Original Article

NT-proBNP in Differential Diagnosis of Acute Dyspnea: A Cross-sectional Study

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Abstract

Background: Dyspnea is common in emergency departments, often linked to cardiac or pulmonary causes, with congestive heart failure (CHF) being a major contributor. N-Terminal Pro-B-Type Natriuretic Peptide (NT-proBNP) has limited diagnostic performance in distinguishing between cardiac and non-cardiac causes of dyspnea. Thus, this study aimed to explore the differential diagnosis of acute onset dyspnea and evaluate NT-pro BNP's role in identifying these causes.

Materials and Methods: A cross-sectional study was conducted with 100 patients aged over 40 years presenting with acute dyspnea to the emergency department. Based on clinical diagnosis, patients were categorized into two groups: acute CHF and those without acute CHF which included mainly pulmonary and other miscellaneous non cardiac causes of dyspnea. Clinical characteristics, laboratory evaluations including electrocardiography, chest X-ray, echocardiography, and left ventricular ejection fraction (LVEF) measurement were documented. An automated immuno-analytical test for NT-proBNP was performed.

Results: NT-proBNP levels were significantly higher in patients with acute CHF (NT-proBNP >300 pg/mL) compared to those without acute CHF (NT-proBNP <300 pg/mL). NT-proBNP levels positively correlated with hospital stay duration ($r = 0.689$, $p < 0.05$) and negatively correlated with LVEF ($r = -0.723$, $p < 0.05$), indicating poorer heart function. At a cut-off of 300 pg/mL, NT-proBNP demonstrated excellent diagnostic accuracy for differentiating acute CHF from those without acute CHF, with sensitivity 100%, specificity 85%, negative predictive value 100%, and positive predictive value 80%.

Conclusions: NT-proBNP is a valuable biomarker in differential diagnosis of acute CHF and non-cardiac causes of dyspnea due to the high sensitivity and strong association with the severity of CHF.

Keywords: Amino-terminal pro B-type natriuretic peptide, biomarker, congestive heart failure, dyspnea, emergency

INTRODUCTION

In emergency settings, the differential diagnosis of dyspnea is complex, particularly when congestive heart failure (CHF) or other cardiac and pulmonary conditions are involved. Globally, the prevalence of dyspnea among adults ranges from 10 to 20%.[1], while in India, it affects around 44% of the population, with 4% experiencing severe symptoms.[2] Current diagnostic tests, including blood analysis, echocardiograms, chest X-rays, bronchoscopy, and angiography, though effective, often lack the necessary sensitivity and specificity to differentially diagnose an acute dyspnea condition.[3,4]

In recent decades, cardiovascular natriuretic hormones, including atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), and N-terminal pro-B-type natriuretic peptide (NT-proBNP), have gained prominence as valuable biochemical tools in the management of CHF.[5] The European Society of Cardiology and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines highlight the importance of biomarkers, particularly NT-proBNP in assessing heart failure (HF) and distinguishing it from non-cardiac causes of dyspnea.[6,7] NT-proBNP is released from cardiac myocytes in response to myocardial stretch and volume overload, and correlates closely with left ventricular ejection fraction (LVEF) and overall cardiac function.[8, 9] NT-proBNP serves as a sensitive and specific prognostic marker for ventricular dysfunction, proving more effective for early HF detection compared to BNP.[5] Notably, NT-proBNP measurements are reliable and cost-effective for diagnosing HF and guiding subsequent treatment decisions.[10]

NT-proBNP has been extensively validated as a diagnostic tool for differentiating between cardiac and non-cardiac causes of dyspnea with levels exceeding 300 pg/mL linked to adverse cardiac events risk in patients with HF.[11] Despite the established utility of NT-proBNP in various populations, there is a noticeable lack of research examining its diagnostic accuracy for distinguishing between acute cardiac and non cardiac causes of dyspnea within the Indian context.[1213] Therefore, the present study aimed to explore the differential diagnosis of acute onset dyspnea, evaluate the diagnostic performance of NT-proBNP, and assess the correlation between NT-proBNP levels and prognosis in HF.

