD, Department of General Medicine, SDM College of Medical Sciences and Hospital, Dharwad, Karnataka 580009, India.

E-mail: drkiranaithal@yahoo.com

Abstract

Context: There is strong and convincing evidence that B-type Natriuretic Peptide (BNP) is a reliable and useful biomarker in acute dyspnea due to heart failure (HF) and has a diagnostic as well as prognostic value. when used with clinical information, rapid measurement of BNP may reduce the total treatment cost of patients. *Aim:* To understand the significance of BNP in predicting the severity of Heart Failure. *Materials and Methods:* The study was conducted in SDM Hospital, Dharwad, on 100 patients admitted in with features of HF, during the period of one year i.e. from Nov. 2017 to Oct. 2018. Left ventricular ejection fraction (EF) was measured by 2D Echocardiography and EF of above 40% was considered as preserved ejection and lesser than 40% as reduced. Serum BNP levels were estimated and levels higher than 100 pg./ml., were considered to be significant. *Statistical analysis used:* Data entry was done using Microsoft Excel and analysis using Statistical Package for Social Sciences (SPSS) version 22. *Results:* Majority of patients with preserved EF(28/58 patients), who developed signs and symptoms of HF, the levels of serum BNP were in the range of 1000 to 2000 pgs/ml., whereas, majority of patients with reduced EF(29/42 patients),who developed signs and symptoms of HF, the levels of serum BNP were in the range of 100 to 1000 pgs/ml. *Conclusion:* In the study, serum BNP levels were found to be highly significant in assessing the severity of heart failure and in management of the patients.

Keywords: Brain natriuretic peptide (BNP); Ejection Fraction; Heart Failure; Markers; Prognosis.

Introduction

Heart Failure, (HF) is a complex clinical syndrome that results from structural or functional impairment of ventricular filling or ejection of blood, which in turn leads to the cardinal clinical symptoms of dyspnea and fatigue and signs of HF, namely edema and rales as defined by American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) guidelines. Most of the patients present without signs or symptoms of volume overload, so the term "heart failure" is preferred over the older term "congestive heart failure".[1]

The prevalence of HF in India is 0.12-0.44%. It is an important cardiovascular disease because of its increasing prevalence, rapidly expanding health care cost, significant morbidity, and high mortality. There are continuing efforts to improve risk stratification of HF using biomarkers, imaging and genetic testing.[2]

In India HF affects younger age group, unlike in western countries where heart failure is

predominantly a disease of elderly and the important risk factors for HF are coronary artery disease, diabetes, hypertension, valvular heart diseases, rheumatic heart disease and primary muscle disease.[3]

There is strong and convincing evidence that B-type Natriuretic Peptide (BNP) is a reliable and useful biomarker in acute dyspnea due to HF and has a diagnostic as well as prognostic value. When used along with clinical information, rapid measurement of BNP may reduce the total treatment cost of patients.[4]

Natriuretic peptides (NPs) are hormones which are mainly secreted from heart and have important natriuretic and kaliuretic properties. There are four different groups NPs identified till date [atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), C-type natriuretic peptide (CNP) and dendroaspis natriuretic peptide, a D-type natriuretic peptide (DNP)], each with its own characteristic functions. The N-terminal part of the prohormone of BNP, NT-proBNP, is secreted alongside BNP and has been documented to have important diagnostic value in heart failure.

Elevated NP levels have shown predictive value in various diseases that have direct or indirect influences on the heart functions in many non-heart failure circumstances, even in the absence of depressed cardiac function.[5]

Objective

- To understand the significance of BNP in predicting the severity of Heart Failure.

Materials and Methods

This was a hospital based prospective study conducted in the Department of General Medicine, SDM College of Medical Sciences and Hospital Manjushree Nagar, Sattur, Dharwad, from November 2017 to October 2018. 100 cases with features of heart failure admitted in the hospital, were included in the study. This study was done after ethical committee approval and written informed consent was obtained from all patients included in the study.

Inclusion Criteria

1) Patients admitted with signs and symptoms of heart failure

2) Patients of heart failure with preserved or reduced left ventricular ejection fraction

3) Age group of patients - more than 18 years.

