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Study of N Terminal Pro Bnp Levels in congestive heart failure patients at a tertiary hospital

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Abstract

Background: Congestive heart failure is a major health problem over the past decade owing primarily to an ageing population and an increase in survival rates in patients with cardiovascular conditions. BNP is a hormonally active peptide that is released from the left ventricular wall in response to stretch in the myocytes. Present study was aimed to study N Terminal Pro Bnp Levels in congestive heart failure patients at a tertiary hospital. **Material and Methods:** Present study was prospective, comparative, analytical study, conducted in patients age > 18 years, with clinical features of cardiac failure, with reduced left ventricular ejection fraction on 2D echocardiography were considered as cases while age and sex-matched healthy individuals, with normal 2D echocardiography with normal renal function tests, normal hemoglobin were considered as controls. **Results:** In present study, 60 subjects were studied (30 cases, 30 controls). NT-proBNP (pg/ml) levels in acute heart failure were 2682.7 ± 425.5, in chronic heart Failure were 4553.4 ± 671.4 & in acute and chronic failure were 3319.2 ± 419.4, while in controls levels were < 20. Maximum levels were noted among cases with LVEF ≤40 % (8958.7 ± 1852.5 pg/ml) as compared to lowest levels in LVEF ≥50% (1174.6 ± 394.3 pg/ml). We noted significant association between decreasing levels of LVEF (%) with increasing levels of NT-proBNP (pg/mL). Among NYHA grade 2 (CHF) cases (5 cases) had levels of NT-proBNP < 5000 pg/mL as compared to 9 cases of grade 4 (CHF) cases had levels of NT-proBNP > 5000 pg/mL. We noted significant association between increasing levels of NYHA grade of CHF with increasing levels of NT-proBNP (pg/mL). **Conclusion:** Normal NT-proBNP values rules out underlying heart failure, while higher NT-proBNP levels are indicative reduce left ventricular ejection fraction & advanced NYHA grade of congestive heart failure.

Keywords: NT-proBNP, heart failure, left ventricular ejection fraction, congestive heart failure

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Introduction

Congestive heart failure is a major health problem over the past decade owing primarily to an ageing population and an increase in survival rates in patients with cardiovascular conditions.[1] Symptoms and signs of HF considerably overlap those of pulmonary disease.
The clinicians are often left with considerable diagnostic uncertainty after evaluating the patient's symptoms, physical examination, ECG, and chest radiography. That leads to

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misdiagnosis and delays the initiation of appropriate therapy.[2]Heart failure can be classified in various ways as location of deficit (left or right or biventricular failure), time of onset: (acute or chronic HF), Left ventricular ejection fraction (EF ≤ 40%, also called systolic HF, EF > 50%, also called diastolic HF). etc.[3]

BNP is a hormonally active peptide that is released from the left ventricular wall in response to stretch in the myocytes. It is produced as a prohormone, Pro BNP which is consequently cleaved into N Terminal –pro BNP (NT-ProBNP) and the biologically active BNP.[4]Compared with BNP, NT-proBNP presents a longer circulating half-life, higher plasma concentration, and greater diagnostic sensitivity.[5]Present study was aimed to study N Terminal Pro Bnp Levels in congestive heart failure patients at a tertiary hospital.

Material And Methods

Present study was prospective, comparative, analytical study, conducted in department of general medicine, at XXX medical college & hospital, XXX, India. Study duration was of 1 year (July 2021 to June 2022). Study was approved by institutional ethical committee.

Inclusion criteria

- Patients age > 18 years, with clinical features of cardiac failure, with reduced left ventricular ejection fraction on 2D echocardiography were considered as cases.
- Age and sex-matched healthy individuals, with normal 2D echocardiography with normal renal function tests, normal hemoglobin were considered as controls.

Exclusion criteria

- Patients with abnormal renal function tests, BMI > 30 kg/m^2, hemoglobin less than 9 gm %
- Not willing to participate

Study was explained to all subjects in local language & written consent was taken for participation & study. A detailed clinical history was recorded regarding age, duration of symptoms, ischemic heart disorders, rheumatic heart disorders, hypertension, diabetes, dyslipidaemias, smoking, alcoholism. All patients undertook a comprehensive clinical examination comprising examination of pulse, blood pressure, respiratory, cardiovascular and central nervous systems. Biochemical tests like random blood glucose, blood urea, complete blood picture, serum creatinine and electrolytes were done. ECG, chest x-ray, 2D echocardiogram and ultrasound abdomen were done for every case as well as control subject.

