Cross-Sectional Study

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Diagnostic accuracy of plasma brain natriuretic peptide for evaluation of dyspnea NYHA-III and NYHA-IV in emergency department of tertiary care hospital

Hina Saghir, MBBS[a], Hina Andaleeb, MBBS[b], Amina Azhar, MBBS[e], Sadia Babu, MBBS[d], Saadia Fatima, MBBS[d], Hassan Mumtaz, MBBS, MSPH[c,*]

Objective: To determine the diagnostic accuracy of breathing not properly (BNP) for evaluation of dyspnea NYHA III and IV due to systolic heart failure in emergency department patients keeping echocardiography as the gold standard.

Study design: Cross-sectional validation study. Setting: Department of Accident and Emergency Duration of Study: 25 July 2022–25 January 2023.

Subjects and methods: A total of 115 of both sexes presenting with acute onset of dyspnea and having NYHA Class III and IV were included. Emergency nursing staff had immediately taken a single venous blood sample for BNP and creatinine levels and a 2D echo was performed. Ejection fraction was recorded, and the diagnosis of systolic heart failure on the basis of an ejection fraction, that is less than or equal to 45% was documented.

Results: The age range in this study was from 18 to 65 years, with a mean age of 49.147 ± 8.73 years. Mean BNP levels were 139.452 ± 84.04 pg/ml. Patients with NYHA class III was 67.8 and 32.2% belongs to NYHA class IV. BNP levels greater than or equal to 100 pg/ml diagnosed 76 (66.1%) and echocardiography has diagnosed 68 (59.1%) patients with heart failure. BNP levels greater than or equal to 100 pg/ml had shown sensitivity 94.1%, specificity 74.5%, and diagnostic accuracy 86%, positive predictive value 84.21%, negative prediction value 89.74%, likelihood positive ratio 3.68 and likelihood negative ratio was 0.08 in diagnosis of heart failure.

Conclusion: BNP estimation is a sensible and particular procedure for diagnosing CHF in patients who present to the emergency department with acute dyspnea and may add extra advantages to the administration of patients with congestive heart failure (CHF) in our population.

Keywords: BNP, echocardiography, heart failure, shortness of breath

Introduction

Patients who get admitted to the emergency department (ED) most of them came with the complaint of undifferentiated dyspnea, it is usually difficult to distinguish that the dyspnea is due to a cardiac or pulmonary cause. Systolic heart failure is one of the most important causes of dyspnea, which is usually associated with a high risk of mortality and morbidity. Therefore, early diagnosis is important for starting effective treatment and improving prognosis[1].

Traditionally, clinical assessment and transthoracic echocardiography has been used for evaluating acutely decompensated heart failure. Systolic heart failure is normally defined as an ejection fraction of less than 45%[2,3].

Echocardiography represents the 'Gold standard' for the diagnosis of systolic dysfunction. It has an excellent diagnostic accuracy with a sensitivity of 98% and a specificity of 91% for the detection of acute decompensated heart failure[4].

Making a diagnosis of HF can be difficult because the cardinal triad of edema, fatigue, and dyspnea are neither sensitive nor specific manifestations and atypical presentations should be recognized particularly when evaluating women, obese patients, and the elderly.

Biomarkers of category amino-terminal pro-B natreureticpeptite (NT-proBNP) and breathing not properly (BNP) emerged as

HIGHLIGHTS

- This study reveals that breathing not properly measurement is a sensible and specific strategy for diagnosing CHF in patients with acute dyspnea.
- Breathing not properly levels greater than or equal to 100 pg/ml shows sensitivity 94.1%, specificity 74.5%, diagnostic accuracy 86%, positive predictive value 84.21%, and negative prediction value 89.74%.

[a]HBS Medical and Dental College, [b]Rawal Institute of Health Sciences, [c]Maroof International Hospital Public Health Scholar, Health Services Academy, Islamabad, [d]Department of Wah Medical College, Rawalpindi and [e]Cardiologist Government City Hospital, Talagang, Pakistan

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*Corresponding author. Address: Maroof International Hospital, Public Health Scholar, Health Services Academy, Islamabad, PM Health Complex, Chak Shahzad Islamabad Pakistan. E-mail: Hassanmumtaz.dr@gmail.com (H. Mumtaz).

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Table 1
Mean ± SD of patient's demographics.