Exclusion Criteria

1) Recent myocardial infarction or angina (< 1 month),

2) Patients with Acute Coronary Syndrome

3) Chronic obstructive pulmonary disease cases

Functional status and severity of the disease in the patients was assessed according to New York Heart Association Classification. To assess type of heart failure, left ventricular ejection fraction was measured by 2D Echocardiography and ejection fraction of above 40% was considered as preserved ejection and lesser than 40% as reduced or depressed.

In all the cases, serum BNP levels were assayed by chemiluminescence method. Results were analyzed and presented as frequency, percentage and mean. *Chi*-square test was applied to find the association between two variables. p value <0.05 was taken as statistically significant. Data entry was done using Microsoft Excel and analysis using Statistical Package for Social Sciences (SPSS) version 22.

Results

The study group comprized of 100 (n) patients with features of HF after applying inclusion and exclusion criteria. Following were the observations made.

The mean age of the patients in the study group was 59.2 ± 14.513 years, youngest being 18 years and eldest 88 years old. There were 53 (53%) female and 47(47%) male patients.

The percentage of cases in different NYHA class were I-1%, II-14%, III-31%, IV-54%. Majority belonged to Class IV.

Majority, i.e, 55 patients, (55%) were hypertensives and 34 (34%) were diabetics and 66(66%) were non diabetics.

Ischemic heart disease was found to be the most common cause of HF in the study (51%). Other causes were, rheumatic heart disease in 10 cases, valvular heart disease in 10 cases, hypertension in 13 cases, infections in 3 cases and other causes in 13 cases.

Among 100 cases, 86 cases (86%) improved, 7 cases died (7%) and 7 cases' condition remained unchanged and were discharged against medical advise (DAMA).

The highest mortality was seen in the age group 60-70 years and >70 years of age, accounting for 28.5% each for the overall mortality.

In the study group of 100, 53 were females and 47 were males. Of the females, 47 patients (88.7%) improved, 3 patients (5.7%) died and 3 patients' (5.7%) condition remained unchanged. Of the 47 male patients, 39 patients (39%) improved, 4 patients (4%) died and 4 cases (4%) condition remained unchanged. The mortality rate in females was 5.7% and in males was 8.5%. The correlation between the gender and outcome was not statistically significant.

BNP values in patients with, Heart Failure with preserved EF (HFpEF) and Heart Failure with reduced EF(HFrEF), were, (Table 1)

Table 1: BNP Values in Patients with HFpEF and HFrEF.

Serum BNP Levels(pgs./ml)	Preserved Ejection Fraction (number of cases)	Reduced Ejection Fraction (number of cases)
100-500	3	16
500-1000	12	13
1000-1500	18	6
1500-2000	10	3
2000-2500	4	1
2500-3000	5	2
3000-3500	4	0
3500-4000	1	1
4000-4500	0	0
4500-5000	1	0
Total	58	42

Majority of patients with preserved EF(28/58 patients), who developed signs and symptoms of HF, the levels of serum BNP were in the range of 1000 to 2000pgs/ml., whereas, majority of patients with reduced EF(29/42 patients), who developed signs and symptoms of HF, the levels of serum BNP were in the range of 100 to 1000pgs/ml.

Statistical details related to age, BNP levels and EF% are (Table 2)

Table 2: Statistical Details Related to Age, BNP Levels and EF%.

	Age(years)	BNP pg/ml	LVEF (%)
N	100	100	100
Mean	59.200	1354.100	36.430
Median	61.000	1125.000	30.000
Standard deviation	14.513	936.441	14.282
Range	70.000	4852.000	50.000
Minimum	18.000	148.000	10.000
Maximum	88.000	5000.000	60.000
Percentile(25)	50.250	647.000	25.000
Percentile(75)	70.000	1727.500	50.000

Statistical analysis of serum BNP levels in relation to type of Heart Failure (Table 3)

Table 3: Statistical Analysis of Serum BNP Levels in Relation to Type of Heart Failure.

Type of HF	N	Mean	Std.Deviation	Z
HFpEF	42	952.17	787.052	4.295
HFrEF	58	1645.16	933.953	P<0.001

Serum BNP levels were found to be very highly significant in patients with HF with reduced EF.