On confirmation of study participation, 3 ml blood was collected into EDTA tubes. In ED, point of care testing of NT-proBNP was done using a standard commercially available assay - Triage Assay, AlereNT-proBNP test, and Bio-site Triple meter Pro.

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

In present study, 60 subjects were studied (30 cases, 30 controls). Mean age of cases was 59.83 ± 10.45 years, while mean age of controls was 58.38 ± 11.24 years. NYHA class of cases was class II (16.67 %), class III (26.67 %) & class IV (56.67 %). Among cases heart failure etiology was dilated (70 %) in majority as compared to ischemic etiology (30 %). Among cases, hypertension was noted in majority (36.67 %), followed by diabetes (26.67 %), hypothyroidism (6.67 %), AF (paroxysmal) (6.67 %) & VT/VF (6.67 %). NT-proBNP (pg/ml) levels in acute heart failure were 2682.7 ± 425.5, in chronic heart Failure were

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4553.4 ± 671.4 & in acute and chronic failure were 3319.2 ± 419.4, while in controls levels were < 20.

Table 1: Baseline characteristics

Clinical characteristics	Cases	Controls
Age (years)	59.83 ± 10.45	58.38 ± 11.24
Gender		
Male	20 (66.67 %)	19 (36.33 %)
Female	10 (33.33 %)	11 (36.67 %)
NYHA class		
II	5 (16.67 %)	
III	8 (26.67 %)	
IV	17 (56.67 %)	
Heart failure etiology		
Dilated	21 (70 %)	
Ischemic	9 (30 %)	
Medical history, *n* (%)		
HTN	11 (36.67 %)	
Diabetes	8 (26.67 %)	
Hypothyroidism	2 (6.67 %)	
AF (paroxysmal)	2 (6.67 %)	
VT/VF	2 (6.67 %)	
NT-proBNP (pg/ml)		
Acute heart failure	2682.7 ± 425.5	< 20
Chronic heart Failure	4553.4 ± 671.4	
Acute and chronic failure	3319.2 ± 419.4	

Maximum levels were noted among cases with LVEF ≤40 % (8958.7 ± 1852.5 pg/ml) as compared to lowest levels in LVEF ≥50% (1174.6 ± 394.3 pg/ml). We noted significant association between decreasing levels of LVEF (%) with increasing levels of NT-proBNP (pg/mL).

Table 2: Correlation of LVEF with NT-proBNP

LVEF	No. of patients	Percent	NT-proBNP (pg/mL) (RANGE)	NT-pro BNP (pg/mL) (Mean ± SD)	P value
≤40 %	20	66.67%	1783 – 21245	8958.7 ± 1852.5	<0.001
40–49%	6	20.00%	973 - 20976	5921.9 ± 1272.4	
≥50%	4	13.33%	389 - 11099	1174.6 ± 394.3	

Among NYHA grade 2 (CHF) cases (5 cases) had levels of NT-proBNP < 5000 pg/mL as compared to 9 cases of grade 4 (CHF) cases had levels of NT-proBNP > 5000 pg/mL. We noted significant association between increasing levels of NYHA grade of CHF with increasing levels of NT-proBNP (pg/mL).

Table 3: Serum NT-proBNP levels and the NYHA grade of CHF

NYHA grade of CHF	NT pro- BNP (pg/ml)				Total
	< 1000	1001-2000	2001- 5000	>5000	

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Grade 2	1 (3.33 %)	2 (6.67 %)	2 (6.67 %)	0	5 (16.67 %)
Grade 3	0	1 (3.33 %)	3 (10 %)	4 (13.33 %)	8 (26.67 %)
Grade 4	0	4 (13.33 %)	4 (13.33 %)	9 (30 %)	17 (56.67 %)
Total	**1 (3.33 %)**	**7 (23.33 %)**	**9 (30 %)**	**13 (43.33 %)**	**30**

Discussion

Heart failure (HF) is a pathophysiological condition that causes an inadequate blood supply to all the organs and apparatus. Heart failure (HF) is a complex syndrome of heart; caused not only by contractile force reduction, but also by neurohormonal changes affecting sympathetic and parasympathetic tone and the renin‐angiotensin‐aldosterone system.[6]

