

## Prognostic Role of B-Type Natriuretic Peptide in Adults with Acute Dyspnea Requiring Emergency Admission

### Abstract

**Objective:** The aim of the study was to evaluate the role of B-type natriuretic peptide (BNP) in patients presenting with acute dyspnea admitted in emergency services. **Materials and Methods:** A prospective observational study was conducted on 100 patients presenting to the emergency of Dayanand Medical College and Hospital and Hero DMC Heart Institute with acute dyspnea of <48 h duration, in which BNP levels were done on arrival to emergency. **Results:** BNP levels were significantly higher in patients having left ventricular dysfunction, both systolic and diastolic. Patients with systolic dysfunction had slightly higher BNP (1251.50 ± 950.14 pg/mL) compared to patients with diastolic dysfunction (905.62 ± 618.10 pg/mL) though statistically insignificant ( $P = 0.055$ ). BNP levels were also inversely related to ejection fraction. Mean BNP levels in patients with EF <31%, 31%–45%, 46%–59%, and ≥60% were 1464.63 ± 1058.29, 968.24 ± 751.59, 841.64 ± 503.41 and 781.67 ± 504.21 ( $P = 0.009$ ), respectively. Patients having higher BNP levels had significantly prolonged duration of stay compared to patients with lower BNP. Patients who expired had slightly higher levels of BNP though statistically nonsignificant. BNP had no significant statistical relation with age, heart rate, creatine phosphokinase-MB, Trop-T levels, systolic blood pressure. **Conclusion:** We conclude that high BNP levels are a marker of cardiac dysfunction and increased duration of hospital stay in patients presenting to the emergency with acute dyspnea. Hence, BNP can be used as a screening test for the evaluation and management of dyspnea.

**Keywords:** B-type natriuretic peptide, cardiac dysfunction, dyspnea

### Introduction

Dyspnea is a common chief complaint in the emergency department (ED). The most important differential diagnosis of acute dyspnea include congestive heart failure (HF) and pulmonary conditions such as respiratory tract infections, pulmonary embolism, asthma, exacerbation of chronic obstructive pulmonary disease (COPD), etc.<sup>[1]</sup> The accurate and prompt differentiation of HF from other causes is a major challenge in the emergency.

Because of the dramatic impact of HF on morbidity, mortality, and cost of care, a rapid, accurate, and reliable tool is needed to differentiate HF from other causes of dyspnea. Based on numerous studies, B-type natriuretic peptide (BNP) is increasingly being used for the diagnosis of HF, especially in the emergency room setting. It is estimated that >70% of hospitals utilize BNP testing in the United States.<sup>[2]</sup> In addition to the clinical

presentation, BNP levels not only help with the diagnosis and monitoring of patients with HF but also provide information on prognosis, and mortality.<sup>[3]</sup> Besides its role in HF, measurement of BNP is useful in other acute emergency settings such as COPD. Pulmonary hypertension due to pulmonary disease is also associated with raised BNP, which can serve as a marker of advanced cardiopulmonary disease.<sup>[4]</sup>

In our country, very sparse data are available on the utility of BNP in acute dyspnea.<sup>[5]</sup> Therefore, there is a need to collect data in our country regarding the role of BNP in patients with dyspnea in the emergency setting. The aim of the current study was to assess the role of BNP in the diagnosis and prognosis of patients presenting to an emergency with acute dyspnea.

### Materials and Methods

This is a prospective observational study duly approved by the institutional ethics committee.

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The study participants included 100 adult patients admitted through emergency services in a tertiary care center. Patient aged >20 years with acute dyspnea within 48 h of presentation in ED were taken. Patients with dyspnea secondary to trauma and with serum creatinine level >2.8 mg/dl in their previous medical records were excluded from the study. Name, age, gender, presenting complaints, history of present illness, treatment history, general physical examination, and systemic examination was recorded on a predesigned pro forma. BNP estimation, Chest X-ray, electrocardiogram, echocardiography complete blood count, liver function tests, and renal function tests were done. Any other investigations such as Troponin T, d-dimer, MB-creatine phosphokinase (CPK) wherever advisable were sent. Written informed consent was obtained.

