***Original Research Article***

**AN OBSERVATIONAL STUDY ON NT pro-BNP LEVELS IN PATIENTS ADMITTED TO A TERTIARY CARE HOSPITAL**

**1-This is a good project**

**2- The very good language and the results clear presentation**

**3- Answer the comments**

**4- Must be increased number of reference**

**ABSTRACT:**

**Background:**

N-terminal pro b-type natriuretic peptide (NT-proBNP) is a well-established biomarker used for diagnosing and evaluating cardiac function, particularly in heart failure, and for assessing the prognosis of cardiovascular diseases. This observational study aimed to evaluate elevated NT-proBNP levels in patients admitted to a tertiary care hospital and explore their association with clinical outcomes.

**Methods:**

An observational study was conducted over six months by reviewing medical records of patients admitted to the pulmonology, cardiology, and internal medicine departments of a tertiary care hospital. Data on demographics, clinical characteristics, laboratory findings, and NT-proBNP levels were extracted from electronic health records. The relationship between NT-proBNP levels and clinical outcomes, including mortality and cardiac events, was analyzed.

**Results:**

A total of 200 patients were included, with a mean age of 60.5 years and a predominance of males (61%). Elevated NT-proBNP levels were significantly associated with older age, male gender, and the presence of comorbidities such as hypertension, diabetes, and chronic kidney disease. Dyspnea was reported in 138 patients, of whom 121 had elevated NT-proBNP levels. Among 62 patients without dyspnea, 56 also had elevated levels. Higher NT-proBNP concentrations were associated with an increased risk of mortality and adverse cardiac events.

**Conclusion:**

This study highlights the diagnostic value of NT-proBNP across various age groups, genders, and clinical conditions, particularly in differentiating between dyspneic and non-dyspneic patients. Elevated NT-proBNP levels were more common among patients with dyspnea, suggesting a strong correlation with respiratory distress. These findings underscore the importance of incorporating NT-proBNP testing into the routine assessment of patients presenting with dyspnea, facilitating early diagnosis and intervention.

**Keywords:** NT-proBNP, Dyspnoea, Hypertension, Diabetes, Chronic kidney disease.

**INTRODUCTION:**

N-terminal pro-brain natriuretic peptide (NT-proBNP) is a 76-amino acid peptide derived from the cleavage of the prohormone brain natriuretic peptide (BNP), which also yields the active 32-amino acid BNP. These peptides are primarily secreted by cardiac myocytes in response to myocardial stretch or injury. Compared to BNP, NT-proBNP has a longer half-life (1–2 hours), resulting in lower inter- and intraindividual variability, making it a more stable biomarker for clinical use 1-3. NT-proBNP levels are influenced by several physiological factors: they tend to be lower in males and obese individuals and are elevated in patients with renal dysfunction due to reduced clearance 4. Levels also increase with advancing age. NT-proBNP and BNP have well-established roles in the diagnosis and prognosis of heart failure (HF), a complex clinical syndrome characterized by impaired ventricular filling or ejection, leading to symptoms such as dyspnea and fatigue 5. Acute heart failure may present as either new-onset (de novo) or acutely decompensated chronic heart failure, often associated with systemic congestion. Common precipitants of acute HF include myocardial ischemia, arrhythmias, infections, non-adherence to medication, uncontrolled hypertension, anemia, and renal impairment 6-7. While natriuretic peptides are reliable markers in HF, their levels may also be elevated in critically ill patients due to non-cardiac causes such as sepsis, pulmonary embolism, multiorgan failure, and various therapeutic interventions like vasopressors or fluid resuscitation 8. Given these factors, there is growing interest in comparing NT-proBNP with other commonly used cardiac biomarkers such as D-Dimer and Troponin-I. This observational study aimed to assess the screening patterns of NT-proBNP, D-Dimer, and Troponin-I in patients admitted to a tertiary care hospital and to explore the clinical relevance of elevated NT-proBNP levels, particularly in relation to patient outcomes such as mortality and cardiovascular events.

**OBJECTIVES:**

* To evaluate the frequency and distribution of NT-pro BNP screening across various age groups and genders.
* To conduct a comparative assessment of D-Dimer, Troponin-I, and NT-pro BNP screening patterns.
* To validate the diagnostic utility of NT-pro BNP for the early detection of heart failure
* To determine the overall prevalence of NT-pro BNP screening among admitted patients.
* To compare NT-pro BNP levels between patients presenting with dyspnea and those without.
* To explore the association between NT-pro BNP levels and underlying medical conditions in dyspneic patients.
* To analyze the correlation between NT-pro BNP levels and coexisting medical conditions in non-dyspneic patients.

