INTRODUCTION

Congestive heart failure (CHF) is a syndrome caused by cardiac dysfunction with a prevalence rate of about 0.8% and 2% in the general population. It has many causes, numerous clinical subsets and variable clinical presentation. Left ventricular dysfunction (LVD) leads to circulatory abnormalities, resulting in fluid retention, shortness of breath and fatigue on exertion. It carries high mortality with frequent hospitalization and poor quality of life. Early diagnosis is important for an effective therapy to be started and for prognosis improvement. Patients identified as at risk for heart failure (HF) require a thorough clinical assessment with appropriate investigations to identify risk factors, in an effort to prevent development of left ventricular failure (LVF).

A simple way of classifying the extent of HF is provided by the functional classification of New York Heart Association (NYHA). After a thorough clinical examination, the first line investigations include echocardiography (ECG), thorax radiography and Doppler echocardiography along with brain natriuretic peptide (BNP) measurement, according to the European guidelines 2008.

Diagnostic Cut-Off Levels of Plasma Brain Natriuretic Peptide to Distinguish Left Ventricular Failure in Emergency Setting

Arif Hussain1, Irfan Amjad Lutfi2 and Faisal Iqbal Afridi1

ABSTRACT

Objective: To determine the diagnostic cut-off values of brain natriuretic (BNP) peptide to establish left ventricular failure in patients presenting with dyspnoea in emergency department.

Study Design: Descriptive study.

Place and Duration of Study: Ziauddin University Hospital, Karachi, from July to December 2011.

Methodology: BNP estimation was done on Axysm analyzer with kit provided by Abbott diagnostics, while the Doppler echocardiography was done on Toshiba istyle (UICW-660A) using 2.5 MHz and 5.0 MHz probes. Log transformation was done to normalize the original BNP values. A receiver operating curve was plotted to determine the diagnostic cut-off value of BNP which can be used to distinguish CHF from other causes of dyspnoea. Statistical analysis was performed by SPSS version 17.

Results: A total of 92 patients presenting with dyspnoea in the emergency department were studied. There were 38/92 (41.3%) males and 54/92 (58.7%) females, and the average age of the study population was 64 ± 14.1 years. These patients had BNP levels and Doppler echocardiography done. The average BNP was found to be 1117.78 ± 1445.74 pg/ml. In log transformation, the average was found to be 2.72 ± 0.58. BNP value of 531 pg/ml was found to be the cut off to distinguish between cardiogenic and non-cardiogenic causes of dyspnoea.

Conclusion: BNP value of 531 pg/ml can distinguish CHF from other conditions as a cause of dyspnoea in emergency.

cardiomyopathy, diastolic dysfunction and ventricular hypertrophy. The effectiveness of determining plasma BNP concentrations in patients presenting with acute dyspnoea is well established. High levels of BNP are related to ventricular dysfunction, but should be carefully interpreted in patients with obesity and renal dysfunction.

With the increasing use of rapid BNP assays, it is important to determine diagnostic and cut-off values of BNP to predict CHF. The clinical utility of BNP is limited in the absence of a universally accepted normal range. If a reliable cut-off value of BNP is found which can reliably differentiate CHF from other causes of dyspnoea this would be of great value in the clinical management of such patients. Therefore, the aim of this study was to determine the diagnostic cut-off values of brain natriuretic peptide to establish left ventricular failure in patients presenting with dyspnoea in emergency department.

**METHODOLOGY**

The study was conducted at Dr. Ziauddin University Hospital, from July to December 2011. Adult patients aged 18 years and above who came to the ER with dyspnoea during the study period were included in the study. All other patients with suspected respiratory diseases due to infective nature are excluded from the study. Venous blood was drawn aseptically for BNP estimation and collected in purple top vacutainer containing ethylenediaminetetraacetic acid (EDTA). The test was performed on the Abbott Axysm analyzer by kit provided by Abbott diagnostics. The controls of BNP were provided by Abbott Diagnostic Lot No. 44K35512. All levels of controls (low, medium, and high) were used.

These patients also had echocardiography done. The echocardiography was done on the Toshiba machine istyle (UICW-660A) using 2.5 MHz and 5 MHz probes. The ejection fraction (EF) of the patients was noted and recorded. Those patients who had EF of less than 45 were considered to have LVF, while a EF of more than 45 was considered to be normal ventricular function according to criteria by Logeart et al.9

Statistical analysis was done on the Statistical Package for Social Sciences (SPSS) version 17. The original BNP values were skewed, and linear log transformation was done. Then a one sample Kolmogorov-Smirnov test was used to assess the normality of log transformed BNP value. Chi-square independent test was applied to determine the proportion difference between BNP cutoff values by ejection fraction. A p-value of less than 0.05 was considered statistically significant. The diagnostic utility of BNP was compared with echocardiographic probability of LVD using receiver operating curve (ROC). The results were expressed in terms of area under the curve (AUC) as 95% confidence interval (CI), under this area.

### RESULTS

A total of 92 patients were studied with mean age of 64.4 ±14.1 years. There were 38/92 (41.3%) males and 54/92 (58.7%) females in the study. The mean BNP level of the overall study population was found to be 1117.78 ±1445.74 pg/ml. These patients were divided into two groups on the basis of EF as shown in Table I. There were 49/92 (53.3%) patients who had EF of less than 45, while 43/92 (46.7%) patients had EF of more than 45. Dyslipidaemia and hypertension was commonly seen in most of the patients.