MATERIALS AND METHODS

Study Design and Ethics

This cross-sectional study was conducted with 100 patients presenting to the Emergency

Department (ED) of a tertiary care hospital. The study was approved by the Institutional Ethical Committee, and written informed consent was obtained from all the patients.

Population

The study included male and female patients aged more than 40 years presented with acute dyspnea in ED. While patients with age more than 80 years, renal failure, liver cirrhosis with ascites, obvious traumatic causes of dyspnea, history of ischemic stroke, and obese patients with BMI more than 30kg/m^2 were excluded.

Study Groups

The patients were categorized on the basis of clinical diagnosis into two categories: 1) Acute CHF and 2) without acute CHF, which included pneumonia, COPD, bronchial asthma, pulmonary embolism, bronchitis, etc. and other causes of dyspnea.

Data Collection

Clinical characteristics of each patient were recorded, including demographics, symptoms, signs, medication use, and diagnostic evaluations in the ED. Electrocardiography, chest X-ray, routine blood tests, bedside echocardiography, and LVEF measurement were performed within one hour of admission. Laboratory testing results, diagnostic test outcomes, and patient discharge information were documented.

CHF was diagnosed based on Framingham Standards,[14] color Doppler echocardiography, chest X-ray, and patient responsiveness to drug treatments. The HF functional classification was based on the guideline of the American Heart Association-NYHA functional classification system.[15] By the Framingham criteria, CHF diagnosis required the simultaneous presence of at least two of the following major criteria or one major criterion in conjunction with two of the minor criteria.[14]

Study Protocol

Upon hospital admission, 2 mL of blood was collected from each patient in a VACUETTE EDTA K2 tube. NT-proBNP levels were measured using the Canada RAMP NT-proBNP Assay. Blood sample was collected for NT-proBNP measurement, and was analyzed using an automated immunoanalytical test with a processing time of less than 20 minutes. All the measurements were conducted following the manufacturer's instructions. The device measured NT-proBNP levels within a range of 5 ng/L to 35,000 ng/L.

Sample size Estimation

The sample size was calculated using the following formula, yielding an estimated requirement of 100 participants.

$$\eta = (Z^2 pq)e^2$$

The parameters included η (sample size), Z (1.96, standard normal value for a 95% confidence interval), p (8%, prevalence of dyspnea in the emergency department),[16] q (92%, calculated as 1-p), and e (5%, margin of error).

Statistical analyses

The data was analysed with SPSS (IBM, Armonk, NY, USA) version 23.0 for Windows. The categorical and continuous variables are represented as frequency (percentage) and mean ± standard deviation, respectively. A chi-square test and independent sample t-test were used to assess significant association of NT-proBNP with various categorical and continuous variables, respectively. Relationships between NT-proBNP and clinical outcomes were determined by Pearson correlation analysis. The Receiver Operating Characteristic curve analysis was performed to assess the diagnostic accuracy of NT-proBNP. The $p < 0.05$ was considered significant.

RESULTS

The patients were slightly male predominant in both groups (55.3% in acute CHF and 67.7% in without acute CHF). The acute CHF group was significantly higher mean age ($p = 0.004$) and had a higher proportion of individuals with hypertension ($p = 0.008$), ischemic heart disease ($p = 0.001$), and hypercholesterolemia ($p = 0.028$). Additionally, acute CHF patients more frequently presented with paroxysmal nocturnal dyspnea ($p = 0.013$), orthopnea ($p < 0.001$), and swelling of feet ($p < 0.001$). However, without acute CHF patients were more likely to report chest pain ($p = 0.032$) and expectoration ($p = 0.014$). In terms of clinical signs, raised JVP ($p = 0.006$), murmur ($p = 0.003$), crepitations ($p = 0.002$), and tender hepatomegaly ($p = 0.009$) were more common in the acute CHF group, while without acute CHF patients had a higher incidence of wheezing ($p = 0.033$) (Table 1).

