

# Study of role of N terminal pro brain natriuretic peptide in congestive heart failure at a tertiary hospital

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## Abstract

**Background:** Heart failure is the end spectrum of most of the cardiovascular diseases and leading cause of death due to cardiac diseases. Recombinant pro brain natriuretic peptide also known as natriuretic peptide has been used in the treatment of congestive heart failure. This study is based on the role of Natriuretic peptides and their implication and role in congestive heart failure. **Material and Methods:** Present study was cross sectional, case-control study, conducted in patients with clinical features of heart failure and reduced left ventricular ejection fraction (ejection fraction less than 40%) by 2D echocardiography finding were selected as cases. 40 patients in the similar age group with no clinical features and imaging evidence of congestive heart failure were selected as controls for the study. **Results:** The mean value of NT PRO BNP among the cases was 2589 pg/ml, and the mean value of NT PROBNP in the control group was 70 pg/ml, indicating a strong correlation of the levels of serum NTPROBNP with congestive heart failure. The mean left ventricular ejection fraction was 34.75% among the cases and 62.5% among the control group. Systemic hypertension was the major risk factor among the cases, 47.5 % of the patients had systemic hypertension, 35% patients had type-2 diabetes, 32.5 % of patients had ischemic heart disease. Maximum number of patients belonged to class III NYHA heart failure, followed by class II NYHA. The mean value of NTPROBNP was the highest among patients with class IV NYHA heart failure, followed by class III NYHA and class II NYHA heart failure. There is a strong correlation between clinical grades of heart failure and the levels of NTPROBNP. **Conclusion:** NT-pro BNP is a good marker of left ventricular dysfunction in the absence of confounding factor like renal dysfunction, elderly age, critical illness and anemia.

**Keywords:** NT-pro BNP, left ventricular dysfunction, congestive heart failure, NYHA class

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## INTRODUCTION

Heart failure is the end spectrum of most of the cardiovascular diseases including structural heart diseases and systemic diseases, it is the leading cause of death due to cardiac diseases, In other words heart failure is the

leading cause of morbidity and mortality all over the world.<sup>1</sup> There are enzyme studies to determine an ongoing myocardial ischemia in the form of troponins, creatine kinase, lactate dehydrogenase, aspartate transaminase, but heart failure is more of a clinical diagnosis than a lab value based diagnosis.<sup>2</sup> Recombinant pro brain natriuretic peptide also known as natriuretic peptide has been used in the treatment of congestive heart failure,<sup>3</sup> even though cardiac transplantation has gained pace in the modern scenario and also with the advent of implantable cardiac devices, drug therapy still remains the mainstay of treatment due to affordability and patient issues.<sup>4</sup> This study is based on the role of Natriuretic peptides and their implication and role in congestive heart failure, whenever a patient presents to the emergency department with clinical signs of tachypnea and breathlessness, to differentiate the cause of breathlessness between a respiratory pathology or due to

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congestive heart failure, a serum N-TERMINAL PRO BNP can be measured.

**MATERIAL AND METHODS**

Present study was cross sectional case-control study, conducted in department of medicine, at Shri Sathya Sai medical college and research institute. Study duration was of 2 years (July 2018 to June 2019). Study was approved by institutional ethical committee.

**Inclusion criteria:** Adults in the age group of 40-80, of either gender. Patients with clinical features of heart failure and reduced left ventricular ejection fraction (ejection fraction less than 40%) by 2D echocardiography finding were selected as cases. 40 patients in the similar age group with no clinical features and imaging evidence of congestive heart failure were selected as controls for the study.

**Exclusion criteria:** Patients with abnormal renal function tests. (urea >50, creatinine >3.0). Morbid Obesity, patients with a body mass index greater than 35 were not be included in the study. Patients with iron deficiency anemia with features of hyperdynamic circulation and heart failure with volume overload

The study was done with a written and informed consent from the patient and in some cases from the patient’s attenders. This is a study enrolling 80 patients of which 40 patients were selected as cases and 40 patients were enrolled into the control group.