**METHODOLOGY:**

**Study Design:** Observational study.

**Sample Size:** A total of 200 subjects were included in the study.

**Place of Study:** The study was conducted at Continental Hospitals, located in Nanakramguda, Gachibowli, Hyderabad, Telangana, India.

**Duration of the Study:** Data was collected from patient records of individuals admitted over a period of six months.

**Inclusion Criteria:**

The study included patients aged 18 years and above who had a documented history of cardiovascular disease and other comorbid conditions. Individuals who presented with clinical symptoms such as chest pain, shortness of breath (SOB), or syncope were also considered. Additionally, critically ill patients admitted to intensive care units (ICUs), as well as those with a history of percutaneous coronary intervention (PCI) or surgical myocardial revascularization, were included in the study.

**Exclusion Criteria:**

Patients with active cancer, a recent history of surgery or trauma, or those undergoing dialysis were excluded from the study. Individuals with known hepatic diseases and pregnant women were also not considered for inclusion. Additionally, patients who had signed a Do Not Resuscitate (DNR) form were excluded from participation.

**Data collection:**

A structured data collection form was specifically developed for the study to capture essential information, including demographic details, medical and medication history, laboratory investigations, and clinical diagnoses of the study participants. Relevant data were systematically collected and documented. Patients were enrolled based on the predefined inclusion and exclusion criteria. The gathered data were subsequently compiled and analyzed using appropriate statistical methods.

**Statistical Analysis:**

Statistical analysis was performed using specialized software, and the t-test was applied to assess NT-proBNP levels.

**RESULTS & DISCUSSION:**

Out of the total 200 patients, 122 were male and 78 were female, representing approximately 61.0% and 39.0% respectively. This indicates a male predominance in the study population. Similarly, a study conducted by Daniels LB, Clopton P, et al. reported higher NT-proBNP levels in males compared to females, attributing this difference to hormonal variations, particularly the lower estrogen levels observed in men 9. NT-proBNP screening was most frequent in the 61–70 age group (30.5%), followed by the 71–80 age group (24.0%). The mean age of the study population was 60.5 years.

Among the clinical symptoms assessed—dyspnea, cough, swelling, chest pain, and sweating—dyspnea was the most common, observed in 138 patients (35.7%) out of 200. This was followed by cough in 113 patients (29.2%), swelling in 61 patients (15.8%), chest pain in 58 patients (15%), and sweating in 17 patients (4.4%). A study by Martinez-Rumayor et al. reported a 65% prevalence of dyspnea among patients with congestive heart failure (CHF), underscoring its importance as a key clinical manifestation in heart failure cases.

**Table 1** indicates that Troponin-I (Trop-I) was elevated in 64.3% of patients (n = 142), while D-Dimer levels were elevated in 79 patients (35.7%). All three biomarkers—NT-proBNP, Troponin-I, and D-Dimer—were screened in 61 out of the 200 subjects included in the study. Table 2 shows that 200 patients evaluated, NT-proBNP levels were assessed in all cases, with 182 patients (78.5%) showing abnormal levels and 18 patients (21.5%) falling within the normal range. Troponin-I (Trop-I) was screened in 142 patients, of which 99 (44.83%) had abnormal values and 43 (19.47%) had normal levels. D-Dimer was tested in 79 patients, revealing abnormal levels in 62 patients (28.01%) and normal levels in 17 patients (7.68%). In a study by Celia Maria Cassaro Strunz et al., elevated Troponin-I levels were linked to increased risk of death and heart failure hospitalization in 53.3% of stable CAD patients. Byung Sik Kim et al. reported abnormal D-Dimer levels in 63.3% of screened patients, associating it with higher risks of heart disease, stroke, and kidney disease. Hendricks et al. found that elevated NT-proBNP levels were significantly associated with increased cardiovascular events and mortality, highlighting its vital role in clinical assessment.

Out of the 200 patients (100%) screened for NT-proBNP, the test was performed only once in the majority of cases, accounting for 153 patients (77%). Among these 200 patients, 138 (69%) presented with dyspnea, while the remaining 62 (31%) did not report any symptoms of dyspnea. Table 3 shows that the 138 patients with dyspnea, 121 (87.7%) had abnormal NT-proBNP levels (>400 pg/ml), while 17 (12.3%) had normal levels (<400 pg/ml). In comparison, among the 62 patients without dyspnea, 56 (90.3%) had abnormal NT-proBNP levels and 6 (9.7%) had normal levels. This indicates a high prevalence of elevated NT-proBNP levels in both dyspneic and non-dyspneic patients.