### Testing method

Serum BNP levels were measured by the Alere BNP triage test. This is a rapid, point of care fluorescence immunoassay used for the quantitative measurement of BNP in ethylenediaminetetraacetic acid anticoagulated whole blood or plasma specimens. Samples were immediately sent for analysis due to the urgent requirement of results. If a specimen appeared to be hemolyzed, another specimen was obtained and tested. The BNP range reported by the test system was 5 pg/mL to 5000 pg/mL.

### Statistical analysis

Discrete categorical data were presented as *n* (%); continuous data were written as mean  $\pm$  standard deviation. The normality of quantitative data was checked by measures of Kolmogorov–Smirnov tests of normality. For more than two groups, Kruskal–Wallis test or ANOVA was applied. Categorical data were compared using Chi-square or Fisher's exact test. All statistical tests were two-sided and performed at a significance level of  $\alpha = 0.05$ . The analysis was conducted using SPSS for Windows (version 17.0; SPSS Inc., Chicago, IL, USA).

### Results

This was a prospective observational study conducted on 100 patients presenting to the ED of Dayanand Medical College and Hospital and Hero DMC Heart Institute with acute dyspnea of duration <2 days.

Demographic characteristics are shown in Table 1. The mean age of our population was  $65.30 \pm 11.92$  years. About 53% of the patients were male. Percentage of diabetics and hypertensive were 48% and 49%, respectively. 14% of patients were smokers, while 13% gave a history of alcohol intake. The majority of the patients had cardiac disease. The most common was ischemic heart disease (55%), while nonischemic dilated cardiomyopathy was present in 16% of patients. 11% patients had COPD.

It was observed that BNP level had significant relation with duration of stay and ejection

**Table 1: Demographic and clinical characteristics of the study population**

Characteristics	Cases (n=100)
Age (years)*	65.30 $\pm$ 11.92
Sex (male/female)	53/47
Diabetes mellitus	48
Hypertension	49
Smoking	14
Alcohol	13
Diagnosis	
IHD	55
Dilated cardiomyopathy	16
COPD	11
Normal EF heart failure	6
Hypertensive heart disease	1
Rheumatic heart disease	1
Nonrheumatic valvular disease	3
Anxiety neurosis	2
Bronchial asthma	2
Pneumonia	1
Pulmonary embolism	1
Interstitial lung disease	1

\*Values are in mean $\pm$ SD. SD: Standard deviation, IHD: Ischemic heart disease, COPD: Chronic obstructive pulmonary disease; EF: Ejection fraction

**Table 2: Relation of B-type natriuretic peptide with length of stay**

Length of stay (days)	n (%)	Mean BNP levels (pg/ml)*
Upto 5	27 (27)	987.83 $\pm$ 867.01
6-10	49 (49)	1009.55 $\pm$ 675.85
11-15	17 (17)	1393.08 $\pm$ 1241.52
16-20	4 (4)	1735.25 $\pm$ 703.16
21-25	1 (1)	1070.00
>25	2 (2)	1365.00 $\pm$ 1590.99
<i>P</i>		0.032**

\*Values are in mean $\pm$ SD; \*\*Significant *P* value. *n*: Number of patients; BNP: B-type natriuretic peptide

fraction [Tables 2-4]. In this study, 7 patients (7%) had BNP < 100 pg/ml, 18 patients (18%) had BNP 100–500 pg/ml and 75 patients (75%) had BNP >500 pg/ml [Table 3]. Mean BNP levels (mean  $\pm$  SD) in our study were  $1105 \pm 86$  pg/ml.

It was observed that higher BNP levels were associated with a significantly increased duration of stay (*P* = 0.032) [Table 2]. Patients having the length of stay up to 5 days had mean BNP levels of  $987.83 \pm 867.01$  pg/ml, patients having the length of stay 6–10 days, 11–15 days, 16–20 days had mean BNP levels of  $1009.55 \pm 675.85$  pg/ml,  $1393.08 \pm 1241.52$  pg/ml, and  $1735.25 \pm 703.16$  pg/ml, respectively. The mean length of stay in patients having BNP <100, 100–150 and >500 was  $6.38 \pm 2.82$  days,  $7.59 \pm 5.29$  days and  $8.65 \pm 4.81$  days, respectively [Table 3].

