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Brain Natriuretic Peptide in The Diagnosis of Heart Failure

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ABSTRACT

Introduction: Heart failure (HF) is a global problem, with more than 20 million people affected. The overall prevalence of heart failure in developed countries is around 2%. The significance of natriuretic peptides (NPs) is well established in the diagnosis of heart failure (HF).

Materials and Methods: In this cross-sectional study, 100 consecutive patients who presented with acute dyspnea to the Emergency department of a tertiary medical centre in Palakkad were included from December 2019-April 2020. The initial diagnosis for dyspnea was assigned to the emergency department. Later the patient was evaluated in the cardiology department and a final diagnosis was made. A rapid microparticle enzyme immunoassay (AXSYM SYSTEMS ABOBT) was used for the quantitative determination of BNP measurement. EDTA plasma of the patients was subjected to the estimation of BNP according to the manufacturer's instructions.

Results: Out of 100 patients, 79 % had abnormal BNP levels ($>100\text{pg/ml}$); Out of these, 6 In this study, among patients with elevated BNP levels 55 % had abnormal ECG changes and 45 % had normal ECG 1% ($n=47$) were diagnosed to have CCF($p<0.01$) and 39% had another diagnosis.

Conclusion: The results conclude that the measurement of BNP levels will help the clinicians to differentiate cardiac and non-cardiac causes of dyspnea in the emergency setting.

Key Words: BNP, Dyspnea, Heart failure, ECG, Axsym Systems Abbott

INTRODUCTION

Heart failure (HF) is a global problem with more than 20 million people affected worldwide. The overall prevalence of heart failure in developed countries is about 2%. Heart failure prevalence rises with age and affects 6–10% of people over the age of 65.¹

Heart failure was once thought to arise primarily in the setting of a depressed left ventricular (LV) ejection fraction (EF). Several epidemiological research in this field has shown that approximately 50% of patients developing heart failure have a normal or preserved ejection fraction (EF 40–50%). Accordingly, heart failure patients are now broadly categorized into one of two groups:

- (1) HF with a depressed EF as(systolic failure) or
- (2) HF with a preserved EF (diastolic failure).¹

There is a significant challenge in the diagnosis of heart

failure as there are no specific signs and symptoms of heart failure. The key for a correct and prompt diagnosis is to have a high index of suspicion, particularly for high-risk patients. The routine diagnostic aids include Electrocardiogram (ECG), 2D ECHO, Doppler and Chest X-Ray.

The role of Natriuretic peptides (NPs) is well established in the diagnosis of heart failure (HF) with low levels of NPs being especially significant to exclude heart failure (HF).²

A meta-analysis published in 2015, studied the value of brain (B-type) NP (BNP), N-terminal proBNP (NT proBNP) and mid regional pro-atrial NP (MR-proANP) in the acute setting. It showed a high negative predictive value while using low cutoff levels (i.e. BNP $<100\text{ pg/ml}$; NT-proBNP $<300\text{ pg/ml}$, MR-proANP $<120\text{ pmol/l}$).³

This study aimed to assess the role of BNP in the diagnosis of heart failure in patients presenting with acute breathlessness.

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MATERIALS AND METHODS

In this cross-sectional study, 100 consecutive patients who presented with acute dyspnea to the Emergency department of Karuna Medical College, Palakkad were included.

Study period: December 2019-April 2020

Besides clinical examination, laboratory tests (renal function tests, BNP, Hb%) and chest radiography, Echocardiography was done to all patients presenting with dyspnea.

Patients with left ventricular fractional shortening equal to or less than 25% were considered as having systolic dysfunction.

The initial diagnosis for dyspnea was assigned to the emergency department. Later the patient was evaluated in the cardiology department and a final diagnosis was made. Patients with both CCF and other concomitant diagnoses (such as sepsis leading to decompensated CCF) were considered as having CCF as the ultimate diagnosis because the study aimed to assess the ability of BNP in diagnosing CCF.

The study has been done by the ethical standards of the institutional ethical committee on human experimentation and with the Helsinki Declaration of 1975, as revised in 2013. The institutional ethical committee clearance has been obtained for the same. (No.KMC/IHEC/09/2019)

BNP measurements

A rapid microparticle enzyme immunoassay (AXSYM SYSTEM (ABOTT) was used for the quantitative determination of BNP measurement. Under aseptic conditions 3 ml of blood was taken by venipuncture into an EDTA containing vacutainer and plasma was separated by centrifuging at 3000 g for 15 minutes. The EDTA plasma of the patients was further subjected to the estimation of BNP according to the AXSYM SYSTEMS operation manual.

Test principle

This test is a microparticle enzyme immunoassay forming antigen and antibody complexes coated microparticles. If BNP is present, there is a complex formed with corresponding monoclonal antibody coated on the wells. The BNP values are calculated using AXSYM SYSTEM with standard calibrators.

A p-value of lesser than 0.05 was considered statistically significant. The data are reported as the mean $\pm$ SD or the median, depending on their distribution.

