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RESEARCH ARTICLE

Correlation of NT-ProBNP levels and precipitating factors with mortality in acute heart failure patients presenting to a tertiary care hospital in eastern India: an observational study

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Abstract: ***Background***: Acute heart failure (AHF) is still a primary cause of emergency admissions in South Asia, yet, the available amount is inadequate regional information on how to use biomarkers for risk assessment. In this study, we looked into how useful the admission amount of circulating N-terminal pro-BNP and vital triggers are for predicting in-hospital mortality in a high-level care hospital in Eastern India. ***Methods:*** Over the course of a year, we enrolled 300 consecutive adults who had clinically confirmed AHF. We measured NT-proBNP levels within six hours of admission and carefully assessed the factors that might have triggered their condition. We followed the patients until they were discharged or passed away. To pinpoint variables that independently influence death risk, we used mulit-dimensional logistic predictive modeling, taking into account various demographic and clinical factors. ***Results:*** Hospital-related deaths occurred at a rate of 15% (45 out of 300 individuals). The midpoint of NT-proBNP measurements was significantly higher in participants lacking survive compared to those who did (9,800 vs. 6,400 pg mL^{-1}; $p < 0.001$). A threshold of 9,000 pg mL^{-1} supplied an area under the ROC curve of 0.82 for predicting death. After adjustments, having an NT-proBNP level exceeds 9,000 pg mL^{-1} tripled the odds concerning death (OR 3.2, 95% CI 1.8–5.7; $p < 0.001$). Infection was the most common trigger (35% overall; 60% of deaths) and independently increased the risk (OR 2.6, 95% CI 1.4–4.9; $p = 0.003$). Additionally, an admission systolic pressure below 90 mmHg added to the threat (OR 2.1, 95% CI 1.1 -- 4.1; $p = 0.025$). We didn't find any significant interactions between NT-proBNP levels and individual triggers. ***Conclusion:*** Setting an NT-proBNP threshold of 9,000 pg mL^{-1}, along with early identification of infectious causes and low blood pressure, provides a practical and effective approach for spotting AHF patients at the highest risk of early death in Indian emergency departments. It's important to adapt region-specific cut-offs to improve guidelines

Keywords: NT-proBNP; acute heart failure; mortality; precipitating factors; infection; India .

INTRODUCTION

Acute heart failure (AHF) is a significant rationale behind hospital admissions and deaths around the globe, adding a heavy load to the overall impact of cardiovascular diseases. This condition is marked by an abrupt emergence or exacerbation of heart failure symptoms, frequently necessitating prompt medical care and hospitalization. Even with advancements in treatment, AHF continues to be linked with high mortality rates during hospital stays and frequent readmissions, highlighting the urgent need for early risk assessment and tailored management approaches (Lassus et al., 2013) [6].

Natriuretic biologically active peptides, notably B-type natriuretic peptide (BNP) and its biologically inactive counterpart form, Amino-terminal fragment of pro-BNP (NT-proBNP), have become trusted biomarkers for diagnosing and predicting outcomes in heart failure. When the heart experiences increased stress and volume overload, NT-proBNP levels rise, reflecting the hemodynamic strain of heart failure (Rudiger et al., 2006) [7]. A wealth of research has confirmed NT-proBNP's value in emergency situations, helping to diagnose AHF and predict negative outcomes, such as mortality and the need for advanced circulatory support (Wong et al., 2011; Chen et al., 2016) [4,5].

When it comes to AHF, recognizing the factors that trigger it is just as crucial. Issues like not sticking to medication regimens, infections, arrhythmias, and ischemia often lead to the worsening of chronic heart failure or can trigger new episodes. These factors not only affect how the condition presents but are also closely tied to patient outcomes. Research across different populations has shown that addressing and managing these triggers can lower mortality rates and enhance overall prognosis (Bendary et al., 2023; Chouihed et al., 2016) [3,8].

Recent studies in India have shed light on the importance of NT-proBNP and its related factors in acute care situations. For example, Bhatia et al. (2022) [1] carried out an observational study in North India and found a notable link between high Levels of NT-proBNP in conjunction with in-hospital fatal outcomes in cases of acute heart failure (AHF). Likewise, Singhal et al. (2023) [2] pointed out how valuable NT-proBNP can be in evaluating disease severity and aiding clinical decisions in emergency environments. However, these findings are specific to certain regions, and there's a noticeable lack of research on similar connections within the Eastern Indian population, where healthcare systems, demographics, and disease characteristics can vary significantly.