Table 4 indicated that out of the 138 patients (69%) presenting with dyspnea, the majority (n=64) with abnormal NT-proBNP levels were diagnosed primarily with respiratory conditions, followed by 44 patients with cardiovascular conditions as the primary diagnosis. Among the 64 dyspneic patients with respiratory illnesses, 40 had lower respiratory tract infections (LRTI) and 14 had chronic obstructive pulmonary disease (COPD), all showing elevated NT-proBNP levels. In a study by Fengming Tian et al., NT-proBNP levels >400 pg/ml were found to be elevated in COPD patients with dyspnea. However, in our study, higher NT-proBNP levels were observed more frequently in patients with LRTI, followed by COPD, highlighting the importance of cardiac monitoring in respiratory illnesses.

The overall dataset included 99 patients with respiratory conditions as the primary diagnosis, of whom 74 (74.7%) also had cardiovascular comorbidities, while 25 (25.3%) did not. These findings highlight the significant overlap between respiratory and cardiovascular conditions, emphasizing the interconnected nature of these systems in clinical practice. Among 58 dyspneic patients with respiratory conditions and coexisting cardiovascular (CVS) comorbidities, LRTI was the most common primary diagnosis, accounting for 36 cases. Figure 1 indicated that among 19 dyspneic patients with respiratory conditions but without CVS comorbidities, LRTI also predominated, with 13 cases, indicating it as a major contributor to dyspnea regardless of cardiovascular involvement. Additionally, out of 44 patients with abnormal NT-proBNP levels and cardiovascular diagnoses, heart failure (HF) was observed in 17 patients (38.6%) and coronary artery disease (CAD) in 14 patients (31.8%), reflecting the strong association between elevated NT-proBNP and these conditions.

Among patients with abnormal NT-proBNP levels and neuro-endocrine conditions, 6 cases were identified, with acute febrile illness (AFI) and shock each accounting for 2 cases (40% each). Elevated NT-proBNP in AFI is linked to systemic inflammation affecting cardiac function, while in shock, myocardial strain due to hypotension and poor perfusion contributes to elevated levels.

In the gastro/metabolic category, 3 patients showed abnormal NT-proBNP levels, with 2 cases of gastritis (66.7%). One dyspneic patient diagnosed with urinary tract infection (UTI) also showed elevated NT-proBNP, representing 100% of nephrology-related cases in this context. Additionally, among 3 patients with skin-related conditions, 2 with cellulitis had abnormal NT-proBNP levels (66.7%).

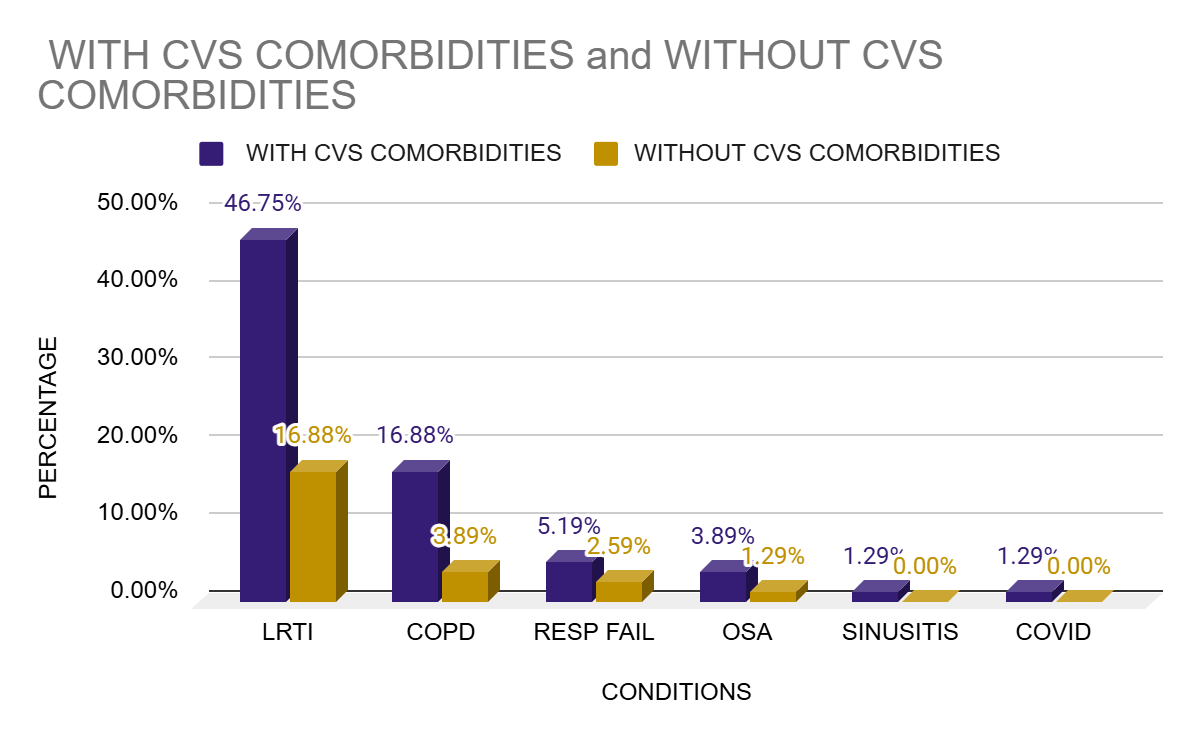
Table 5 indicated that among the 62 non-dyspneic patients, the majority with abnormal NT-proBNP levels had respiratory conditions (n=18), primarily LRTI (n=12) and COPD (n=3), followed by neuro-endocrine conditions (n=9), equally distributed among AFI, shock, and stroke (33.3% each). Cardiovascular causes accounted for 7 cases, with heart failure present in 4 patients (57.1%).

