

## CORRELATION OF NT-PRO BRAIN NATRIURETIC PEPTIDE LEVEL WITH SEVERITY OF CHRONIC HEART FAILURE

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### ABSTRACT

**Background:** Heart failure is currently the most common cause of death among all cardiovascular diseases. Biochemical markers of heart failure are potential laboratory tools for determination of severity and prognosis of heart failure, however the correlation of level of biomarkers, N- terminal pro-BNP (NT-pro BNP), in particular with severity of heart failure to be established. Aims and objective is to find the correlation between NT Pro-BNP level with severity (Based on New with York Heart association classification & different 2D-Echocardiographic parameters) of heart failure admitted to the medicine ward. **Materials and Methods:** Approximately 31 newly admitted and clinically diagnosed patients of heart failure, more than 12 years age, are taken into consideration for this Hospital Based Descriptive-correlational Study. **Result:** In our study EF (55-75%) was negatively correlated with quantitative NT Pro-BNP level and this was statistically Significant. **Conclusion:** NT- Pro Brain Natriuretic Peptide level can predict future outcomes and thus may aid physicians in making triage decisions about severity of chronic heart failure patients.

## INTRODUCTION

Heart failure is a progressive disease that is currently the most common cause of death among all cardiovascular diseases. The prevalence of heart failure continues to rise due to an increase in the proportion of elderly people as well as an increase in the number of patients with chronic heart failure who have survived acute heart failure because of new therapies.<sup>[1,2]</sup> Therefore, heart failure is a very important disease from both a medical and socioeconomic standpoint.<sup>[3]</sup> Echocardiography is the gold standard for diagnosing heart failure; it is the most useful method and the basis for diagnostic and therapeutic decision-making. Its disadvantages include high cost and ineffectiveness in patients who are obese or have concomitant chronic lung diseases with respiratory distress. Therefore, biochemical markers have become useful and essential clinical tools for the easy and accurate diagnosis and prognosis of heart failure by clearly determining its incidence and stage.<sup>[4]</sup> B-type natriuretic peptide

(BNP) and N- terminal pro-BNP (NT-pro BNP) have been used as routine laboratory tests; a large number of studies have proven their clinical usefulness in the differential diagnosis of serious acute respiratory distress syndrome and the diagnosis and prognostic rating of heart failure.<sup>[5,6]</sup> Natriuretic peptides, including B-type natriuretic peptide (BNP) and N-terminal-pro BNP (NT-pro BNP), have emerged as powerful markers of cardiovascular risk in patients with heart failure. Circulating natriuretic peptide (NP) levels add incremental prognostic value to standard clinical risk stratification algorithms for both ambulatory and hospitalized heart failure patients, with a steady increase in the risk of mortality and recurrent heart failure hospitalization as NT-pro BNP levels rise above 1000 pg/mL. A systematic review of 19 studies of patients with heart failure demonstrated that for every 100-pg/mL rise in BNP concentration, there was a corresponding 35% increase in the relative risk of death.<sup>[7]</sup> The prevalence of chronic heart failure (HF) is increasing in many developed countries. Both bioactive brain-

type natriuretic peptide (BNP) and an inactive marker molecule (NT- pro BNP), which is derived from the BNP precursor have been used for the diagnosis and pharmacological management of HF.<sup>[8,9]</sup> BNP clearance occurs in the kidney, liver, and vascular endothelium through clearance receptor and neutral endopeptidase,<sup>[10]</sup> whereas NT-pro BNP is believed to be cleared solely in the kidney through unknown mechanism.<sup>[11]</sup> Because NT-pro BNP has some advantages over BNP, including higher circulating levels and superior stability, and only a small amount of serum is required for its measurement.<sup>[12-14]</sup>

## MATERIALS AND METHODS

In this descriptive cross-sectional hospital-based study 31 treatment naïve adolescent and adult (> 12 yrs.) patients with newly diagnosed chronic heart failure as per Framingham criteria of CHF are enrolled after exclusion of conditions listed below. NT pro BNP is estimated in all cases after Echocardiographic evaluation. Severity of chronic

heart failure is defined by Echocardiographic parameters. Standard Statistical methods are applied to work out correction between level of NT pro BNP and severity of CHF.