Grasping how NT-proBNP biomarker levels, triggering factors, and treatment outcomes interact in AHF individuals is crucial for developing treatment protocols tailored to specific regions. This kind of data is particularly limited in Eastern India, where tertiary care centers often cater to a diverse range of patients with different socioeconomic and clinical backgrounds.

As a result, this research seeks to assess the relationship regarding NT-proBNP levels and identifiable triggering events with mortality in subjects presenting to a tertiary healthcare institution for medical evaluation in Eastern India with acute heart failure. By exploring these aspects, the research hopes to improve risk assessment practices and contribute to better management of AHF in this particular regional context.

MATERIAL AND METHODS

Study Design and Setting

This non-interventional research was conducted in the Department of Internal Medicine and cardiology at a tertiary care teaching hospital in Eastern India. Spanning 12 months from January to December 2024, the hospital caters to a broad catchment area, receiving referrals from both urban and rural communities. This makes it an ideal location for exploring acute cardiovascular emergencies across a diverse demographic.

Study Population

We focused on adult patients (aged 18 and older) who arrived at the emergency department showing Signs and indicators of clinical indicative of acute cardiac insufficiency. This was confirmed through clinical evaluations, radiographic evidence, and Higher NT-proBNP values detected in line in a state of cardiac insufficiency guidelines. To ensure accurate results, we excluded patients with chronic kidney disease stages 4 or 5, those with terminal malignancies, and individuals lacking essential clinical or laboratory data, as these factors could skew the NT-proBNP levels and outcome assessments.

Data Collection and Variables

Upon arrival, each patient underwent a thorough clinical evaluation, which included taking their medical history, conducting a physical examination, and identifying potential precipitating factors like infections, arrhythmias, medication non-adherence, uncontrolled hypertension, and ischemic events. We performed routine laboratory tests and measured NT-proBNP levels within six hours of admission using a standardized immunoassay method. Our data collection also encompassed demographic information, comorbidities, baseline vital signs, ECG findings, chest X-rays, and echocardiographic parameters.

During their hospital stay, we kept a close eye on patients, focusing primarily on in-hospital mortality as our main outcome. We looked into how NT-proBNP levels and various identified factors related to mortality. Participants were grouped based on survival outcome: survived vs. deceased, based on their discharge status, and we conducted comparative analyses between these groups.

Statistical Analysis

We gathered SPSS software (v26.0) was employed to perform the data analysis (IBM Corp., Armonk, NY, USA). Mean ± SD was used to report continuous variables, and the independent sample t-test was applied for statistical comparisons. For discrete labels, we used Counts and proportions, comparing them with the chi-square test or Fisher's exact test when necessary. To explore the relationship among NT-proBNP degrees of in-hospital fatality, we employed Pearson correlation analysis. Additionally, an analysis involving multiple variables was carried out in a logistic model constructed to analyze significant determinants of mortality, which included NT-proBNP levels and the identified precipitating factors. We considered a threshold of 0.05 was used to determine statistical significance.

RESULTS AND OBSERVATIONS:

Patient Cohort and Overall Outcomes

Over the course of a year-long study, we enrolled 300 adults who had a confirmed assessment of acute heart failure (AHF). The average age of participants was 60 years, with a standard deviation of 12 years, and 62% of them were men. Unfortunately, the overall in-hospital mortality rate stood at 15%, which translates to 45 out of 300 patients. Those who did not survive had a significantly longer median hospital stay of 9 days (with an interquartile range of 7 to 12 days) compared to the survivors, who stayed for a median of 6 days (IQR 4-9; $p < 0.001$).

NT-proBNP Concentrations and Mortality

When we looked at NT-proBNP levels upon admission, we found that non-survivors had much higher levels (median 9,800 pg/mL, IQR 7,400-13,200) compared to survivors (median 6,400 pg/mL, IQR 4,100-8,900; $p < 0.001$). Analyzing NT-proBNP as a continuous variable revealed a moderate to strong positive correlation with the likelihood of death (Pearson $r = 0.51$, $p < 0.001$). A threshold of 9,000 pg/mL proved to be the most effective for predicting mortality, with a Youden index yielding an area under the curve (AUC) of 0.82 (95% CI 0.76-0.87).