RESULTS

In our study, 62% were males and 38% were females. 51% of the patients were in the age group between 40-60 years; 36% were above 60 years and 13% were below 40 years. Among

these, 7 % in the age group of fewer than 40 years, 42 % in the age group 40-60 years and 25 % in the age group greater than 60 years had elevated BNP levels. [TABLE 1]

Out of 100 patients, 79 % had abnormal BNP levels (>100 pg/ml); Out of these, 61% (n=47) were diagnosed to have CCF ($p<0.01$) and 39% had other diagnosis. [CHART 1]

Among the study population, 62% were hypertensives, 63% were diabetics, 26% had renal failure, 43% were smokers. 58% were diagnosed with Coronary Artery Disease.

49 patients had abnormal chest X-Ray findings. The relation between these parameters and BNP are shown in [TABLE 2]

In this study, among patients with elevated BNP levels, 55 % had abnormal ECG changes and 45 % had normal ECG. [CHART 2]

41 % of the patients with abnormal BNP had normal ejection fraction, 23 % had mild ejection fraction, 20 % had moderate ejection fraction and 16 % had severe ejection fraction. [TABLE 3]

Among patients with elevated BNP levels, 56 % had Akinesia / Dyskinesia and 23% had normal regional wall motion. [CHART 3]

DISCUSSION

Natriuretic peptides are hormones of cardiac origin having natriuretic, diuretic, and vasodilatory effects.⁴ BNP belongs to a family of natriuretic peptides, which includes atrial natriuretic peptide (ANP) and C-type natriuretic peptide (CNP), with the latter mainly secreted by vascular endothelium. ANP and BNP are cardiac natriuretic peptides secreted by myocytes, with BNP mainly secreted by atrial myocytes in the normal heart.⁴ With an increase in cardiac wall stress, Brain natriuretic peptide (BNP), is secreted into the circulation. Thus, BNP is a robust biomarker to aid in differentiating cardiac and non-cardiac causes of breathlessness.^{5,6}

The largest study using the Triage R POC in the Emergency room was the Breathing Not Properly trial enrolling 1586 patients presenting to the Emergency Room with acute dyspnea. 744 of the patients (47%) were diagnosed to have heart failure based on clinical data. Mean BNP plasma concentrations at admission were 675 and 110 pg/L in patients with and without HF, respectively.⁷

The level of BNP was by itself the strongest predictor of a correct diagnosis of HF, with a cut-off of 100 pg/L (sensitivity 90%, specificity 76% for distinguishing HF from other causes of dyspnea).

In our study, A B-type natriuretic peptide cut off value of 100 pg per millilitre had a sensitivity of 97 percent, a specificity of 60 %, and an accuracy of 82 % for differentiating congestive heart

failure from other causes of dyspnea. Lower values were associated with more accurate negative predictive values of about 94%. This is consistent with the Breathing Not Properly trial.⁷

Among the patients with elevated BNP levels, 61% (N=47) were diagnosed to have CCF ($p < 0.01$). This is in comparison with a study done by Sheikh Ishaq, et al.⁸ where 54% of CCF patients had elevated BNP levels.

Thus, in determining the correct diagnosis of heart failure, including BNP in the routine investigation along with clinical judgement would enhance the diagnostic accuracy.

CONCLUSION

Majority of the patients presenting with Congestive Cardiac Failure fall in the age group of 40 to 60 years with males being affected more often than females. BNP levels can also be elevated in other condition like acute pulmonary embolism, renal failure, myocardial infarction and acute coronary syndrome. Using the cut off values of BNP of 100 pg/ml, it can be concluded that low BNP levels are highly reliable in ruling out heart failure, whereas a value > 100 pg/mL is only a fair indicator of disease.

The results conclude that the measurement of BNP levels will help the clinicians to differentiate cardiac and non-cardiac causes of dyspnea in the emergency setting.

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Table 1: AGE VS BNP

AGE	BNP NORMAL	BNP ABNORMAL	TOTAL
< 40 years	7	6	13
40 - 60 yrs	9	42	51
> 60 years	5	31	36
Total	21	79	100
(%)	21%	79%	100%

BNP: Brain Natriuretic Peptide

Chart 1: BNP.

Table 2: Correlation between Various Parameters Tested with BNP

PARAMETER	ABNORMAL BNP	NORMAL BNP	TOTAL
HYPERTENSION	54	08	62
DIABETES	56	07	63
RENAL FAILURE	24	02	26
SMOKING	40	03	43
CAD	45	03	48
ABNORMAL CXR	41	08	49

Chart 2: ECG VS BNP.

Table 3: EF VS BNP

EF	BNP		Total	(%)
	Normal	Abnormal		
Normal	13	18	31	52%
Mild	2	10	12	20%
Moderate	1	9	10	17%
Severe	0	7	7	12%
Total	16	44	60	100%
(%)	27%	73%	100%	

EF: Ejection Fraction

AK: Akinesia, DK: Dyskinesia

Chart 3: AK/DK VS BNP.