### Inclusion Criteria

- Age should be >12 yrs.
- Framingham clinical criteria for heart failure.
- Echocardiography proven systolic and diastolic dysfunction.

### Exclusion Criteria

Patient having the below mentioned criteria are excluded from the study:

- Cardiac surgery
- Cardioversion
- Anaemia
- Renal failure
- Pulmonary: severe pneumonia, pulmonary hypertension
- Critical illness, bacterial sepsis
- Severe burns

## RESULTS

Tables of distribution of Age, Sex, Systemic Hypertension:

**Table 1**

| Age Group (years) | Frequency | Percent |
|-------------------|-----------|---------|
| ≤ 40              | 4         | 12.9%   |
| 41 – 50           | 7         | 22.6%   |
| 51 – 60           | 8         | 25.8%   |
| 61 – 70           | 10        | 32.3%   |
| 71 – 80           | 2         | 6.5%    |
| Total             | 31        | 100%    |

**Table 2**

| Sex    | Frequency | Percent |
|--------|-----------|---------|
| Female | 13        | 41.9%   |
| Male   | 18        | 58.1%   |
| Total  | 31        | 100.0%  |

**Table 3**

| Systemic Hypertension | Frequency | Percent |
|-----------------------|-----------|---------|
| No                    | 18        | 58.1%   |
| Yes                   | 13        | 41.9%   |
| Total                 | 31        | 100.0%  |

Table: Distribution of Clinical severity of heart failure (NYHA) Grading:

**Table 4**

| Clinical severity of heart failure (NYHA) Grading | Frequency | Percent |
|---------------------------------------------------|-----------|---------|
| II                                                | 11        | 35.5%   |
| III                                               | 5         | 16.1%   |
| IV                                                | 15        | 48.4%   |
| Total                                             | 31        | 100.0%  |

Table: Distribution of Grade of LV Diastolic Dysfunction:

**Table 5**

| Grade of LV Diastolic Dysfunction | Frequency | Percent |
|-----------------------------------|-----------|---------|
| I                                 | 17        | 54.8%   |
| II                                | 12        | 38.7%   |
| III                               | 2         | 6.5%    |

|       |    |        |
|-------|----|--------|
| Total | 31 | 100.0% |
|-------|----|--------|

Table: Distribution of mean Age (in years):

**Table 6**

|                | Number | Mean    | SD      | Minimum | Maximum | Median  |
|----------------|--------|---------|---------|---------|---------|---------|
| Age (in years) | 31     | 55.5161 | 12.6567 | 20.0000 | 74.0000 | 58.0000 |

Tables of Distributions of Echocardiographic Parameters:

**Table 7**

|                 | Number | Mean    | SD     | Minimum | Maximum | Median  |
|-----------------|--------|---------|--------|---------|---------|---------|
| LVIDD (35-57mm) | 31     | 58.3677 | 7.6117 | 46.0000 | 69.2000 | 60.0000 |

**Table 8**

|                 | Number | Mean    | SD     | Minimum | Maximum | Median  |
|-----------------|--------|---------|--------|---------|---------|---------|
| LVISD (25-41mm) | 31     | 48.3935 | 7.5124 | 34.0000 | 58.0000 | 51.3000 |

**Table 9:**

|                       | Number | Mean    | SD     | Minimum | Maximum | Median  |
|-----------------------|--------|---------|--------|---------|---------|---------|
| LA diameter (20-40mm) | 31     | 39.1323 | 4.1653 | 30.0000 | 46.0000 | 40.0000 |

Correlation of Quantitative NT Pro-BNP level in all parameters in Case:

**Table 10**

|                        |                                     | Quantitative NT Pro-BNP level | Remarks              |
|------------------------|-------------------------------------|-------------------------------|----------------------|
| LA diameter (20-40 mm) | Pearson Correlation Coefficient (r) | .965**                        | Positive correlation |
|                        | p-value                             | <0.0001                       | Significant          |
|                        | Number                              | 31                            |                      |
| LVIDS (25-41 mm)       | Pearson Correlation Coefficient (r) | .990**                        | Positive correlation |
|                        | p-value                             | <0.0001                       | Significant          |
|                        | Number                              | 31                            |                      |
| LVIDD (35-57 mm)       | Pearson Correlation Coefficient (r) | .965**                        | Positive correlation |
|                        | p-value                             | <0.0001                       | Significant          |
|                        | Number                              | 31                            |                      |
| EF (55-75%)            | Pearson Correlation Coefficient (r) | -.978**                       | Negative correlation |
|                        | p-value                             | <0.0001                       | Significant          |
|                        | Number                              | 31                            |                      |
| Age (in years)         | Pearson Correlation Coefficient (r) | -.322                         | Negative correlation |
|                        | p-value                             | .077                          | Not Significant      |
|                        | Number                              | 31                            |                      |