Table 1: Demographic characteristics

Characteristics	Acute CHF (n=38)	Without acute CHF (n=62)	p
Age, years, mean ± SD	63.0 ± 9.0	57.2 ± 10.0	0.004
Sex, n (%)			0.210
Male	21 (55.3)	42 (67.7)	
Female	17 (44.7)	20 (32.3)	

Risk factor, n (%)			
Diabetes	11 (28.9)	12 (19.4)	0.269
Hypertension	19 (50.0)	15 (24.2)	0.008
IHD	15 (39.5)	7 (11.3)	0.001
Smoking	10 (26.3)	14 (22.6)	0.671
Hypercholesterolemia	7 (18.4)	3 (4.8)	0.028
Hypertriglyceridemia	29 (76.3)	46 (74.2)	0.812
Symptoms, n (%)			
Dyspnea	38 (100.0)	62 (100.0)	-
Paroxysmal nocturnal dyspnea	9 (23.7)	4 (6.5)	0.013
Orthopnea	18 (47.4)	5 (8.1)	<0.001
Swelling of feet	13 (34.2)	4 (6.5)	<0.001
Cough	18 (47.4)	30 (48.4)	0.921
Expectoration	0 (0.0)	9 (14.5)	0.014
Chest pain	8 (21.1)	26 (41.9)	0.032
Fever	3 (7.9)	10 (16.1)	0.232
Signs, n (%)			
Tachycardia	23 (60.5)	32 (51.6)	0.384
Raised JVP	12 (31.6)	6 (9.7)	0.006
S3 gallop	2 (5.3)	0 (0.0)	0.068
Murmur	7 (18.4)	1 (1.6)	0.003
Crepitations	20 (52.6)	14 (22.6)	0.002
Wheezing	7 (18.4)	24 (38.7)	0.033
Tender hepatomegaly	4 (10.5)	0 (0.0)	0.009

Among the 100 patients, 38 had acute CHF and 62 did not have acute CHF. In the without acute CHF group, the majority had COPD (24.19%), followed by pneumonia (19.35%) and bronchial

asthma (17.74%). Pulmonary embolism, Acute respiratory distress syndrome, and bronchitis were each diagnosed in 5 patients (8.06%), while 9 patients had other diagnoses (Table 2).

Table 2: Without acute CHF diagnosis

Without acute CHF diagnosis	n=62 (%)
COPD	15 (24.19)
Pneumonia	12 (19.35)
Bronchial asthma	11 (17.74)
Pulmonary embolism	5 (8.06)
Acute respiratory distress syndrome	5 (8.06)
Bronchitis	5 (8.06)
Others (Lung cancer, Hyperventilation, Anxiety, allergy etc.)	9 (14.52)

On ECG, a significantly higher proportion of acute CHF patients had Q waves ($p = 0.001$), while without acute CHF patients were more likely to exhibit bundle branch block ($p = 0.032$) and P pulmonale ($p = 0.014$). However, sinus tachycardia, T inversion, and poor progression of R wave did not differ significantly in both groups ($p > 0.05$). Chest X-ray findings revealed a higher incidence of cardiomegaly, interstitial oedema, and pleural effusion in the acute CHF group (all $p < 0.001$), while without acute CHF group had more instances of hyperinflation ($p = 0.021$), infiltrates ($p = 0.002$), consolidation ($p = 0.021$), and normal findings ($p < 0.001$). On 2D echocardiography, without acute CHF patients had significantly higher LVEF ($p < 0.001$), while acute CHF patients showed more regional wall motion anomalies, global hypokinesia, and diastolic dysfunction (all $p < 0.001$). However, there were no significant differences in valvular dysfunction and LVH between the groups ($p = 0.298$). Laboratory findings revealed higher serum cholesterol ($p = 0.012$), NT-proBNP levels ($p < 0.001$), and a greater proportion of elevated Troponin T ($p = 0.001$) in the acute CHF group. Acute CHF patients also had longer hospital stays ($p < 0.001$) and a higher mortality rate ($p = 0.019$) (Table 3).