Seven patients died in the hospital. Their serum BNP levels, type of HF and other associated comorbidities were, (Table 4)

IHD-Ischemic Heart Disease, T2DM-Type2 Diabetes Mellitus, RHD–Rheumatic Heart Disease, MS-Mitral Stenosis, MR-Mitral Regurgitation, ASD-Atrial Septal Defect, DCM-Dilated Cardio Myopathy, TR-Tricuspid Regurgitation, PAH–Pulmonary Arterial Hypertension, AF-Atrial Fibrillation)

Five out of seven patients who died, had HF with reduced EF, and their serum BNP levels were in the range of 907 to 1470 pgs/ml.

Table 4: Serum BNP Levels, Type of HF and other Associated Conditions in Seven Patients who Died in the Hospital.

Sl. No.	Age/sex	Serum BNPlevels Pgs/ml.	Type of HF	Other associated conditions
1	81/M	3640	HFpEF	IHD
2	83/F	1350	HFrEF	IHD, T2DM, Hypertension.
3	55/F	1240	HFrEF	RHD, Severe MS with MR with left hemiparesis and cardioembolic stroke
4	18/M	1240	HFrEF	ASD, DCM
5	50/M	907	HFrEF	Severe AS, MR
6	68/F	578	HFpEF	RHD with severe MR severe TR, severe PAH, AF, Hypertension, Anemia.
7	65/M	1470	HFrEF	IHD, T2DM, Hypertension

Discussion

The mean age of the patients in the group was 59.2 ± 14.513 years, youngest being 18 years and eldest 88 years old, which is similar to the Indian Study, "Epidemiology of acute decompensated heart failure in India". The AFAR study (Acute failure registry study)", conducted by Sandeep Seth et al.[6], where the mean age was 53.5±17.7 years, but lower compared to western studies (ranging from 65 to 73 years) such as Euro Heart Failure (EURO-HF) study[7], the Acute Decompensated Heart Failure National Registry (ADHERE)[8] and the Organized Program to Initiate Life-Saving 60 Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF)[9] hence this supports the concept that cardiovascular disease affects patients in India at a younger age than their Western counterparts.

Among the study population (n=100), 53 were female and 47 were male which is contrary to the worldwide incidence which is higher in males.[2]

Ischemic heart was found to be the most common cause of HF in the present study (51%), which is also the most common cause world wide and also in India according to study conducted by Seth S et al.[6] Satyamurthy et al., stated that, multi-factorial cause was the commonest etiology for HF with coronary artery disease being the single most common factor contributing to 66% of cases of HF.[10]

Satyamurthy et al. in their "Indian Consensus document on Cardiac Biomarkers" reviewed that, Maisel et al. performed the largest studies for BNP and Januzzi et al. for NT-proBNP, and the observations from these studies were noteworthy,

A BNP concentration >100 pg/mL is a strong independent predictor of CHF.

Accuracy of BNP (83%) was more than either the NHANE criteria (67%) or the Framingham criteria (73%), two commonly used sets of criteria for diagnosing CHF.

The diagnostic accuracy of BNP at a cut off of 100 pg/ml was 83.4%.

The negative predictive value of this threshold was particularly high (98%) [10]

Arati A. Inamdar and Ajinkya C. Inamdar, in their review article, discussed that, the evaluation for HF is performed using various parameters: physical examination to determine the presence of clinical symptoms and signs, blood tests, including complete blood count, urinalysis, complete metabolic profile for levels of serum electrolytes (including calcium and magnesium), blood urea nitrogen, serum creatinine, glucose, fasting lipid profile, liver function tests and thyroid-stimulating hormone.

Other HF-specific laboratory tests (especially in patients with a high possibility of heart failure) include Brain Natriuretic Peptide (BNP) with 70% sensitivity and 99% specificity and N-terminal proBNP (NT-proBNP) with 99% sensitivity and 85% specificity. During the diagnosis of HF, in patients presenting with acute dyspnea, BNP levels of less than 100 pg/mL have a 90% negative predictive value (NPV), and values of more than 500 pg/mL have an 81% positive predictive value (PPV). The BNP level is a strong predictor of risk of death and cardiovascular events in patients previously diagnozed with heart failure or cardiac dysfunction. Patients with BNP level of less than 200 pg/mL at admission have been associated with 2% mortality rate as opposed to 9% mortality rate seen in patients with admission BNP level of more than 200 pg/mL.[11]