#### LA diameter (20-40 mm)

The value of Pearson Correlation Coefficient (r) was .965\*\*. The Positive correlation was found between Quantitative NT Pro-BNP levels LA diameter (20-40 mm). The P-Value was <0.0001. The result was statistically significant.

#### LVIDS (25-41 mm)

The value of Pearson Correlation Coefficient (r) was .990\*\*. The Positive correlation was found between Quantitative NT Pro-BNP levels LVISD (25-41 mm). The P-Value was <0.0001. The result was statistically significant.

#### LVIDD (35-57 mm)

The value of Pearson Correlation Coefficient (r) was .965\*\*. The Positive correlation was found between Quantitative NT Pro-BNP level vs LVIDD (35-57 mm). The P-Value was <0.0001. The result was statistically significant.

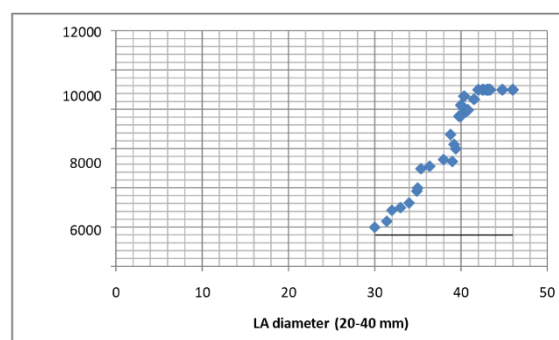
#### EF (55-75%)

The value of Pearson Correlation Coefficient (r) was -.978\*\*. The Negative correlation was found between Quantitative NT Pro-BNP levels EF (55-

75%). The P-Value was <0.0001. The result was statistically significant.

#### Age (in years)

The value of Pearson Correlation Coefficient (r) was -.322. The Negative correlation was found between Quantitative NT Pro-BNP levels Age (in years). The P-Value was .077. The result was not statistically significant.



**Figure 1**

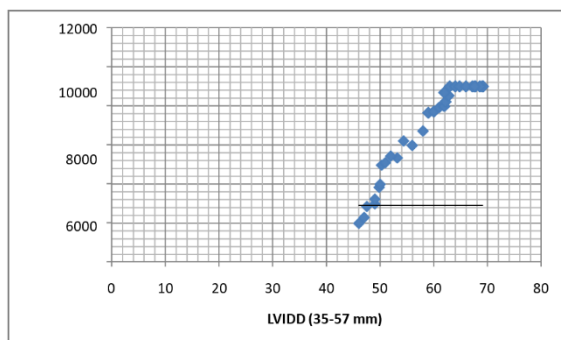


Figure 2

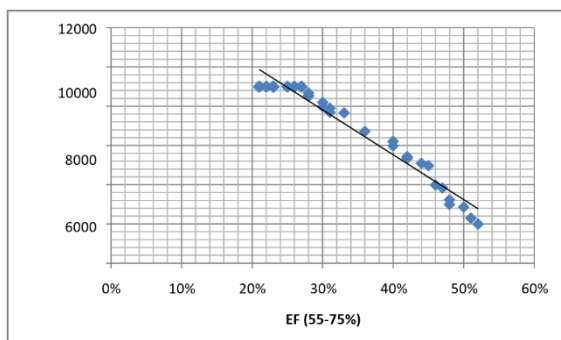


Figure 3

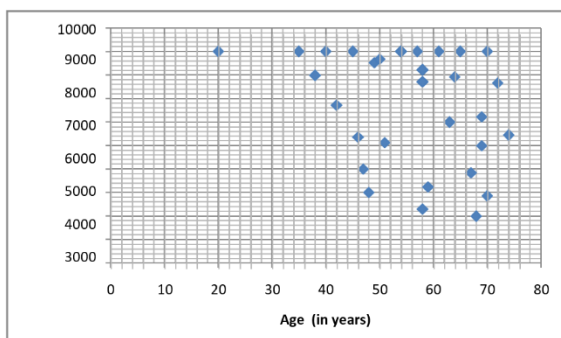


Figure 4

## DISCUSSION

This is a hospital based descriptive analytical Study aiming at finding out correlation between levels of NT pro BNP with severity of chronic heart failure recovering from acute heart failure was conducted at Bankura Sammilani Medical College & Hospital.