Table 3: Association of congestive heart failure with clinical characteristics

Characteristics	Acute CHF (n=38)	Without acute CHF (n=62)	p
ECG findings, n (%)			
Sinus tachycardia	24 (63.2)	29 (46.8)	0.111

Bundle branch block	0 (0.0)	7 (11.3)	0.032
Q waves	6 (15.8)	0 (0.0)	0.001
P Pulmonale	0 (0.0)	9 (14.5)	0.014
T inversion	12 (31.6)	11 (17.7)	0.110
Poor progression of R wave	7 (18.4)	6 (9.7)	0.207
Chest X-ray, n (%)			
Cardiomegaly	28 (73.7)	11 (17.7)	<0.001
Interstitial oedema	19 (50.0)	0 (0.0)	<0.001
Pleural effusion	8 (21.1)	0 (0.0)	<0.001
Hyperinflation	0 (0.0)	8 (12.9)	0.021
Infiltrates	0 (0.0)	13 (21.0)	0.002
Consolidation	0 (0.0)	8 (12.9)	0.021
Normal	0 (0.0)	24 (38.7)	<0.001
2D ECHO, n (%)			
LVEF, mean ± SD	30.8 ± 11.3	58.6 ± 5.3	<0.001
Regional wall motion anomalies	14 (36.8)	0 (0.0)	<0.001
Global hypokinesia	9 (23.7)	0 (0.0)	<0.001
Valvular dysfunction	3 (7.9)	2 (3.2)	0.298
LVH	3 (7.9)	2 (3.2)	0.298
Diastolic dysfunction	18 (47.4)	1 (1.6)	<0.001
Normal	0 (0.0)	52 (83.9)	<0.001
Laboratory			

findings, mean ± SD			
RBS	147.8 ± 61.5	142.0 ± 64.6	0.761
Serum cholesterol	194.1 ± 53.9	168.4 ± 38.5	0.012
Serum triglycerides	138.0 ± 41.1	125.5 ± 40.0	0.305
Troponin T	6 (15.8%)	0 (0.0%)	0.001
NT pro-BNP, pg/ mL, mean ± SD	4020.84 ± 4882.049	188.39 ± 135.571	<0.001
Outcome, n (%)			0.019
Death	14 (36.8)	10 (16.1)	
Survive	24 (63.2)	52 (83.9)	
Duration of hospital stay, days, mean ± SD	10.42 ± 2.95	6.23 ± 2.64	<0.001

Among the 100 patients, 53 had NT-proBNP levels ≤300 pg/mL, and 47 had levels >300 pg/mL. Patients with NT-proBNP levels >300 pg/mL were significantly older ($p < 0.001$). Additionally, hypertension ($p = 0.034$) and ischemic heart disease (IHD) ($p = 0.006$) were more prevalent in this group. However, there were no significant differences in gender or other risk factors, such as diabetes, smoking, hypercholesterolemia and hypertriglyceridemia between the two groups ($p > 0.05$) (Table 4).

Table 4: Association of demographics with NT-proBNP level

Characteristics	**NT-proBNP (pg/ml)**		**p**
	≤300 (n=53)	**>300 (n=47)**	
Age, years, mean ± SD	55.5 ± 9.4	63.8 ± 8.8	<0.001
Sex, n (%)			0.504
Male	35 (66.0)	28 (59.6)	
Female	18 (34.0)	19 (40.4)	
Risk factors, n (%)			
Diabetes	11 (20.8)	12 (25.5)	0.571
Hypertension	13 (24.5)	21 (44.7)	0.034

IHD	6 (11.3)	16 (34.0)	0.006
Smoking	14 (26.4)	10 (21.3)	0.548
Hypercholesterolemia	3 (5.7)	7 (14.9)	0.125
Hypertriglyceridemia	14 (26.4)	14 (29.8)	0.708