Data was collected in a pretested proforma consist of detailed clinical history, clinical examination. Relevant investigations like complete hemogram, erythrocyte

sedimentation rate, urea, creatinine, liver function tests, fasting lipid profile, electrocardiogram, 2D Echocardiography and serum N-Terminal Pro Brain Natriuretic peptide (Quantification assay of N terminal pro bnp in picograms. Electro chemiluminescent sandwich immunoassay using two polyclonal antibodies directed at the NTp BNP molecule.) Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi- square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

**RESULTS**

With regards to age distribution among cases and controls, 40 % of the patients were in the age group of 46- 60 years followed by 32.5 % of patients in the age group of 61- 75 years. Prevalence of heart failure follows an exponential pattern with age, data suggests a greater number of patients above the age of 60 years. 71.2 % of the patients were males and 28.2% of the patients were females. The mean value of NT PRO BNP among the cases was 2589 pg/ml, and the mean value of NT PROBPNP in the control group was 70 pg/ml, indicating a strong correlation of the levels of serum NTPROBNP with congestive heart failure. The mean left ventricular ejection fraction was 34.75% among the cases and 62.5% among the control group.

**Table 1: General Characteristics**

RANGE	CASES	CONTROLS	TOTAL
AGE (in years)			
≤ 45	6 (15%)	11(27.5%)	17 (21.3%)
46-60	14 (35%)	18 (45%)	32 (40%)
61-75	18 (45%)	8 ( 20%)	26 (32.5%)
> 75	2 (5%)	3 (7.5%)	5 ( 6.2%)
GENDER			
FEMALE	10 (25.0%)	13 (32.5 %)	23 (28.8 %)
MALE	30 (75 %)	27 (67.5 %)	57 (71.2 %)
Other			
NTPROBNP levels	2589 pg/ml	70 pg/ml	
Mean left ventricular ejection fraction	34.75 %	62.5 %	

Systemic hypertension was the major risk factor among the cases, 47.5 % of the patients had systemic hypertension, 35% patients had type-2 diabetes, 32.5 % of patients had ischemic heart disease. Among the patients in the control group 11 patients had type-2 diabetes as a risk factor, 5 patients had systemic hypertension, 1 patient had diabetes, systemic hypertension and ischemic heart disease. 1 patient had COPD, 1 patient suffered from bronchial asthma, 1 patient had seizure disorder, 1 patient had pulmonary tuberculosis, rest of the patients did not have any significant risk factor.

**Table 2: Risk factors**

Risk Factors	Cases	Controls
Systemic hypertension	19 (47.5 %)	5 (12.5 %)
Diabetes mellites	14 (35 %)	11 (27.5 %)
Ischemic heart disease	13 (32.5 %)	1 (2.5 %)
COPD	1 (2.5 %)	1 (2.5 %)
Bronchial asthma	1 (2.5 %)	1 (2.5 %)
Tuberculosis	0	1 (2.5 %)
Seizure disorder	0	1 (2.5 %)

14 patients had NYHA class II heart failure, 19 patients had NYHA class III heart failure, 7 patients had NYHA class IV heart failure. Maximum number of patients belonged to class III NYHA heart failure, followed by class II NYHA. The mean value of NTPROBNP was the highest among patients with class IV NYHA heart failure, followed by class III NYHA and class II NYHA heart failure. There is a strong correlation between clinical grades of heart failure and the levels of NTPROBNP.

**Table 3: NYHA GRADES OF HEART FAILURE AMONG THE CASES**

NYHA CLASS HF	Frequency	Percent	NTPROBNP levels (Mean $\pm$ Std. Deviation)
2	14	35.0	1122.07 $\pm$ 642.684
3	19	47.5	2559.84 $\pm$ 963.285
4	7	17.5	5602.43 $\pm$ 2024.354
<b>Total</b>	<b>40</b>		<b>2589.08 <math>\pm</math> 1897.149</b>

Mean levels of NTPROBNP were higher in cases with high risk factors such as Diabetes mellites, Systemic hypertension and ischemic heart disease as compared to those without these high risk factors, but difference was not statistically significant ( $p > 0.05$ ).