Our study showed that, 17 (54.8%) patients had Grade I Diastolic Dysfunction, 12 (38.7%) patients had Grade II Diastolic Dysfunction, and 2 (6.5%) patients had Grade III Diastolic Dysfunction. The value of z is 1.2727. The value of p is 20408. The result is not significant at  $p < .05$ .

A study done by Carsten Tschö pe, Mario Kaš ner, Dirk Westermann, Regina Gaub, Wolfgang C. Poller, Heinz-Peter Schultheiss (89) NT-pro BNP levels were four-fold elevated in patients with diastolic abnormalities when compared with control patients [189.54 pg/mL (86.16– 308.27) vs. 51.89 pg/mL (29.9–69.7);  $P < 0.00$ .

In our study we found the mean LA diameter (20-40 mm) of patients was  $39.1323 \pm 4.1653$ . The Positive

correlation [.965\*\*] was found between Quantitative NT Pro-BNP level vs LA diameter (20-40 mm). The P-Value was  $< 0.0001$ . The result was statistically significant.

In a study done by 1Kemalpaşa State Hospital, Clinic of Cardiology, İzmir, Turkey 2 Dadaist Analytics, Dublin, Ireland(91). larger LAD was correlated to higher levels of NT pro BNP ( $r = 0.451$ ,  $p < 0.001$ ).

We examined that the mean LVIDD (35-57 mm) of patients was  $58.3677 \pm 7.6117$ , the mean LVISD (25-41 mm) of patients was  $48.3935 \pm 7.5124$

In our study the Positive correlation [.990\*\*] was found between quantitative NT Pro-BNP level vs LVISD (25-41 mm). The P-Value was  $< 0.0001$ . The result was statistically significant. We observed that the Positive correlation [.965\*\*] was found between Quantitively NT Pro-BNP level vs LVIDD (35-57 mm). The P-Value was  $< 0.0001$ . The result was statistically significant.

In a study done by Kaleemullah Shaikh 1, Bashir Hanif, et al.(93) showed that The group of patients with LV dilation, had significantly higher BNP levels than those with normal LVEDD ( $12416 \pm 1060$  pg/ml vs.  $6113 \pm 960$ ,  $p = 0.009$ ) and LVESD ( $10416 \pm 1160$  vs.  $4513 \pm 960$  pg/ml,  $p = 0.008$

In our study EF (55-75%) (mean $\pm$ s.d.) of patients was  $34.84 \pm 10.31$

Our study showed that the Negative correlation [-.978\*\*] was found between Quantitative NT Pro-BNP level vs EF(55-75%). The P-Value was  $< 0.0001$ . The result was statistically significant.

Study done by Amulya C. Belagavi, Medha Rao, Aslam Y. Pillai, and U.S. Srihari said that NT pro-BNP levels correlated well with reduced LVEF. Patients with a final diagnosis of LV dysfunction had significantly higher levels of NT pro-BNP than those without LV dysfunction ( $P > 0.001$ ).

Liang Xu, Yanchun Chen, Yanniji, and Song Yang et al. (95) has done correlation analysis between NT-pro-BNP and LVEF levels in patients with different degrees of cardiac function. The analysis suggests that NT-pro-BNP level is negatively related to LVEF level [ $r = -0.8517$ ,  $p < 0.001$  ( $< 0.05$ )]. NT-pro-BNP, N-terminal pro-brain natriuretic peptide; LVEF, left ventricular ejection fraction.

## CONCLUSION

Level of NT-pro BNP is a potential parameter for assessing severity of chronic heart failure in treatment naïve patient.

### Limitations of the Study

1. In the present study the sample size is too small.
2. The study was conducted in a single centre hence there is possibility of regional bias.
3. The method used to estimate NT pro-BNP level not able to measure more than 9000 pg/ml.

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