Ishaq S, et al.,[4] study sample comprized of 100 patients (55 males and 45 females), out of which 60 were diagnosed as having CHF. Serum BNP was more than 100 pg/ml in 54 patients and it was less than 100 pg/ml in 6 patients. In their study, it was seen that 18/60 patients had BNP levels of more than 700 pg/ml at the time of admission, whereas, in the present study, 74/100 patients, had BNP levels of more than 700pg/ml. These patients had severe heart failure and majority had markedly reduced ejection fraction. In their study, eight patients (8/18), died within 7 days of hospital stay, indicating the correlation of BNP levels with severity of CHF and also its prognostic significance. In the present study, seven patients (7/74), died in the hospital (Table 5).

Table 5: Comparizon of BNP levels and Mortality of patients.

Study	No. of patients with BNP levels >700pg/ml	No. of patients who died in the hospital
Ishaq S, et al.[4]	18/60 (30%)	8/18 (44.44%)
Present study	74/100 (74%)	7/74 (9.46%)

Seven patients were dischared against medical advice and they could not be followed up.

Saha S, et[12]., opined that their study of 100 participants gave insight about common etiologies among the patients presenting with acute dyspnea in which HF was a competing diagnosis.[12] Mean BNP values were found to be similar in both the studies.(Table 6)

Table 6: Comparizon Between Mean BNP Levels, Mean and Standard Deviation (SD) of EF

Study	Mean BNP level(pg/ml)	Mean EF(%)	SD of EF(%)
Saha S, Meena L P, Chakravarty J, et al.[12]	1383.70	46.07	10.243
Present study	1354.10	36.430	14.282

Gong. H, et al., conducted a study to investigate the association between BNP levels and the prognosis of patients with left ventricular (LV) diastolic dysfunction. A total of 708 inpatients with cardiovascular disease (mean age, 66 years; 395 males and 313 females) were grouped according to initial BNP and were followedup for 2051 months (average, 30.86 months) until endpoint events occurred. Endpoints were defined as mortality or readmission due to cardiovascular disease, or mortality due to any other reason. A total of 67 and 77 events were reported in the BNP ≤80 pg/ml and BNP >80 pg/ml groups, respectively. They found that the occurrence rate of the endpoint was significantly higher in the BNP >80 pg/ml group, as compared with the BNP ≤80 pg/ml group (26.28 vs. 16.14%; relative risk=1.63) and the durations of patient survival were significantly shorter in the BNP >80 pg/ml group, as compared with the BNP ≤80 pg/ml group (P=0.0006), and patient survival decreased as BNP levels rose (P=0.0074). The prognoses of patients with elevated BNP levels were correspondingly worse in their study and these correlations were demonstrated to be significant in patients with LV diastolic dysfunction. Therefore, they concluded that BNP levels may be used to predict the prognosis of patients with cardiovascular disease.[13]

In the present study, serum BNP level of more than 100pgs/ml, was considered to be significant in the diagnosis of HF and the levels were found to be very highly significant in patients with HF with reduced EF.

Navid Iqbal, et al., opined that, cardiac biomarkers with their objectivity, reproducibility and accessibility are excellent adjuncts to physical examination and imaging studies in HF diagnosis and risk stratification. With advances in medical research, newer biomarkers continue to emerge, providing an ever clearer risk profile for patients with HF.[14]

Chapman. AR, et al., in their pilot study on measurement of plasma BNP in a 'real life' setting in primary care had a similar sensitivity, specificity and negative predictive value to that observed in trial populations. BNP aids early diagnosis of heart failure in primary care and may help to facilitate prompt introduction of evidence based therapies to modify patient outcomes. The costs of measuring plasma BNP in suspected cases of heart failure are modest, and its use would increase the diagnostic capacity of primary care if supported by local cardiology services.[15]

Doust J, et al., opined that, patients with treated chronic stable heart failure may have levels in the normal range (i.e., BNP less than 100 pg per mL and N-terminal proBNP less than 125 pg per mL in patients younger than 75 years. Increases in BNP levels may be caused by intrinsic cardiac dysfunction or may be secondary to other causes such as pulmonary or renal diseases (e.g., chronic hypoxia). BNP tests have to be correlated with other measures of cardiac status such as New York Heart Association classification.[16]