The NT-proBNP level ranged from 101 to 150 pg/mL in the ≤300 pg/mL group (median 130 pg/mL) and from 876 to 3592 pg/mL in the >300 pg/mL group (median 1620 pg/mL) ($p < 0.001$). Patients with NT-proBNP levels >300 pg/mL had more frequent ECG abnormalities, including sinus tachycardia ($p = 0.041$), Q waves ($p = 0.007$), T inversion ($p = 0.013$), and poor progression of R wave ($p = 0.020$), whereas the ≤300 pg/mL group exhibited normal ECG findings ($p < 0.001$). Chest X-ray findings revealed that cardiomegaly ($p < 0.001$), pleural effusion ($p = 0.002$), and infiltrates ($p = 0.002$) were more common in the >300 pg/mL group, while hyperinflation ($p = 0.005$) and consolidation ($p = 0.005$) were more prevalent in the ≤300 pg/mL group. Normal chest X-ray findings were significantly associated with ≤300 pg/mL group ($p = 0.003$). In 2D echocardiography, patients with NT-proBNP levels >300 pg/mL had lower LVEF ($p < 0.001$) and a higher prevalence of regional wall motion anomalies ($p < 0.001$), global hypokinesia ($p = 0.001$), and diastolic dysfunction ($p < 0.001$), while the ≤300 pg/mL group had more normal echocardiographic findings ($p < 0.001$). Serum cholesterol was significantly higher in the >300 pg/mL group ($p = 0.048$), but other laboratory parameters did not differ significantly ($p > 0.05$). Additionally, the majority of patients with NT-proBNP levels >300 pg/mL had acute CHF ($p < 0.001$) and a longer hospital stay ($p = 0.001$), with no significant difference in mortality rates between the two groups ($p = 0.202$) (Table 5).

Table 5: Association of clinical characteristics with NT-proBNP level

Characteristics	**NT-proBNP (pg/ml)**		**p**
	≤300 (n=53)	**>300 (n=47)**	
ECG findings, n (%)			
Sinus tachycardia	23 (43.4)	30 (63.8)	0.041
Bundle branch block	5 (9.4)	2 (4.3)	0.311
Q waves	0 (0.0)	6 (12.8)	0.007
P Pulmonale	6 (11.3)	3 (6.4)	0.381

T inversion	7 (13.2)	16 (34.0)	0.013
Poor progression of R wave	3 (5.7)	10 (21.3)	0.020
Normal	20 (37.7)	1 (2.1)	<0.001
Chest X-ray, n (%)			
Cardiomegaly	8 (15.1)	31 (66.0)	<0.001
Pleural effusion	0 (0.0)	8 (17.0)	0.002
Hyperinflation	8 (15.1)	0 (0.0)	0.005
Infiltrates	12 (22.6)	1 (2.1)	0.002
Consolidation	8 (15.1)	0 (0.0)	0.005
Normal	19 (35.8)	5 (10.6)	0.003
2D ECHO, n (%)			
LVEF, mean ± SD	59.2 ± 4.7	34.8 ± 13.2	<0.001
Regional Wall Motion Anomalies	0 (0.0)	14 (29.8)	<0.001
Global hypokinesia	0 (0.0)	9 (19.1)	0.001
Valvular dysfunction	2 (3.8)	3 (6.4)	0.550
LVH	2 (3.8)	3 (6.4)	0.550
Diastolic dysfunction	1 (1.9)	18 (38.3)	<0.001
Normal	48 (90.6)	4 (8.5)	<0.001
Laboratory findings, mean ± SD			
RBS	144.2 ± 68.5	144.1 ± 57.3	0.980
Serum cholesterol	169.6 ± 40.9	187.9 ± 50.5	0.048
Serum triglycerides	127.5 ± 41.3	133.3 ± 38.8	0.475
NT pro BNP, pg/mL, median (Range)	130.0 (101.0-150.0)	1620.0 (876.0-3592.0)	**<0.001**
Outcome, n (%)			0.202

Death	10 (18.9)	14 (29.8)	
Survive	43 (81.1)	33 (70.2)	
Duration of hospital stay, days, mean ± SD	5.9 ± 2.7	9.8 ± 2.9	0.001
Diagnosis, n (%)			<0.001
Acute CHF	0 (0)	38 (80.85)	
Without acute CHF	53 (100)	9 (19.15)	

NT Pro-BNP levels showed a moderate, significant positive correlation with the duration of hospital stay (r = 0.689, p = 0.000) and a moderate, significant negative correlation with LVEF (r = -0.723, p = 0.000).