	Demographics	Mean ± SD
1	Age (years)	49.147 ± 8.73
2	BNP levels (pg/ml)	139.452 ± 84.04

alternative for the diagnosis of heart failure in the ED setting they help clinicians in accurately diagnosing heart failure. The American College of Emergency Physician has recommended that adding a single BNP test can help in accurate diagnoses of heart failure as compared to standard clinical judgment or echocardiography[5].

A BNP level of greater than or equal to 100 pg/ml has a sensitivity and specifity of 95% (area under the curve = 0, 98) for diagnosing heart failure in patients who come with acute dyspnea[5]. The value of BNP is the strongest independent predictor of CHF [Odds ratio = 29.6]. A BNP less than or equal to 100 pg/ml has a negative predictive value of 94% for ruling out heart failure. This data was calculated assuming a heart failure prevalence of 39%[6]. European Society of Cardiology Guidelines for heart failure 2021 recommended plasma B-type natriuretic peptide has excellent ability to exclude acute heart failure[7].

In an international study published in BMJ 2015 showed the sensitivity and specificity of BNP as 95 and 94%, respectively[8] while a local study done in 2015 showed sensitivity of 88% and specificity of 66%[5]. The rationale of my study is to validate the diagnostic accuracy of BNP for the determination of systolic heart failure in patients who present to the ED with acute dyspnea. It is of great value in screening patients of acute dyspnea in the ED for appropriate management and referrals as echocardiography is not available in the ED of most tertiary care centers in Pakistan.

Objective

To determine the diagnostic accuracy of BNP for evaluation of dyspnea NYHA III and IV due to systolic heart failure in ED patients keeping echocardiography as the gold standard.

Material and methods

Study design

Cross-sectional validation study.

Setting

Department of Accident and Emergency and the Department of Medicine.

Duration of study

This study was conducted from 25 July 2022 to 25 January 2022.

Table 2
% age of patients according to sex.

Sex	Number of patients	% age
Male	76	66.1%
Female	39	33.9%
Total	115	100%

Table 3
% age of patients according to NYHA class.

NYHA class	Number of patients	% age
III	78	67.8%
IV	37	32.2%
Total	115	100%

Sample size

With the help of the WHO calculator,

- Sensitivity = 80%[9]
- Specificity = 66%[9]
- Prevalence = 39%[5]
- Desired precision = 10%
- CI = 95%[5]
- Sample size = 115patients
- Sampling technique: consecutive nonprobability sampling.

Inclusion criteria

- Patients of age 18–65 years.
- Both male and female.
- Present with an acute onset of dyspnea.
- Patients classified as having NYHA Class III and IV.

Exclusion criteria

- Patients who were classified as having dyspnea in NYHA Class I and II.
- Patients who were having severe renal insufficiency, which was defined as serum creatinine greater than 2.5 mg/dl.
- Patients who developed dyspnea after chest trauma.

Data collection procedure

After taking informed consent and permission from the ethical committee, we enrolled the patients attending the ED. We entered the patient's medical record number, age, and sex in the performa, assessing the patients and classify them into one of the NYHA class according to the operational definition. The ED nursing staff then immediately takes a single venous blood sample for BNP and creatinine levels. We entered the value of BNP in pg/ml.

An echocardiography was done by a cardiologist. We recorded the ejection fraction from the final echo report. We made and documented the diagnosis of systolic heart failure on the basis of an ejection fraction, that is less than or equal to 45%.

Table 4
Overall results of BNP and echocardiography.

Heart failure	BNP ≥ 100 pg/ml	Echocardiography
Positive	76 (66.1%)	68 (59.1%)
Negative	39 (33.9%)	47 (40.9%)
Total	115 (100%)	115 (100%)

Table 5

Comparison of BNP versus echocardiography.

	Echocardiography		
BNP	**Positive**	**Negative**	**Total**
Positive	64 (TP)	12 (FP)	76
Negative	4 (FN)	35 (TN)	39
Total	68	47	115

X^2, 58.33.
P-value, 0.000.
FN, false negative; FP, false positive; TN, true negative; TP, true positive.

Data analysis procedure

SPSS (version 24) was used to enter and analyze the data.

Mean ± SD was calculated for quantitative variable like age and BNP levels in patients. Frequency and percentages were calculated for qualitative variables like sex, NYHA class, true positives, and true negatives. Sensitivity, specificity, positive predictive value (PPV), negative prediction value (NPV) was calculated according to 2 × 2 table. The ROC and likelihood ratio was calculated. Effect modifiers like age, sex, NYHA class III and IV was controlled by stratification. Poststratification diagnosis accuracy was measured.