Wright G A and Struthers A D, concluded that, elevated plasma concentrations of BNP have been shown to be excellent independent predictors of mortality and readmission in this group of patients. If BNP does not fall after aggressive treatment, then it is indicative of a very poor prognosis. This simple and quick test may outperform other ways of risk stratifying heart failure patients. Patients with a persistently high BNP despite pharmacological treatment, should be considered for other treatments to improve survival, such as an ICD or cardiac transplantation.[17]

Conclusion

The present study has helped us to understand the significance of serum BNP level in confirming the diagnosis of heart failure, and in identifying high-risk patients who need close monitoring and more aggressive treatment.

Disclosure of Potential Conflicts of Interest: The authors indicate no potential conflicts of interest.

References

1. Mann DL, Chakinala M. Heart failure: Pathophysiology and Diagnosis. In: Jameson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Loscalzo J(eds). Harrison's Principles of Internal Medicine 20th ed. USA. Published McGraw– Hill Companies 2018;pp.1763–69.

2. Choi H, Park M, and Youn J. Update on heart failure management and future directions Korean J Intern Med 2019;34:11–43.

3. Reddy S, Bahl A, Talwar KK. Congestive heart failure in Indians: How do we improve diagnosis & management? Indian J Med Res 2010;132:549–560.

4. Ishaq S, Afaq S, Harnam Kaur, et al. Brain natriuretic peptide (BNP). A diagnostic marker in congestive heart failure–induced acute dyspnea. International Journal of Medicine and Public Health 2012;2(4):20–23.

5. Pandit K, Mukhopadhyay P, Ghosh S et al. Natriuretic peptides: Diagnostic and therapeutic use. Indian J Endocr Metab 2011;15, Suppl S4:345–53.

6. Seth S, Khanal S, Ramakrishnan S et al. Epidemiology of acute decompensated heart failure in India: The AFAR study (Acute failure registry study). Journal of the Practice of Cardiovascular Sciences. 2015;1(1):35.

7. Cleland JG, Swedberg K, Follath F et al. The EuroHeart Failure survey program – A survey on the quality of care among patients with heart failure in Europe. Part 1: Patient characteristics and diagnosis. Eur Heart J 2003;24:442–63.

8. Adams KF, Fonarow GC, Emerman CL et al. Characteristics and outcomes of patients hospitalized for heart failure in the United States: Rationale, design, and preliminary observations from the first 100,000 cases in the Acute Decompensated Heart Failure National Registry (ADHERE). Am Heart J 2005;149:209–16.

9. Fonarow GC, Abraham WT, Albert NM et al. Influence of a performance–improvement initiative on quality of care for patients hospitalized with heart failure: Results of the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE–HF). Arch Intern Med 2007;167:1493–502.

10. Satyamurthy I, Dalal JJ, Sawhney JPS et al. The Indian Consensus Document on cardiac biomarker. Indian Heart Journal 2014;66(1): 73–82.

11. Inamdar AA, Inamdar AC. Heart Failure: Diagnosis, Management and Utilization. Journal of Clinical Medicine.

12. Saha S, Meena P, Chakravarty J et al. Role of B-type natriuretic peptide level in predicting future cardiac events inpatients presenting with dyspnea (a hospital-based study). Heart India 2019;7:49–54.

13. Gong H, Wang X, Shi Y et al. "Correlation between brain natriuretic peptide levels and the prognosis of patients with left ventricular diastolic dysfunction" Experimental and Therapeutic Medicine 2016;11:2583–2589.

14. Iqbal N, Wentworth W, Choudhary R et al. "Cardiac biomarkers: New tools for heart failure management" Cardiovasc Diagn Ther, 2012;2(2):147–164.

15. Chapman AR, Leslie SJ, Walker SW et al. "Potential costs of B–type natriuretic peptide for the identification of people with heart failure in primary care in Scotland – a pilot study" J R Coll Physicians, Edinb, 2015;45:27–32.

16. Doust J, Lehman R, Glasziou P. "The Role of BNP Testing in Heart Failure" American Family Physician, December 1, 2006;74(11):1893–98.

17. Wright GA, Struthers AD, "Natriuretic peptides as a prognostic marker and therapeutic target in heart failure" Heart, 2006;92:149–151.