**Table 4: RISK FACTORS VERSUS LEVELS OF NTPROBNP**

RISK FACTORS		No. of cases	Mean $\pm$ Std. Deviation	P value
Diabetes mellites	Absent	14	2603.79 $\pm$ 2140.169	0.972
	Present	26	2581.15 $\pm$ 1797.987	
Systemic hypertension	Absent	13	2689.92 $\pm$ 1907.284	0.819
	Present	27	2540.52 $\pm$ 1926.727	
Ischemic heart disease	Absent	21	2094.86 $\pm$ 1817.912	0.083
	Present	19	3135.32 $\pm$ 1877.843	

## DISCUSSION

As NTPROBNP has a renal mediated clearance, very high values may be seen in patients with estimated glomerular filtration rate less than 60ml/min, unlike brain natriuretic peptide whose values are also higher in patients with chronic kidney disease, the values of NTPROBNP are significantly elevated.<sup>5</sup> Seino *et al.*,<sup>6</sup> had used BNP and NT-proBNP assays, compared 105 patients having chronic heart failure with 67 healthy control subjects and found that the peptide levels were significantly correlated with CHF symptoms. The levels were measured using the New York Heart Association (NYHA) classification of heart failure. The primary value of BNP and NT-pro BNP testing in the emergency department is its diagnostic value in the differential diagnosis of acute dyspnea and possible CHF. levels of the natriuretic peptides may also assist the emergency physician in appropriately triaging the patient with CHF. Studies have shown that measurements of BNP or NT- Pro BNP in the emergency can be used to establish the diagnosis of CHF. Bay M *et al.*,<sup>7</sup> showed that a raised NT pro BNP ( $>357$  pmol/L) identified patients with acute LVF of  $<40\%$  with a sensitivity of 73% and specificity of

82%. The negative predictive value of having a NT pro BNP concentration below 357 pmol/L was 98%. An international pooled analysis of 1256 patients of acute heart failure cases,<sup>8</sup> showed that with age related cut offs of 450, 900 and 1800 pg/ml for ages of  $<50$ , 50-75, and  $>75$  years of age, the NT pro BNP level measurement showed a sensitivity of 90% and a specificity of 84% for acute heart failure. An age independent cut off of 300 pg/ml had 98% negative predictive value to exclude acute Heart failure. Among those with acute heart failure, a presenting NT pro-BNP concentration of  $>5180$  pg/ml was strongly predictive of death by 76 days. Tsao CW, *et al.*,<sup>9</sup> showed that serial NT-proBNP levels especially at 2<sup>nd</sup> week of therapy is predictive of cardiovascular events; those patients with events showed no significant reductions at week 1-4. Also elevated levels of NT-proBNP predicts cardiovascular morbidity and mortality independent of other prognostic markers and thus is helpful to guide risk stratification of high-risk individual, such as those with coronary artery disease. In the PROTECT study<sup>10</sup> which studied the benefits of NTPROBNP guided therapy of heart failure patients with severe left ventricular systolic

dysfunction, there was a significant correlation with the severity of symptoms and the levels of NT PRO BNP. The STARS- BNP study<sup>11</sup> and Berger *et al.*,<sup>12</sup> also showed close correlation with the data and analysis as that of PROTECT. NT-proBNP guided HF treatment was associated with greater reverse ventricular remodeling, presumably reflecting increased personalized application of anti-remodeling therapies (angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers,  $\beta$ -adrenergic blockers, mineralocorticoid receptor antagonists) in those patients most vulnerable to this deleterious process.<sup>13</sup> These data not only suggest that biomarker-guided HF management improves outcomes but also support the contention that NT-proBNP monitoring may be used as a surrogate for echocardiography for the serial assessment of ventricular remodeling. BNP levels of less than 100pg/ml and of more than 500pg/ml have a 90% negative predictive value (NPV) and positive predictive value (PPV), respectively, for the diagnosis of congestive heart failure (CHF) in patients presenting with acute dyspnea.<sup>14</sup> For intermediate levels between 100 and 500pg/ml, physicians must also consider underlying left ventricular (LV) dysfunction, effects of renal insufficiency, or right ventricular (RV) dysfunction secondary to cor pulmonale or acute pulmonary embolism. In addition, if clinical suspicion is high for CHF but the natriuretic peptide levels are lower than expected, obesity or flash pulmonary edema should be considered. The information BNP testing provides should always be considered an adjunct in decision making about the patient's treatment.

## CONCLUSION

NT-pro BNP is a good marker of left ventricular dysfunction in the absence of confounding factor like renal dysfunction, elderly age, critical illness and anemia. It has been shown to be useful both as a diagnostic tool as well as a prognostic tool.

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