Table 6

Sensitivity, specificity, diagnostic accuracy, and likelihood ratio of BNP greater than or equal to 100 pg/ml.

Sensitivity $= \frac{\text{True Positive}}{\text{True Positive + False Negative}} \times 100 =$

$\frac{64}{64 + 4} \text{X } 100 =$ **94.1%**

Specificity $= \frac{\text{True Negative}}{\text{True Negative + False Positive}} \times 100$

$\frac{35}{35 + 12} \text{ X } 100 =$ **74.5%**

Diagnostic Accuracy $= \frac{\text{True Positive + True Negative}}{\text{True Positive +True Negative + False Positive + False Negative}} \times 100$

$\frac{64 + 35}{64+35+12+4} \text{X } 100 =$ **86%**

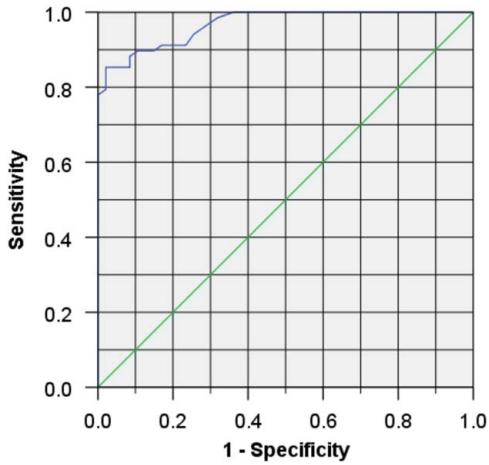
PPV= $\frac{\text{True Positive}}{\text{True Positive+ False Positive}}$

= **84.21%**

NPV= $\frac{\text{True Negative}}{\text{False Negative+ True Negative}}$

= **89.74%**

Likelihood Ratio Positive= Sensitivity/ (1-Specificity)
LR+ = 3.68
Likelihood Ratio Negative = (1-Sensitivity)/Specificity
LR- = 0.08



Graph I. ROC curve.

Results

The age range in this study was from 18 to 65 years with mean age of 49.147 ± 8.73 years. Mean BNP levels were 139.452 ± 84.04 pg/ml as shown in Table 1. The majority of patients were male, that is 66.1% as shown in Table 2. A patient with NYHA class III was 67.8 and 32.2% belongs to NYHA class IV as shown in Table 3. BNP levels greater than or equal to 100 pg/ml diagnosed 76 (66.1%) and echocardiography has diagnosed 68 (59.1%) patients with heart failure as shown in Table 4.

BNP levels greater than or equal to 100 pg/ml had shown sensitivity 94.1%, specificity 74.5%, and diagnostic accuracy by 86%, PPV 84.21%, NPV 89.74%, likelihood positive ratio 3.68 and likelihood negative ratio was 0.08 in diagnosis of heart failure as shown in Tables 5 and 6.

A cutoff level of BNP 111.5 pg/ml had shown the sensitivity of 89.7% and specificity of 89.4% in the diagnosis of heart failure as shown by the ROC curve and its coordinates as shown in Graph I and Table 7.

Stratification with respect to age, sex, and NYHA class of BNP levels greater than or equal to 100 pg/ml versus echocardiography are shown in Tables 8, 9, 10, 11, 12, and 13, respectively.

Discussion

The natriuretic peptide framework contains three peptides, the A-type peptide (ANP, discharged from the atria), the B-type peptide (BNP, discharged basically from the ventricles), and the C-type peptide (CNP, discharged from endothelial cells)[10,11].

Since BNP is discharged specifically from the ventricles, it has been recommended that it is more precise than other natriuretic

Table 7

Coordinates of the ROC curve.

