

# Role of Pro-BNP in predicting outcome in acute heart failure patient presenting to a medical emergency: An observational study from North India

Arjun K. Singhal<sup>1</sup>, Gaurav Singh<sup>2</sup>, SK Singh<sup>3</sup>, Busi Karunanand<sup>1</sup>, Sonu Agrawal<sup>4</sup>

<sup>1</sup>Department of Biochemistry, Faculty of Medicine and Health Sciences, SGT Gurugram, Haryana, India, <sup>2</sup>Department of Microbiology, ESIC Medical College and Hospital, Bhita, Patna, Bihar, India, <sup>3</sup>Department of Medical Health and Family Welfare, Shree Guru Gobind Singh Tricentenary University, Pilibhit, Uttar Pradesh, India, <sup>4</sup>Department of Microbiology, Vimta Labs. Limited, New Delhi, India

## ABSTRACT

**Background:** Acute heart failure (AHF) is a clinical syndrome defined as the new onset or acutely decompensated heart failure (ADHF) leading to signs and symptoms of heart failure (HF). The critical cut-off values for these biomarkers that suggest high mortality are not clearly defined in previous studies. More studies are required to better understand the correlation of Pro- BNP and its association with HF. The primary objective is to study the role of Pro-BNP and critical factors in predicting outcomes in AHF patients presenting to a medical emergency. **Materials and Methods:** The data from the patients presented with symptoms of HF in the Department of Medical Emergency at our hospital were recorded and analysed. AHF is a clinical syndrome defined as the new onset or ADHF leading to signs and symptoms of HF, as based on the European Society of Cardiology. **Results:** The present study highlights the various risk factors of AHF in patients and their association with mortality. In the present study, mortality in patients with very high Pro-BNP levels  $\geq 2000$  pg/ml was significantly higher than in patients with moderately elevated Pro-BNP. The patients who survived after 5 days of hospitalization had Pro-BNP levels  $\leq 2000$  pg/ml, suggesting that very high Pro-BNP levels  $\geq 2000$  pg/ml are associated with fatal outcomes. **Conclusion:** To conclude, diabetes and sepsis are critical factors for the hospitalization and mortality of patients with AHF in northern India. Very high Pro-BNP levels  $\geq 2000$  pg/ml in patients with AHF requiring hospitalization and associated with fatal outcomes.

**Keywords:** Biomarker, emergency department, heart failure, patients, Pro-BNP

## Introduction

Heart failure (HF) is a clinical syndrome often caused by a structural and/or functional impairment of ventricular filling or cardiac output, resulting in clinical symptoms of dyspnoea, orthopnoea, oedema and rales.<sup>[1]</sup> Acute heart failure (AHF) is a clinical syndrome defined as the new onset or acutely decompensated heart failure (ADHF) leading to signs and

symptoms of HF, as based on the European Society of Cardiology (ESC) definition.<sup>[2]</sup> HF is a disease entity affecting people worldwide, resulting in significant mortality, morbidity and cost of care. The prevalence of HF in India was 1.2 per 1000 population, as shown in one Indian study.<sup>[3]</sup> One study estimates that the overall lifetime risk of developing HF is 33% for men and 28% for women.<sup>[4]</sup> Despite the recent advances in the treatment of HF, it still carries a poor prognosis. In contrast, the management of patients presenting with AHF is less understood. Data from the UK and US demonstrate a mortality rate of 4–6% and 9%, respectively.<sup>[5,6]</sup> Uncontrolled diabetes, uncontrolled hypertension (HTN), myocardial ischemia, poor

**Address for correspondence:** Dr. Arjun K. Singhal, Department of Biochemistry, Faculty of Medicine and Health Sciences, SGT Gurugram - 122 413, Haryana, India. E-mail: singhal2075@yahoo.co.in

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adherence to medications, arrhythmias, infection, anaemia, renal impairment, and diet are various known precipitating factors for hospitalization with AHF.<sup>[7,8]</sup> Previous studies have shown that biomarkers like BNP and NT-pro-BNP are independent predictors of mortality and cardiac outcomes in patients with HF and AHF.<sup>[9-11]</sup> However, the critical cut-off values for these biomarkers that suggest high mortality are not clearly defined in previous studies. Only pockets of studies are there from India defining the role of Pro-BNP in the management of AHF patients. More studies are required for a better understanding of the correlation of Pro-BNP and its association with HF.

Therefore, primary objective is to study the role of Pro-BNP and other critical factors in predicting outcomes in AHF patients presenting to medical emergency.