The diagnostic performance of NT pro-BNP in differentiating acute CHF vs those without acute CHF at a cutoff of 300 pg/mL showed a sensitivity of 100%, specificity of 85.5%, negative predictive value (NPV) of 100%, and positive predictive value (PPV) of 80.9%.

DISCUSSION

The principal findings of the study indicate that NT-proBNP effectively distinguishes acute CHF from those without acute CHF at a cut-off of 300 pg/mL, with significantly elevated levels in acute CHF linked to greater cardiac dysfunction and dyspnea severity. NT-proBNP also showed a significant positive correlation with hospital stay duration and a negative correlation with LVEF.

In the present study, the acute CHF group demonstrated significantly higher NT-proBNP levels compared to without acute CHF group, reflecting greater myocardial stress and fluid overload characteristic of acute HF exacerbation and poor hemodynamic status. NT-proBNP, released in response to ventricular wall tension, correlates with HF severity.[17] Elevated NT-proBNP levels not only signify the acute nature of the condition but also serve as a prognostic marker, with higher levels linked to worse cardiac outcomes, including increased mortality.[5] The prolonged hospital stays observed in acute CHF patients can be attributed to the complexity of their condition, requiring intensive monitoring and interventions like diuretics and other HF therapies to address severe symptoms such as pulmonary congestion and fluid retention.[18] In contrast, those without acute CHF patients typically have more stable conditions, allowing for outpatient management or shorter hospital stays. These findings align with Benmachiche et al., who also reported NT-proBNP as a reliable predictor of acute HF, with elevated levels

associated with higher mortality risk and longer hospital stays.[19]

In the present study, NT-proBNP levels ranged from 101 to 150 pg/mL (median 130 pg/mL) in the ≤300 pg/mL group, compared to 876 to 3592 pg/mL (median 1620 pg/mL) in the >300 pg/mL group, demonstrating a significant difference and highlighting the role of NT-proBNP role as a biomarker for distinguishing acute CHF from those with non-cardiac causes of dyspnea. These findings align with Patel et al., who observed a statistically significant difference in NT-pro BNP levels (2234 pg/mL in cardiovascular causes vs. 677 pg/mL in non-cardiovascular causes), reinforcing its reliability in indicating cardiac involvement in acute dyspnea.[13]

In the present study, NT-proBNP levels >300pg/ml exhibited greater frequency of ECG abnormalities suggesting a correlation between elevated NT-proBNP levels and the severity of cardiac dysfunction. This correlation can be primarily attributed to the increased myocardial wall stress that occurs as the heart struggles to pump effectively in HF which can lead to electrical disturbances, manifested as the observed ECG abnormalities. This aligns with Tymińska et al. findings who reported that ECG abnormalities were more prevalent in patients with HF with reduced ejection fraction, further supporting the notion that higher NT-proBNP levels correlate with more severe cardiac impairment and associated ECG changes.[20] Contrastingly, Andrade et al. highlighted that while ECG abnormalities are common in HF, they may not always correlate directly with NT-proBNP levels, suggesting that other factors, such as comorbidities or the duration of HF, may also play a role in the relationship between ECG findings and NT-proBNP.[21] Moreover, Nilsson et al. reported that a substantial proportion of HF patients exhibited abnormal ECG findings and were associated with dyspnea, with most patients presenting NT-proBNP levels exceeding the clinical threshold (>125 ng/L). However, the severity of dyspnea was not independently correlated with NT-proBNP levels.[22] This is in contrast to our study findings, where the ≤300 pg/mL group showed normal ECG results, indicating less cardiac stress and dysfunction.