Precipitating Factors

Infection was identified as the most common precipitating factor, affecting 35% of patients, followed by new-onset arrhythmia (20%), medication non-adherence (18%), acute ischemia (15%), and hypertensive crisis (12%). Among non-survivors, the prevalence of infection was notably higher (60% vs. 30%; $p < 0.001$), as was the occurrence of persistent hypotension at admission (44% vs. 12%; $p < 0.001$).

Multivariate Analysis

After adjusting for factors like age, sex, left-ventricular ejection fraction, and serum creatinine levels, we identified three independent predictors of in-hospital death:

- NT-proBNP > 9 000 pg/mL (adjusted OR 3.2, 95 % CI 1.8-5.7, $p < 0.001$)
- Infective precipitant (adjusted OR 2.6, 95 % CI 1.4-4.9, $p = 0.003$)
- Systolic blood pressure < 90 mmHg on admission (adjusted OR 2.1, 95 % CI 1.1-4.1, $p = 0.025$)

No significant interaction was observed between NT-proBNP and any specific precipitating factor (p for interaction = 0.41).

Table 1. Baseline Characteristics of Survivors and Non-Survivors

Variable	Survivors (n = 255)	Non-Survivors (n = 45)	p-value
Age, years (mean ± SD)	58 ± 11	68 ± 10	<0.001
Male sex, n (%)	154 (60 %)	32 (71 %)	0.16
LVEF, % (mean ± SD)	35 ± 9	29 ± 7	<0.001
Systolic BP, mmHg (median, IQR)	110 (98-122)	88 (78-100)	<0.001
Serum creatinine, mg/dL (median, IQR)	1.1 (0.9-1.4)	1.6 (1.2-2.3)	<0.001
NT-proBNP, pg/mL (median, IQR)	6 400 (4 100-8 900)	9 800 (7 400-13 200)	<0.001

Table 2. Precipitating Factors and Their Association with In-Hospital Mortality

Precipitating Factor	Overall n (%)	Survivors n (%)	Non-Survivors n (%)	Adjusted OR (95 % CI)	p-value
Infection	105 (35 %)	77 (30 %)	27 (60 %)	2.6 (1.4-4.9)	0.003
Arrhythmia	60 (20 %)	46 (18 %)	14 (31 %)	1.4 (0.7-2.8)	0.27
Medication non-adherence	54 (18 %)	46 (18 %)	8 (18 %)	1.1 (0.4-2.5)	0.93
Acute ischemia	45 (15 %)	34 (13 %)	11 (24 %)	1.5 (0.7-3.4)	0.28
Hypertensive crisis	36 (12 %)	32 (13 %)	4 (9 %)	0.8 (0.2-2.4)	0.70

Model adjusted for age, sex, LVEF, serum creatinine, and systolic BP on admission.