## Materials and Methods

### Study area, population, and period

The present study was carried out in the Department of Biochemistry, tertiary care hospital India. Between the year of February 2022 and February 2023, the data from the patients presented with symptoms of HF in the Departments of Medical Emergency at our hospital were recorded and analysed. All patients who were aged  $\geq 16$  admitted to the medical emergency and diagnosed with AHF were enrolled. AHF is a clinical syndrome defined as the new onset or ADHF leading to signs and symptoms of HF, as based on the ESC.<sup>[2]</sup>

### Data collection

A total of 100 patients were included in the present study from February 2022 and February 2023 who meet inclusion criteria were enrolled in this study. Detailed medical history (coronary artery disease, arrhythmias, HF, etc.), recent history of any infection and comorbidity history of all the patients were recorded. All patients underwent basic routine investigations like complete haemogram, liver function test and kidney function test. Pro-BNP, procalcitonin and troponin T levels at the time of admission were measured in all patients. Enrolled patients were subjected to echocardiography. The patients were followed for five days, and their outcomes were recorded.

### Data analysis

We have also specified that included participants with AHF would be categorized into moderately high Pro-BNP values group ( $\leq 2000$ ) and very high Pro-BNP values group ( $>2000$ ), and mortality in these two groups was compared. The patients with AHF who died within 5 days of hospitalization were compared with patients who survived with respect to Pro-BNP.

The data collected were analysed using the STATA/SE version 14.0 statistical software (Stata Corp, Texas, USA). Categorical data were described using numbers and percentages. Data generated from the present study have been presented in the form of tables, and all descriptive analyses have been shown

in percentages. *p*-value has been calculated to analyse statistical significance.

## Results

A total of 100 adult patients ( $n = 100$ ) were included in the present study. Among these 100 patients, 61.31% were males and 38.69% were females, and the male-to-female ratio was 1.58:1. The results showed that males are at higher risk of AHF than females ( $\chi^2 = 17.2, p = 0.02$ ). The mean age for males was 47.87, and the mean age for females was 51.57. The mean age of patients in our study was 49.72. As the cardiac illness, out of 100 patients, 81% ( $n = 81$ ) had an ejection fraction less than 50% and 19% ( $n = 19$ ) had an ejection fraction  $\geq 50\%$ . Patients with an ejection fraction less than 50% had a mortality rate of 12.5% ( $n = 10$ ), which did not statistically differ from patients with an ejection fraction greater than 50%, who had a mortality rate of 6.21% ( $n = 1$ ), 95% CI (0.484-18.6788), and  $p = 0.589$ . Atrial fibrillation and arrhythmias as risk factors were present in 31% ( $n = 31$ ) and 34% ( $n = 34$ ) patients, respectively. Acute coronary syndrome as a risk factor was defined based on ECG changes (ST elevation and non-ST elevation) and cardiac troponin values. ST depression changes were present in 53.5% ( $n = 53.5$ ), ST-elevation was present in 19.5% ( $n = 19.5$ ) patients and 27% ( $n = 27$ ) patients have no changes on ECG. Troponin T was positive in 47.5% ( $n = 47.5$ ) of patients. There was no difference in the outcome of patients who had ACS as compared to those who did not have Acute coronary syndrome (ACS) as a precipitating factor,  $p = 0.645$ , which was not statistically significant. The most common comorbid condition in the present study was diabetes. It was present in 69% ( $n = 69$ ) of the patients. Out of which, poorly controlled glycaemic status was seen in 73.91% (51) had poorly controlled glycaemic status. Diabetes was absent in 31% ( $n = 31$ ) of patients only. The mortality was significantly higher in patients with diabetes as compared to non-diabetic patients, where mortality was ( $P = 0.02$ ). Sepsis was one of the most common risk factors for AHF in this study, and it was present in 39% ( $n = 39$ ) of patients. The mortality was higher in patients with AHF who had sepsis as a risk factor as compared to those who did not have sepsis as a risk factor  $p = 0.002$ , which was statistically significant. The moderately high Pro-BNP values group ( $\leq 2000$ ) was found in 76 patients, and the very high Pro-BNP values group ( $>2000$ ) was found in 24 patients. The mortality in the group of patients with very high Pro-BNP levels  $\geq 2000$  pg/ml was significantly higher than the group of patients who had moderately elevated Pro-BNP.