BNP levels	Sensitivity	1-specificity
24.0000	1.000	1.000
25.5000	1.000	0.936
29.5000	1.000	0.915
38.5000	1.000	0.766
44.5000	1.000	0.702
46.0000	1.000	0.660
51.0000	1.000	0.596
55.5000	1.000	0.489
59.5000	1.000	0.468
65.0000	1.000	0.404
70.5000	1.000	0.362
76.0000	0.985	0.319
82.5000	0.971	0.298
94.5000	0.941	0.255
103.5000	0.912	0.234
107.0000	0.912	0.191
109.5000	0.912	0.170
110.5000	0.897	0.149
111.5000	0.897	0.106
114.0000	0.882	0.085
116.5000	0.853	0.085
118.0000	0.853	0.021
121.0000	0.794	0.021
128.5000	0.779	0.000
144.0000	0.750	0.000
159.5000	0.676	0.000
167.0000	0.632	0.000
172.0000	0.603	0.000
175.5000	0.574	0.000
178.0000	0.529	0.000
184.0000	0.500	0.000
188.5000	0.471	0.000
189.5000	0.441	0.000
193.0000	0.412	0.000
197.5000	0.382	0.000
199.5000	0.353	0.000
200.5000	0.324	0.000
208.0000	0.294	0.000
218.5000	0.265	0.000
227.0000	0.221	0.000
238.5000	0.191	0.000
260.5000	0.162	0.000
283.0000	0.132	0.000
306.5000	0.103	0.000
345.0000	0.029	0.000
368.0000	0.000	0.000

peptides for the determination of CHF[12,13]. Like ANP, it advances diuresis, natriuresis, fringe vasodilation, renin angiotensin-aldosterone framework hindrance, and sympathic sensory system restraint. BNP is a 32-aa polypeptide, containing a 17-aa structure regular to every natriuretic peptide[13].

The nucleic corrosive arrangement of the BNP quality contains the destabilizing grouping 'tatttat', which proposes that turnover of BNP delegate RNA is high and that BNP is blended in blasts (uniquely in contrast to ANP, which is incorporated and after that put away in granules inside the atria). These discoveries brought together with the way that BNP has a short half-life (just 22 min)[14], recommend that BNP is a cardiovascular crisis

Table 8

Stratification with respect to age groups (18–40 years) of BNP versus echocardiography ($n = 24$).

	Echocardiography			
BNP	Positive	Negative	Total	*P*
Positive	6 (TP)	7 (FP)	13	0.745
Negative	18 (FN)	17 (TN)	35	
Total	24	24	48	

Sensitivity: 25%.
Specificity: 70.8%.
DA = 48%.
PPV = 46.15%.
NPV = 48.57%.
LR+ = 0.85.
LR- = 1.05.
FN, false negative; FP, false positive; TN, true negative; TP, true positive.

neurohormone, and therefore mirrors the present snapshot of ventricular over-burden. Of intrigue, BNP corresponds well with New York Heart Association groupings and pneumonic wedge weight adjustments amid the healing facility treatment of patients with decompensated CHF, drop to normal 33 pg/ml/h with in the initial 24 h of treatment. BNP which does not drop to normal with treatment shows a poor prognosis[15].

As of late, its prognostic significance was likewise shown in patients with intense coronary disorders[16]. In our study BNP levels greater than or equal to 100 pg/ml had shown sensitivity 94.1%, specificity 74.5% and diagnostic accuracy by 86%, PPV 84.21%, NPV 89.74%, likelihood positive ratio 3.68, and likelihood negative ratio was 0.08 in diagnosis of heart failure. Bettencourt *et al*. demonstrated a symptomatic exactness of BNP estimation to be 83.75% in affirming left ventricular dysfunction for BNP levels. Echocardiography has incredible sensitivity and specificity for diagnosing left ventricular dysfunction, be that as it may, this methodology is not all around accessible. Different modalities, for example right heart catheterization with pneumonic supply route wedge weight or left heart catheterization with left ventriculography and estimation of LVEDP are extremely exact yet intrusive methods. Moreover, dreariness is far higher in noninvasive instruments.

In the BNP concentrate on, BNP levels were measured in the crisis room on 1586 patients who gave dyspnea. BNP levels above

Table 9

Stratification with respect to age groups (41–65 years) of BNP versus echocardiography ($n = 91$).

	Echocardiography			
BNP	Positive	Negative	Total	*P*
Positive	70 (TP)	61 (FP)	131	0.137
Negative	21 (FN)	30 (TN)	51	
Total	91	91	182	

Sensitivity: 76.9%.
Specificity: 33%.
DA = 55%.
PPV = 53.43%.
NPV = 58.82%.
LR+ = 1.14.
LR- = 0.7.
FN, false negative; FP, false positive; TN, true negative; TP, true positive.

Table 10

Stratification with respect to sex (male) of BNP versus echocardiography ($n = 76$).