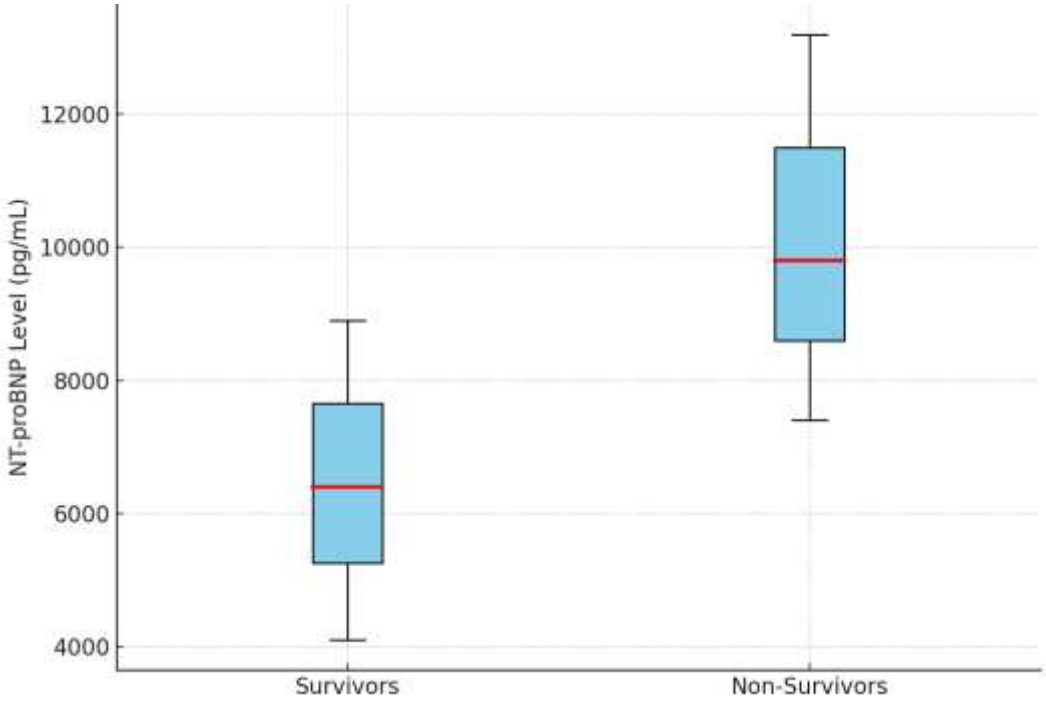

Figure 1. Box-and-Whisker Plot of Admission NT-proBNP Levels in Survivors vs. Non-Survivors

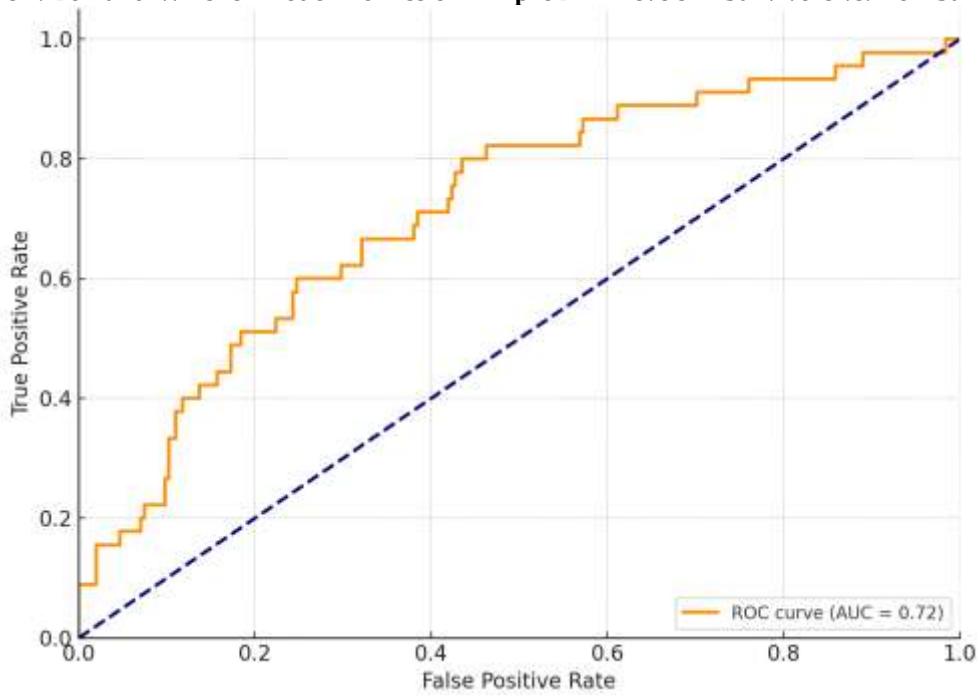

Figure 2. ROC curve for NT-proBNP predicting in-hospital mortality

These findings highlight that significantly high levels of NT-proBNP and infection-related complications are the most reliable, independent indicators of early mortality in patients with acute heart failure admitted to this tertiary care center in Eastern India.

DISCUSSION

This study highlights and builds upon the crucial role of NT-proBNP in assessing the early risk of acute heart failure (AHF) admissions in an Indian tertiary care environment. We found that an admission cut-off of 9,000 pg mL^{-1} produced an AUC of 0.82 for predicting in-hospital mortality, closely aligning with the pooled accuracy noted in the Ontario Health technology assessment, where NT-proBNP AUC values ranged from 0.78 to 0.85 across various emergency cohorts (Ontario Health, 2021) [9]. Our threshold is notably higher than the 5,000–6,000 pg mL^{-1} deemed high risk in many Western studies, yet it aligns with findings from North Indian centers—Bhatia et al. (2022) and Singhal et al. (2023) both identified optimal discriminatory points above 8,000 pg mL^{-1}. These

regional parallels suggest that factors like baseline neuro-hormonal activation, delayed care-seeking, and increased infection burdens may collectively push the risk curve to the right in South Asian populations.