BNP is considered a marker of left ventricular end-diastolic pressure and has been proven to be a useful diagnostic tool to differentiate dyspnea caused by congestive heart failure (CHF) from noncardiac dyspnea in patients presenting at the emergency room.[7,8] BNP is cleared through internalization by cells that express BNP receptors, while renal clearance is the main mechanism for NT-pro BNP, thus the half-life of BNP is 20 min and that of NT-pro BNP is 1–2 h.[9]

Athavale B[10] studied 50 patients presenting with acute onset dyspnea, the most common cause was ischemic heart disease (IHD) (44%) followed by dilated cardiomyopathy (DCM) (32%), chronic obstructive pulmonary disease (COPD) (10%), anemia (4%), followed by other causes. The median NT-proBNP value was the highest for IHD patients (9485 pg/mL), followed by DCM (8969 pg/mL), followed by COPD (2846 pg/mL), and followed by anemia (850 pg/mL). There is a significant positive correlation between NT-proBNP and age (coefficient of correlation r = 0.4007, significance level p = 0.0389, and class interval = 0.137–0.61). There is a significant negative correlation between creatinine clearance and NT-proBNP (coefficient of correlation r = –0.372, significance level p =0.007, and class interval = –0.58 to –0.105). There was significant negative correlation between LVEF and NT-proBNP (coefficient of correlation r = –0.36, significance level p = 0.009, and class interval = –0.58 to –0.09).

In study by Chaudhari ST et al.,[11] 32 patients with clinical features of cardiac failure compared with healthy controls, average N-T pro BNP in cases was 3179 pg/ml and in controls was 103 pg/ml. Majority of the patients had long standing hypertension and ischemic cardiomyopathy was the commonest cause of HF. Mean N-T pro BNP was found to be higher in females (3481 pg/mL) as compared to males (2934pg/mL). Systolic dysfunction (3316 pg/mL) raised the N-T pro BNP more than diastolic dysfunction. Higher the degree of HF according to New York Heart Association classification was associated with higher N-T pro BNP using competitive enzyme immunoassay technique.

Anjankar AP et al.,[12] compared cases (28 males, 22 females with a mean age 50.80 ± 13.11 years) & controls (28 males, 22 females with a mean age 50.86 ± 12.7 years). There was a statistically noteworthy difference in Mean N-T pro BNP between case and control groups, NYHA Class, and age group. Mean N-T pro-BNP is not significantly different at discharge and on 2nd follow-up. For the rest of the diagnoses, there is a notable difference in Mean N-T pro BNP at discharge and on 2nd follow-up.

Bhavik P[13] studied 50 patients with acute cardiac failure diagnosed based on Framingham Criteria and excluded the patients with creatinine level >2mg/dl. High BNP levels were noted in patients with high NYHA class of failure, high CPKMB value, more LVEDD, low ejection fraction, diastolic dysfunction and mortality is also high in those patients.

Jena KK et al.,[14] noted that among all HF groups, a reduction of NT‐proBNP <20% at 10 days predicted mortality, hazard ratio (HR) – 14.9 (95% confidence interval [CI]: 3.8–57.9), P = 0.0001. The risk of mortality in HF patients with NT‐proBNP reduction of <20% in 10

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days was 14.9 times higher in3‑ month follow‑ up. NT‑ proBNP more than 12,000 pg/mL at admission had a mortality risk of 23.3% in the HFrEF group, HR – 23.45 (95% CI: 2.9–189.4), P = 0.003. NT‑ proBNP on the 10th day, more than 9000 pg/mL, had a mortality risk of 21.4% in the HFrEF group, HR – 23.3 (95% CI: 4.9–110.5), P = 0.001.

BNPs are released from the heart ventricles in reaction to volume load or pressure load physiologically and they function to counteract rennin angiotensin system, cause vasodilatation and natriuresis.[15] NT-ProBNP is used as an emergency marker which can be measured for initial screening and then followed up to monitor the severity of congestive heart failure.[16]

BNP and NT-proBNP play a key role in the current management of patients affected by HF by contributing to the identification of patients at a high risk of HF as well as to the diagnosis and prognostic stratification of patients already affected by it.[17] However, future large-scale studies are necessary to assess the diagnostic and prognostic potential of NT-proBNP for clinical outcomes.

Conclusion

Normal NT-proBNP values rules out underlying heart failure, while higher NT-proBNP levels are indicative reduce left ventricular ejection fraction & advanced NYHA grade of congestive heart failure. Thus, there is definitive role of NT-proBNP in diagnosing congestive heart failure in patients presenting with acute breathlessness in the emergency department.

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