In the gastro/metabolic group of non-dyspneic patients, 6 had abnormal NT-proBNP levels, with fatty liver observed in 3 (50%). Among nephrology cases, 3 of 5 patients with abnormal NT-proBNP were diagnosed with UTI (60%). Lastly, 3 of 11 non-dyspneic patients with elevated NT-proBNP had sepsis as the primary diagnosis, contributing to 27.3%.

These findings highlight the diverse range of conditions associated with elevated NT-proBNP levels, reinforcing its role in identifying cardiac strain across various clinical presentations, both with and without dyspnea. Table 6 shows that out of 22 heart failure (HF) patients screened for NT-proBNP levels, the median value was found to be 5041 pg/ml. A t-test was performed to assess the variation in NT-proBNP levels; although a notable difference was observed, the results were not statistically significant.

Extensive research supports the utility of NT-proBNP in identifying left ventricular dysfunction and forecasting outcomes in both cardiac and systemic diseases. Kim et al. have reported its effectiveness in predicting hospital admissions due to heart failure, while Maisel et al. emphasized its early rise in systemic inflammatory responses. Building upon such literature, our study evaluates NT-proBNP not just in cardiac cases but also in system-specific and symptom-specific contexts, including dyspnea-related presentations 9.

**Figure 1: Percentage distribution of respiratory cases having dyspnea with & without CVS comorbidities**

****

**Table 1: Comparison of biomarkers**

|  |  |
| --- | --- |
| BIOMARKERS | PERCENTAGE% (N) |
| TROP-I | 64.3% (142) |
| D - DIMER | 35.7% (79) |

**Table 2: Screening Assessment of Trop-I levels, D-dimer levels and NT-pro BNP levels**

|  |  |  |  |
| --- | --- | --- | --- |
| Range | Number of patients (% patients) | | |
| **Trop-I levels** | **D-dimer levels** | **NT-pro BNP levels** |
| NORMAL | 19.47% (43) | 17 (7.68%) | 18 (21.5%) |
| ABNORMAL | 44.83% (99) | 62 (28.01%) | 182 (78.5%) |
| TOTAL | **64.3% (142)** | **79 (35.7%)** | **100% (200)** |

**Table 3: NT pro-BNP range-based distribution**

|  |  |  |
| --- | --- | --- |
| NT pro-BNP Range | Number of patients (%) | |
| **Dyspnoea** | **Non-Dyspnoea** |
| NORMAL (<400 pg/ml) | 17 (12.3%) | 6 (9.7%) |
| ABNORMAL (>400 pg/ml) | 121 (87.7%) | 56 (90.3%) |
| TOTAL | **138 (100%)** | **62 (100%)** |

**Table 4: Frequency distribution of dyspnea cases in various systems**

| **SYSTEMS** | **NORMAL (n=17)** | **ABNORMAL (n=121)** |
| --- | --- | --- |
| **RESPIRATORY** | **13** | **64** |
| **CVS** | **2** | **44** |
| **NEURO-ENDO** | **1** | **6** |
| **GASTRO/METABOLIC** | **1** | **3** |
| **NEPHROLOGY** | **0** | **1** |
| **OTHERS** | **0** | **3** |
| **TOTAL** | **17** | **121** |
| **MEAN** | **2.833** | **20.17** |