BNP levels were inversely correlated with left ventricular systolic dysfunction ( $P = 0.009$ ) [Table 4]. Mean BNP levels in patients with EF <31%, 31%–45%, 46%–59% and  $\geq 60\%$  were  $1464.63 \pm 1058.29$ ,  $968.24 \pm 751.59$ ,  $841.64 \pm 503.41$ , and  $781.67 \pm 504.21$ , respectively. On intergroup comparisons, BNP was significantly higher in patients with EF <31% compared to patients with EF > 60% (mean difference  $\pm$  SD:  $682.96 \pm 228.62$ ,  $P = 0.004$ ), 46%–59% (mean difference  $\pm$  SD:  $622.99 \pm 283.35$ ,  $P = 0.03$ ), and 31%–45% (mean difference  $\pm$  SD:  $496.39 \pm 200.29$ ,  $P = 0.015$ ), respectively.

About 63% of patients who had systolic dysfunction, whereas 35% had diastolic dysfunction [Table 4]. Patients with systolic dysfunction had higher BNP ( $1251.50 \pm 950.14$ ) compared to patients with diastolic dysfunction ( $905.62 \pm 618.10$ ), but this difference was statistically nonsignificant (0.055).

87 patients (87%) were discharged, 7 patients (7%) were discharged against medical advice (DAMA), and 6 patients (6%) expired [Table 5]. It was observed that patients who were discharged had mean BNP levels of  $1070 \pm 866.61$  pg/ml, patients who were DAMA had mean BNP levels of  $1281 \pm 870.75$  pg/ml, while patients who expired had mean BNP levels of  $1407 \pm 904.91$  pg/ml. Thus, patients who expired had higher BNP though this difference was statistically nonsignificant.

BNP had no statistically significant relationship with age, heart rate, CPK-MB, Trop-T levels, systolic blood pressure ( $P > 0.05$ , data not shown in table).

## Discussion

Dyspnea is the leading symptom in patients with HF, accounting to 2.7% of visits in ED and 15%–25% of all hospital admissions.<sup>[6-8]</sup> It is estimated that 5.8 million people in the United States have HF, with approximately 670,000 new cases occurring each year.<sup>[9]</sup> Reliable estimates of HF in INDIA are not available because of a lack of well-conducted studies and the absence of a systematic surveillance program at national/state level. The prevalence of HF in India is estimated to be around 1% of the population or about 8–10 million individuals.<sup>[10]</sup> Estimated mortality due to HF is around 0.1–0.16 million individuals per year.<sup>[10]</sup>

In this study, the most common cause of dyspnea was HF and etiology was multifactorial. The most common cause was ischemic heart disease, which is in accordance with an Indian study. Ischemic heart disease accounted for 65% of cases of HF in that study.<sup>[11]</sup> Less number of COPD patients (11%) in our study could be due to a few reasons such as referral bias in tertiary care cardiac center and summer season in which this study was carried out. Another important factor is that the incidence of smoking is low in Punjab because of religious reasons.

**Table 3: Relation of B-type natriuretic peptide levels with mean length of stay**

BNP levels (pg/ml)	n	Mean length of stay (days)**
<100	7	6.38 $\pm$ 2.82
100-500	18	7.59 $\pm$ 5.29
>500	75	8.65 $\pm$ 4.81

\*\* $P=0.43$ . n: Number of patients; BNP: B-type natriuretic peptide

**Table 4: Relation of B-type natriuretic peptide with ejection fraction and type of cardiac dysfunction**

	n (%)	Mean BNP levels (pg/ml)*
EF (%) <sup>§</sup>		
$\geq 60$	20 (20)	781.67 $\pm$ 504.21
46-59	11 (11)	841.64 $\pm$ 503.41
31-45	31 (31)	968.24 $\pm$ 751.59
<31 <sup>@</sup>	38 (38)	1464.63 $\pm$ 1058.29
Cardiac dysfunction <sup>^</sup>		
Systolic dysfunction (EF $\leq 45\%$ )	63 (63)	1251.50 $\pm$ 950.14
Diastolic dysfunction (EF $\geq 45\%$ )	35 (35)	905.62 $\pm$ 618.10
No abnormality	2 (2)	10.80 $\pm$ 8.20