## Discussion

The present study highlights the various risk factors of AHF in patients and their association with mortality. The mean age of patients in our study was 49.72, in contrast to a similar study from Israel who had a mean age of  $70 \pm 10$ , suggesting that the Indian population are at risk of AHF approximately one decade earlier as compared to the western population.<sup>[12]</sup> The prevalence of atrial fibrillation as a risk factor for HF ranges from 13% to

27% in previous studies.<sup>[13,14]</sup> However, atrial fibrillation as a risk factor for HF in our study was seen in 34% of the patients. In our study, out of 100 patients, 81% ( $n = 81$ ) had an ejection fraction less than 50% and 19% ( $n = 19$ ) had an ejection fraction  $\geq 50\%$ . Our study has shown a higher prevalence of patients with ejection fraction less than 50% as compared to earlier studies showing 40%–60%.<sup>[15]</sup> The reason for this high prevalence in our study could be due to the fact that these patients are mostly present with AHF. The mortality in patients with an ejection fraction less than 50% is 12.5% ( $n = 10$ ) which did not differ significantly from patients who had an ejection fraction  $\geq 50$  percent and mortality 6.21% ( $n = 1$ ) 95% CI (0.484 to 18.6788), and  $p = 0.589$ . Contrary to past studies where mortality rates were greater in patients with ejection fractions below 50%,<sup>[16]</sup> acute coronary syndrome was identified as a risk factor in 53.5% ( $n = 53.5$ ) of patients with ST depression alterations and in 19.5% ( $n = 19.5$ ) of patients with ST-elevation. There was no difference in the outcome of patients who had ACS as compared to those who did not have ACS as a precipitating factor. Our results were similar to a study from Israel on acute coronary syndrome.<sup>[16]</sup> The most common comorbid condition in the present study was diabetes. Diabetes and HF independently increase the risk for each other. In our study, diabetes was present in 73.91% of patients. The prevalence of diabetes as a precipitating factor for HF ranges from 10% to 47% in previous studies.<sup>[17-19]</sup> The high number of diabetes reported in our study can be explained by the fact that the Indian population have a high prevalence of diabetes. Sepsis was one of the critical risk factors for AHF and was present in 39% ( $n = 39$ ) of patients. The mortality was higher in patients with AHF who had sepsis as a risk factor as compared to those who did not have sepsis as a risk factor. The present study results are inconsistent with another study, showing sepsis is associated with hospitalization and high mortality rates.<sup>[20]</sup> Pro-BNP is an independent predictor of cardiac outcomes in patients with HF, as shown in previous studies.<sup>[21-24]</sup> In the present study, mortality in patients with very high Pro-BNP levels  $\geq 2000$  pg/ml was significantly higher than in patients with moderately elevated Pro-BNP. The patients who survived after 5 days of hospitalization had Pro-BNP levels  $\leq 2000$  pg/ml, suggesting that very high Pro-BNP levels  $\geq 2000$  pg/ml are associated with fatal outcomes.

This topic is relevant to the practice of primary care physicians because they are often the first point of contact for patients with AHF who present to a medical emergency. Primary care physicians need to be aware of the role of Pro-BNP in predicting outcomes in AHF patients, as it can help them in risk stratification, diagnosis, management and referral decisions. It has been shown to be an independent predictor of mortality and other cardiac outcomes in patients with HF. However, there is no consensus on the optimal cut-off values that indicate high mortality risk. A recent study from India suggested that Pro-BNP values above 2000 pg/ml in patients with AHF requiring emergency admission are associated with a poor prognosis. In addition to Pro-BNP, primary care physicians should also consider the precipitating factors of

AHF, as they may influence the patient's outcome and response to treatment. Therefore, primary care physicians should measure Pro-BNP levels and identify precipitating factors in AHF patients presenting to a medical emergency, as they can provide valuable information for prognostic evaluation and clinical decision-making.

## Conclusion

To conclude, diabetes and sepsis are critical factors for the hospitalization and mortality of patients with AHF in northern India. Very high Pro-BNP levels  $\geq 2000$  pg/ml in patients with AHF require hospitalization and associated with fatal outcomes. Considering the scarcity of information available in our country, more region/province-wise studies on precipitating factors and the utility of Pro-BNP levels for AHF patients are required to improve our understanding of better management of AHF.

## Strengths of the study

This study was done in a tertiary care hospital in north India in which patients of different age groups were enrolled. This study not only highlights the role of Pro-BNP and its association with AHF patients but also highlights other risk factors such as diabetes, sepsis other cardiac diseases and their association.

## Limitation of the study

This was a single-centric study with a small sample size, and only in-patients were enrolled.

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## Conflicts of interest

The authors declare that there are no conflicts of interest.

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