A ROC curve was determined for diagnostic BNP value, to use as a cut off to identify CHF patients. A correlation of the log values with the original BNP values to determine the cut off for maximum specificity and optimal sensitivity was found to be 2.73, which corresponds to BNP value of 531 pg/ml. This has a specificity of 75.0% and (1-specificity) of 25.0%. The AUC was found to be 80.5% with a 95% CI of 0.71-0.89 (Figure 1). Hence, according to the present study, a value of BNP of 531 pg/ml can be considered to differentiate CHF due to dyspnoea from other causes of dyspnoea.

Altogether there were 10 (25.0%) patients with BNP less than 531 pg/ml and EF of less than 45. Conversely there were 30 (75.0%) patients with BNP value of more than 531 pg/ml, with EF of less than 45. Significant proportion

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>%</th>
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<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38</td>
<td>41.3</td>
</tr>
<tr>
<td>Female</td>
<td>54</td>
<td>58.7</td>
</tr>
<tr>
<td>Age (years, mean ± sd)</td>
<td>64.4 ± 14.1</td>
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<tr>
<td>BNP (pg/L, mean ± sd)</td>
<td>1117.78 ± 1445.74</td>
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<tr>
<td>Log transformation BNP (mean ± sd)</td>
<td>2.72 ± 0.58</td>
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<tr>
<td>Ejection fraction (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EF &lt; 45</td>
<td>49</td>
<td>53.3</td>
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<tr>
<td>EF ≥ 45</td>
<td>43</td>
<td>46.7</td>
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![Figure 1](https://via.placeholder.com/150)
difference was found between BNP cut-off values and ejection fraction (p < 0.01).

**DISCUSSION**

Acute dyspnoea is one of the main reasons for admission to emergency department. An incorrect diagnosis could increase the risk of mortality, so rapid diagnosis of CHF is important for prompt and appropriate treatment. This can be difficult, especially in elderly or obese patients and in those with associated cardiac or pulmonary diseases. The B-type natriuretic peptide has been described as a powerful diagnostic test to diagnose HF in the emergency setting. This test, along with Doppler echocardiography is used in intensive care units to manage patients with CHF. Studies have shown that BNP and its precursor pro-BNP levels facilitate diagnosis, and guide HF therapy. Elevated NP levels are found to be correlated with the severity of left ventricular systolic dysfunction, right ventricular dysfunctional pressures and left ventricular filling alterations. Several studies have confirmed the effectiveness of determining plasma BNP concentrations in patients presenting with acute dyspnoea. Dao et al. measured BNP levels in 250 subjects who were admitted to the department of emergency medicine with acute dyspnoea and they demonstrated that patients diagnosed with cardiac dyspnoea had significantly elevated plasma BNP concentrations while patients with non-cardiogenic dyspnoea were significantly lower. In a similar larger study, BNP levels were measured in 321 patients which confirmed that the patients with HF had higher BNP levels than in patients with dyspnoea due to respiratory diseases.

The above studies validated that plasma BNP levels are useful in diagnosis of HF with high sensitivity, specificity, and strong predictive value. However, in the interpretation of NP it must be considered that age and gender could potentially alter plasma BNP levels (females have higher levels than males). Thus, increased BNP levels have greater predictive value for adverse events in women. NP also changes on the basis of race. African American and Hispanic patients have higher levels than Caucasians. Renal insufficiency also leads to augmented BNP levels. In the same way, patients with anaemia have higher BNP levels. Conversely, obesity is associated with lower BNP levels. Moreover, the lack of only one set of normal range values, due to the different idiopathic levels and commercially available analysis kits, makes it difficult for optimal use in clinical application. Logeart et al. studied 163 patients admitted in emergency department with dyspnoea and measured compared BNP with Doppler echocardiography. They concluded that BNP cut off value of 300 pg/ml correctly classified 88% of patients as having CHF odds ratio (OR) 85 (19 to 376). In a similar study from Spain, Barrios et al. studied 72 patients attending the ER with complains of dyspnoea, and compared BNP levels with Doppler echocardiography. They concluded that BNP of 100 pg/ml can distinguish LVF, with sensitivity of 25% and specificity of 80.8%. Shaikh et al. also reported the sensitivity of NT-proBNP value of > 300 pg/ml for the diagnosis of CHF as 100% sensitive. The present study supports these findings as it was found that a BNP value of 531 pg/ml was found to reliably differentiate CHF due to dyspnoea from other causes of dyspnoea. This study is unique as it is done in Pakistani population, where associated risk factors like hypertension and dyslipidaemia are common. A reliable value of BNP which can distinguish CHF as a cause of dyspnoea will help in starting the therapy of patients promptly. A limitation of the present study was the sample size. A larger study with larger sample size is desirable to further validate these findings.

**CONCLUSION**

In the present study, a diagnostic BNP value of 531 pg/ml could differentiate CHF as a cause of dyspnoea from other causes of dyspnoea like chronic obstructive pulmonary disease, seen in ER setting. EF of less than 45 was considered to represent impaired left ventricular function.

**REFERENCES**

8. Dao Q, Krishnaswamy P, Kazarnegra R, Harrison A, Amimovin...