	Echocardiography			
BNP	Positive	Negative	Total	*P*
Positive	49 (TP)	41 (FP)	90	0.186
Negative	27 (FN)	35 (TN)	62	
Total	76	76	152	

Sensitivity: 64.5%.
Specificity: 46.1%.
DA = 55%.
PPV = 54.44%.
NPV = 56.45%.
LR + = 1.195.
LR- = 0.77.
FN, false negative; FP, false positive; TN, true negative; TP, true positive.

Table 12

Stratification with respect to NYHA class (III) of BNP versus echocardiography ($n = 78$).

	Echocardiography			
BNP	Positive	Negative	Total	*P*
Positive	50 (TP)	44 (FP)	94	0.939
Negative	28 (FN)	34 (TN)	62	
Total	78	78	156	

Sensitivity: 64.1%.
Specificity: 35.3%.
DA = 51%.
PPV = 53.19%.
NPV = 46.15%.
LR + = 0.99.
LR- = 1.01.
FN, false negative; FP, false positive; TN, true negative; TP, true positive.

100 pg/ml were observed to be connected with congestive heart disappointment with ascertained sensitivity and specificity of BNP to be 90 and 76%, respectively[17].

Similar perceptions were recorded by Maisel *et al.* in 2001. They connected the levels of BNP with LV weight and the measure of dyspnea and inferred that BNP levels increment with seriousness generally as the white cell include do instance of infection.[3,9] This study approves the utilization of BNP estimations in the earnest setting to dependably affirm left ventricular dysfunction and in addition characterizing the solemnity of heart failure[18].

Correlation with different studies – we exhibited that BNP estimations can be valuable in the conclusion of CHF in patients introducing to the ED with dyspnea. In a study, Dao *et al.* assessed 250 patients with intense dyspnea, utilizing a convention like our own. BNP levels in patients with a last conclusion of CHF were fundamentally higher than in the non-CHF amass (1076 ± 138 vs. 38 ± 4 pg/ml). In view of a cutoff estimation of 80 pg/ml, BNP was an exact indicator of a CHF analysis (PPV of 95%) and demonstrated incredible precision to preclude a conclusion of CHF (negative predictive value of 98%). The general precision as evaluated by the range under the bend was 0.97. Of intrigue, BNP execution was superior to that of crisis division doctors (area under the curve of 0.88). Davis *et al.* concentrated-on BNP and ANP in 52 patients with dyspnea and watched that BNP was more precise than launch division or ANP for anticipating the finding of CHF. Our discoveries are as per those from the study by Dao *et al.*[19] and affirm the utility of BNP in this situation. Taken together, this information is overpowering, in light of the fact that it is exceptionally uncommon to have a strategy with amazing sensitivity and specificity in the meantime.

Conclusion

It is concluded that BNP measurement is a sensible and specific strategy for diagnosing CHF in patients who present to the ED with acute dyspnea and may add additional benefits to the management of patients with CHF in our population.

Ethical approval

Data was collected after the ethical approval from HBS General Hospital Islamabad, wide reference no HBS-ERC/Jul/147/22.

Consent

The informed consent from the patients was obtained considering Helsinki's Declaration.

Table 11

Stratification with respect to sex (female) of BNP versus echocardiography ($n = 39$).

	Echocardiography			
BNP	Positive	Negative	Total	*P*
Positive	27 (TP)	27 (FP)	54	1.000
Negative	12 (FN)	12 (TN)	24	
Total	39	39	78	

Sensitivity: 69.2%.
Specificity: 30.8%.
DA = 50%.
PPV = 50%.
NPV = 50%.
LR + = 1.
LR- = 1.
FN, false negative; FP, false positive; TN, true negative; TP, true positive.

Table 13

Stratification with respect to NYHA class (IV) of BNP versus echocardiography ($n = 37$).

	Echocardiography			
BNP	Positive	Negative	Total	*P*
Positive	26 (TP)	24 (FP)	50	0.619
Negative	11 (FN)	13 (TN)	24	
Total	37	37	74	

Sensitivity: 70.3%.
Specificity: 35.1%.
DA = 53%.
PPV = 52%.
NPV = 54.1%.
LR + = 1.08.
LR- = 0.84.
FN, false negative; FP, false positive; TN, true negative; TP, true positive.

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Author contribution

H.S.: Concept formal analysis original draft writing H.A.: formal analysis A.A.: editing and review S.B.: formal analysis H.M.: original draft writing.

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