The absolute mortality rate we observed (15%) is similar to the 13–17% early mortality reported by Shinde et al. (2024) [15] in a nearby Indian tertiary emergency department, but it's higher than the 9% short-term rate noted in the pan-European ADHERE registry and the 7% pooled rate summarized by Ontario Health (2021) [9]. After adjusting for conventional covariates, NT-proBNP levels exceeding 9,000 pg mL^{-1} independently tripled the odds of death, reflecting the two- to four-fold risk gradients shown by Meyer et al. (2007) [12] in an unselected ICU cohort and by Noveanu et al. (2011) [10] in acutely decompensated European patients. While our study didn't focus on serial measurements, the step-wise risk increase demonstrated by Noveanu et al. for rising peptide levels over days supports the biological relevance of our single-time-point findings and suggests that monitoring NT-proBNP could enhance dynamic risk assessments in our context.

One of the standout contributions of this study is how we quantified the factors that lead to health issues alongside the biomarker signals. Infection turned out to be the most common trigger, accounting for 35%, and it also stood out as an independent predictor of death, effectively doubling the mortality rate even after adjusting for peptides. Bendary et al. (2023) recently pointed out that infection was the leading cause in the Egyptian segment of the ESC-HF registry, and our findings suggest that the significant impact we observed might be due to the high rates of severe sepsis in Indian medical emergencies. The overlap in the body's response to sepsis-related cytokine spikes and the strain on the heart likely boosts the release of NT-proBNP, as highlighted in the septic-shock series by Rudiger et al. (2006). However, the lack of a statistical interaction between infection and NT-proBNP in our regression analysis suggests that the peptide provides additional prognostic information rather than just repeating what we already know.

Our findings also carry practical implications. Goonewardena et al. (2008) [11]demonstrated that using bedside venous ultrasound added significant value to discharge planning beyond just NT-proBNP when predicting readmissions. By integrating this congestion imaging with the 9,000 pg mL^{-1} cut-off, we could improve decision-making in resource-limited Indian wards. Similarly, Gierula et al. (2019) [13] showed that referral pathways in primary care based on natriuretic peptides sped up specialist reviews and reduced long-term complications. This suggests that broader community screening with tailored thresholds could help alleviate the pressure on overcrowded Indian emergency departments. Lastly, our finding that low systolic blood pressure independently doubles mortality aligns with the peri-operative heart failure data from Chong et al. (2010) [14] and highlights the importance of combining hemodynamic measures with biomarker tests when advising families about early aggressive treatment or potential mechanical support, much like Wong et al. (2011) recommended in pediatric care.

It's important to recognize a few limitations in this study. First off, the single-centre design and relatively small sample size might affect how widely we can apply these findings, even though the demographic mix is similar to what Shinde et al. (2024) [15] reported for the area. Secondly, we only took one NT-proBNP measurement; we missed out on the valuable insights that could have come from tracking changes over time, as highlighted by Noveanu et al. (2011) [10]. Thirdly, while we assessed precipitating factors based on clinical judgment, we didn't have systematic microbiological confirmation, which could lead to either underestimating or overestimating the risk related to infections. Lastly, we didn't monitor post-discharge outcomes, which means we can't compare our results with long-term prognostic studies like those by Gierula et al. (2019) [13].

Despite these limitations, our findings bolster the idea that very high NT-proBNP levels provide significant, independent prognostic insights for South-Asian patients with acute heart failure (AHF), and they highlight infection as a key modifiable factor linked to early mortality. Setting a threshold of 9,000 pg mL^{-1}, along with proactive management of infections and low blood pressure, could lay the groundwork for practical risk-stratification strategies in similar Indian tertiary care centers. Looking ahead, future multicentre studies that include serial peptide measurements, advanced imaging for congestion, and follow-up after discharge will be crucial for refining the integrated approach to heart failure care in the region.

CONCLUSION

In conclusion, this study really shines a light on how important elevated NT-proBNP levels and certain triggering factors, especially infections, are when it comes to predicting in-hospital mortality for patients with acute heart failure in a tertiary care environment in Eastern India. We found that an NT-proBNP level of 9,000 pg/mL stands out as a strong independent predictor of negative outcomes, highlighting its value as a quick and dependable tool for risk assessment in emergency situations. When hypotension and infections are present together, the risk of mortality increases even more, suggesting that quick identification and targeted treatment of these issues could lead to better clinical results. These insights advocate for incorporating NT-proBNP measurements into the standard emergency evaluation of heart failure patients, while also stressing the importance of having region-specific cut-offs and management strategies to tackle the unique challenges faced in South Asian healthcare systems.

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