In the present study, NT-proBNP levels exceeding 300 pg/mL were associated with reduced LVEF. NT-proBNP is released in response to ventricular wall stress during HF; as the heart's pumping efficiency declines, LVEF decreases, triggering a compensatory rise in NT-proBNP levels. This aligns with Belagavi et al., who found a strong correlation between elevated NT-proBNP levels and reduced LVEF in patients presenting with dyspnea.[23]

Contrastingly, Kragelund et al. noted that elevated NT-proBNP levels in elderly patients could reflect underlying cardiac morbidity independent of left ventricular dysfunction.[24] This highlights the importance of considering the clinical context when interpreting NT-proBNP levels.

The positive correlation between NT-proBNP levels and hospital stay duration reflects the association of elevated NT-proBNP with increased myocardial stress, HF severity, and the need for intensive management and monitoring. This finding aligns with Ozturk et al., who demonstrated that higher NT-proBNP concentrations correlate with worse clinical outcomes and longer hospitalization in HF patients.[25] Conversely, the negative correlation between NT-proBNP levels and LVEF is expected, as lower LVEF indicates poorer cardiac function. This aligns with Su et al. who reported that higher NT-proBNP levels were significantly associated with cardiac structural abnormalities and lower LVEF.[12]

In the present study, the diagnostic performance of NT-proBNP at a cut-off of 300 pg/mL demonstrates a sensitivity of 100%, specificity of 85%, NPV of 100%, and PPV of 80%, underscoring its effectiveness in differentiating acute CHF from those without acute CHF. The high sensitivity indicates that NT-proBNP is excellent at correctly identifying patients with acute CHF, while the specificity suggests it is also reasonably effective at ruling out those without the condition. These results can be attributed to the pathophysiological role of NT-proBNP in HF. This biomarker serves as a reliable indicator of cardiac dysfunction, making it a valuable tool in clinical settings for diagnosing acute CHF. Our findings align with previous reports suggesting NT-proBNP levels >300pg/ml for acute HF diagnosis with a sensitivity around 97-100%, specificity around 93%, PPV between 76-85%, and NPV around 99%.[13,26,27] Moreover, Su et al. reported sensitivity, specificity, PPV, and NPV as 92.0%, 82.2%, 86.7%, and 89.2%, respectively; however, they considered plasma NT-proBNP level cut-off >600 pg/mL for acute HF.[12] Contrastingly, Jafri et al. noted that while NT-proBNP is effective in diagnosing HF, its sensitivity and specificity can be influenced by renal function, particularly in patients with chronic kidney disease.[28]

Limitations

Despite high sensitivity (100%) and reasonable specificity (85%) of NT-proBNP in differentiating acute CHF from those without acute CHF at a cutoff of 300 pg/ml, the study has few limitations that should be acknowledged. Firstly, it was conducted at a

single center, which may limit the generalizability of the findings to broader populations. Secondly, the sample size has been relatively small, which could affect the precision of the estimates and the power of the study to detect differences. Additionally, the study did not account for potential confounding factors such as renal function, age, or comorbidities like liver cirrhosis, obesity and obstructive sleep apnea which can influence NT-proBNP levels and HF outcomes. The cross-sectional study design limits the ability to establish causality between NT-proBNP levels and clinical outcomes, as it cannot control for all variables that may influence the results. Lastly, the echocardiography and NT-proBNP assays were performed at only a single time point, limiting the ability to assess the dynamic relationship between NT-proBNP levels and echocardiographic indices over time.

CONCLUSION

NT-proBNP levels above 300 pg/mL serve as a highly sensitive and specific biomarker for distinguishing acute CHF from those without acute CHF. Patients with NT-proBNP >300 pg/mL demonstrated a significant association with acute CHF and prolonged hospital stays, emphasizing its prognostic value. A moderate positive correlation with hospital stays duration and significant negative correlation with LVEF further highlights its role in evaluating CHF severity. At a 300 pg/mL cutoff, NT-proBNP exhibited excellent diagnostic performance.

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Conflicts of interest

There are no conflicts of interest.

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