\*Values are in mean $\pm$ SD; <sup>§</sup> $P=0.009$ ; <sup>@</sup>On intergroup comparison, BNP was significantly lower in patients with EF <31% compared to other three groups ( $P<0.05$ ); <sup>^</sup> $P$  value between systolic and diastolic dysfunction was 0.055. n: Number of patients; BNP: B-type natriuretic peptide; EF: Ejection fraction; SD: Standard deviation

**Table 5: Relation of B-type natriuretic peptide with clinical outcome**

Clinical outcome	n (%)	Mean BNP levels (pg/ml)*
Discharge	87 (87)	1070 $\pm$ 866.61
Discharged against medical advice	7 (7)	1281 $\pm$ 870.75
Death	6 (6)	1407 $\pm$ 904.91

\* $P=0.56$ . n: Number of patients; BNP: B-type natriuretic peptide

For the acutely sick patient presenting to the ED, a wrong and delayed diagnosis can lead to significant morbidity and mortality. A diligent approach to determine the etiology of acute dyspnea in a rapid and accurate manner is extremely important. The two cardinal causes of dyspnea, HF, and lung disease, are often difficult to differentiate.<sup>[12,13]</sup> In a resource-limited country like India, Echocardiography is not easily available in acute care settings. Most of the Indian hospitals lack the facility and expertise of echocardiography in ED. Having a blood test, such as BNP would aid in the diagnosis and management of patients with dyspnea. In the developed world, the role of BNP has been clearly established as an important diagnostic and prognostic marker of HF in the emergency setting and has been found to have a favorable cost-benefit ratio in the setting acute dyspnea.<sup>[14]</sup>

In this study, it was observed that the mean BNP levels were significantly higher in patients having lower

ejection fraction, which is supported by a study done by Hammerer-Lercher *et al.* in which it was observed that BNP levels were significantly high in patients having ejection fraction <30%.<sup>[15]</sup> Similar trends were observed in various other studies.<sup>[16-19]</sup>

It was observed that the mean BNP levels were highest in systolic dysfunction, followed by diastolic dysfunction and least being in patients with no abnormality. This finding is supported by the study done by Angurana *et al.*, in which it was observed that patients having systolic dysfunction have the highest levels of BNP.<sup>[5]</sup> Similar trends were also observed in various other studies.<sup>[20,21]</sup>

Another important finding is that the mean length of stay was longer in patients having higher levels of BNP and vice versa. In this study, it was observed that patients having lower BNP levels have lesser stay in the hospital, thereby reducing treatment time and reduced cost of treatment. Thus BNP measurement has an important prognostic role. A lower BNP levels would suggest a better clinical outcome and earlier discharge. In a study conducted by Mueller *et al.*, it was found that the median time to discharge was 8.0 days in patients in whom the BNP group was measured compared to 11.0 days in the control group. As a consequence, cost of treatment was also significantly reduced.<sup>[22]</sup>

We observed that mean BNP levels were highest in patients who expired, while patients who were discharged had the lowest mean BNP levels though it did not reach statistical significance probably because of the small sample size in our study. A multivariate analysis of the EPIDASA study observed that BNP levels were a predictor of death.<sup>[23]</sup> A study done by Chenevier-Gobeaux *et al.* observed that patients having higher BNP levels had higher hospital mortality.<sup>[24]</sup> Seeing the magnitude of acute dyspnea in ED, more studies with larger sample size are needed to further define the role of BNP in the emergency setting, especially in the Indian context.

## Conclusion

We conclude that high BNP levels are a marker of cardiac dysfunction, increased duration of hospital stay, and increased in-hospital mortality. Thus, BNP can be used as a prognostic and diagnostic test for the evaluation of acute dyspnea.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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