**Table 5: Frequency distribution of non-dyspnea cases in various systems**

|  |  |  |
| --- | --- | --- |
| **SYSTEMS** | **NORMAL (n=6)** | **ABNORMAL (n=56)** |
| **RESPIRATORY** | **4** | **18** |
| **NEURO-ENDOCRINE** | **0** | **9** |
| **CVS** | **1** | **7** |
| **GASTRO/METABOLIC** | **0** | **6** |
| **NEPHROLOGY** | **1** | **5** |
| **OTHERS** | **0** | **11** |
| **TOTAL** | **6** | **56** |
| **MEAN** | **1** | **9.33** |

**Table 6: Unpaired T-test**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Group** | **HF** | **CAD** | **HTN URGENCY** | **ATRIAL FIBRIL** | **IHD** | **OTHERS** |
| **Mean** | 8605.27 | 7918.38 | 6994.50 | 8364.00 | 3185.00 | 2978.40 |
| **SD** | 9941.28 | 8524.06 | 9691.06 | 6668.02 | 1200.67 | 2486.63 |
| **SEM** | 2119.49 | 2131.01 | 4845.53 | 4715.00 | 849.00 | 1112.05 |
| **N** | **22** | **16** | **4** | **2** | **2** | **5** |

**FUTURE SCOPE:**

To advance the clinical utility of NT-proBNP, future research should focus on its prognostic potential through long-term studies across diverse patient populations. This includes evaluating its predictive value in disease progression and long-term outcomes, expanding studies to include varied ethnic and socioeconomic groups, and exploring genetic and molecular factors influencing NT-proBNP levels. Additionally, integrating machine learning and AI to analyze NT-proBNP alongside other clinical data may reveal new diagnostic insights and support personalized treatment strategies. These directions could significantly enhance its application in clinical practice.

**CONCLUSION:**

This study offers a comprehensive evaluation of NT-proBNP levels across various age groups, genders, and clinical conditions, with a particular focus on differentiating between dyspneic and non-dyspneic patients. Elevated NT-proBNP levels were more commonly observed in patients presenting with dyspnea, especially among those with cardiovascular comorbidities, indicating a strong association between NT-proBNP and respiratory distress. The findings underscore NT-proBNP’s value not only as a diagnostic marker for cardiovascular diseases but also its broader utility in identifying other systemic conditions. These insights are particularly valuable for clinician’s managing patients with complex, multi-system involvement. The study highlights the importance of incorporating NT-proBNP testing into routine evaluations of patients presenting with dyspnea to support early detection of heart failure and improve clinical outcomes.

**REFERENCES:**

1. Weber M, Hamm C. Role of B-type natriuretic peptide (BNP) and NT-proBNP in clinical routine. Heart 2006;92(6):843–849. DOI: 10.1136/ hrt.2005.071233.

2. Ventetuolo CE, Levy MM. Cardiac biomarkers in the critically ill. Crit Care Clin 2011;27(2):327–343. DOI: 10.1016/j.ccc.2010.12.004.

3. Welsh P, Campbell RT, Mooney L, et al. Reference ranges for NT-proBNP (N-terminal pro-B-type natriuretic peptide) and risk factors for higher NT-proBNP concentrations in a large general population cohort. Circ Heart Fail 2022;15(10):e009427. DOI: 10.1161/ CIRCHEARTFAILURE.121.009427.

4. Chaikijurajai T, Demirjian S, Tang WHW. Prognostic value of natriuretic peptide levels for adverse renal outcomes in patients with moderate to severe acute kidney injury with or without heart failure. J Am Heart Assoc 2023;12(21):e031453. DOI: 10.1161/JAHA.123.031453.

5. Rørth R, Jhund PS, Yilmaz MB, et al. Comparison of BNP and NT-proBNP in patients with heart failure and reduced ejection fraction. Circ Heart Fail 2020;13(2):e006541. DOI: 10.1161/CIRCHEARTFAILURE.119.00 6541.

6. Ibrahim NE, Januzzi JL. Established and emerging roles of biomarkers in heart failure. Circ Res 2018;123(5):614–629. DOI: 10.1161/ CIRCRESAHA.118.312706.

7. Searle J, Frick J, Möckel M. Acute heart failure facts and numbers: acute heart failure populations. ESC Heart Fail 2016; 3: 65-70.

8. Phua J, Lim TK, Lee KH. B-type natriuretic peptide: Issues for the intensivist and pulmonologist. Crit Care Med 2005;33(9):2094−2113. DOI: 10.1097/01.ccm.0000178351.03327.9f.

9. Maisel, A. S., Daniels, L. B., Breidthardt, T., Conen, D., Christenson, R. H., Andrey, J.L., & Bayes-Genis, A. (2008). Natriuretic peptides in heart failure with preserved ejection fraction. Heart Failure Clinics, 4(4), 511-523.