



## N-TERMINAL PRO BRAIN NATRIURETIC PEPTIDE: A POTENTIAL PREDICTOR FOR INTENSIVE CARE ADMISSIONS IN PATIENTS WITH ACUTE EXACERBATION OF COPD.

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### ABSTRACT

**BACKGROUND:** Cardiovascular disease is one of the major causes of mortality and is frequently unrecognized in COPD patients. Serum N-terminal pro-brain natriuretic peptide (NT-pro BNP) is an established risk factor in patients with Heart failure. However NT-pro BNP levels may also be elevated during acute exacerbation of COPD(AECOPD) even without heart failure. Objectives of the study are-(a)To find the levels of Serum NT-pro BNP in AECOPD patients. (b) To find out the association of Serum NT-pro BNP with clinical and physiological parameters in AECOPD patients.

**METHODS:** This cross-sectional study was carried out on 60 AECOPD patients admitted in department of Respiratory Medicine, Institute of Respiratory Diseases, SMS Medical College, Jaipur during July 2019–June 2020. Clinical data including vitals, Electrocardiogram (ECG), arterial blood gas analysis (ABG), Serum NT-pro BNP levels were assessed. Previous ECG and spirometry details were also recorded.

**RESULTS:** The mean levels of Serum NT-pro BNP were higher in very severe COPD patients. The association of Serum NT-pro BNP were significantly higher with AECOPD patients having increased exacerbations per year, longer hospital stay duration, decreasing Spo<sub>2</sub> levels and decreasing blood pH levels.

**CONCLUSION:** Patients with AECOPD who had elevated Serum NT-pro BNP levels had higher likelihood of ICU admission and longer hospital stay. Thus elevated NT-pro BNP levels warrants the need of Intensive care for early and better management of COPD patients.

**KEYWORDS :** Cardiovascular disease, COPD, NT-pro BNP, Intensive care.

### INTRODUCTION

Exacerbations of COPD are a leading cause of hospitalization and healthcare expenditures. It alters the health-related quality of life and the natural course of disease, increasing the risk of mortality, both during and after the acute event<sup>(1)</sup> So COPD exacerbations account for the greatest proportion of the total COPD burden on the health care system.

Cardiovascular disease is a major cause of mortality in COPD. Moreover it often remains undiagnosed in these patients<sup>(2)</sup> because the symptoms and signs of MI and heart failure may mimic an acute exacerbation of COPD (AECOPD) and also because the classic symptom and sign of MI i.e. chest pain and ECG changes are poorly associated with myocardial injury during AECOPD<sup>(3)</sup>

The cardiac peptide N-terminal fragment of its prohormone pro-BNP (NT-pro BNP) is mainly released by cardiac myocytes in ventricles owing to volume overload states as in Heart failure, chronic kidney disease, Pressure overload states as in heart valve abnormalities and myocardial ischemia as in coronary artery disease. It is an established biomarker of heart failure<sup>(4)</sup> and is primarily used for diagnosis, risk stratification and management of heart failure. However NT-pro BNP levels may also be elevated during acute exacerbation of COPD(AECOPD) even without heart failure<sup>(5)</sup> secondary to hypoxemia, secondary pulmonary hypertension and cor-pulmonale which act as stimuli for its release from ventricles of heart.

Present study aims at assessing the association of NT-pro BNP with clinical and physiological parameters in AECOPD patients apart from assessing the levels of NT-pro BNP among them.

### MATERIALS AND METHODS

The present study consisted of 60 acute exacerbation of COPD patients of either sex, aged >45 years who have admitted at the department of the hospital from July 2019 to June 2020. Patients were excluded based on the following criteria:(i) Patients having diabetes mellitus and systemic hypertension(ii) Cardiovascular diseases with congestive heart failure(iii) Other respiratory diseases such as bronchial asthma, suppurative lung disease, interstitial lung diseases, lung malignancy, obstructive sleep apnea. Approval of the Institutional Ethical Committee was taken prior to the study.

COPD Exacerbation is recognized based on Clinical symptoms(increased shortness of breath/increased cough frequency or severity/increased sputum amount or purulence),Physical examination(use of accessory muscles of respiration, wheezing). The admitted AECOPD patients clinical data including symptoms and physical examination, number of admissions with AECOPD during the 12 months prior to admission, Previous ECG records and spirometry records to grade severity of COPD were recorded. Vitals including heart rate, blood pressure, body temperature, respiratory rate, arterial oxygen saturation (Spo<sub>2</sub>) by pulse oximetry were also recorded. Chest Radiography, Arterial blood gas analysis, Electrocardiography(ECG) were done.

### Laboratory analysis of NT-pro BNP

5ml of venous blood sample is taken from antecubital vein and is transferred to a tube containing ethylenediaminetetraacetic acid and centrifuged at 3000 revolutions/min for 15 min. The plasma was stored at -70°C until analysis. NT-pro BNP was measured via enzyme immunoassay.

### Statistical analysis:

Data analysis was performed using descriptive statistics, independent samples t-test, and one way analysis of variance in the SPSS software, version 20. In all the measurements, P-value less than 0.05 was considered statistically significant.

**RESULTS**

Our study showed that majority of the patients (55%) were seen in more than 60 years of age group and majority were male(43/60) with most common complaint being shortness of breath(90%).

Table 1 depicts that the mean value of NT -PRO BNP level with mild, moderate, severe and very severe subgroups of AECOPD were 213.2 60.44, 303.53 54.21, 352.93 46.47, 462.6 76.15 respectively. The comparison of NT -PRO BNP level was statistically significant (P<0.0001\*\*\*) in between severity of AECOPD among cases group.

Table 2 depicts that the mean levels of NT -PRO BNP with no. of exacerbations of 1, 2, 3, 4 and 5 per year were 213.2 64.27, 213.2 62.03, 333.95 85.62, 412.47 90.28, 386.73 71.35 respectively. The comparison of NT -PRO BNP level was statistically significant (P<0.0001\*\*\*) in between no. of exacerbation per year among cases group.

Table 3 depicts that the mean levels of NT-PRO BNP with duration of hospital stay of 3 days, 4-6 days and >6 days were 325.07 122.71, 339.73 97.95, 344.8 78.65 respectively. The mean levels of NT- PRO BNP was statistically significant (P=0.0480) in between duration of hospital stay among cases group.

Table 4 depicts that the mean levels of NT -PRO BNP with SPO2 levels of 60%, 61%-70%, 71%-80%, 81% - 90%, 90% were 484.0 20.15, 379.57 85.15, 399 90.15, 289.96 82.82, 213.14 57.73 respectively. The comparison of NT -PRO BNP level was statistically significant (P<0.0001\*\*\*) in between various SPO2% levels among cases group.

**Table 1:-NT -PROBNP Level with Severity of AECOPD in patients**

Severity of AECOPD	No. of patients	NT -PRO BNP Level (Mean SD)	P-value
Mild	12	213.2 60.44	<0.0001***
Moderate	10	303.53 54.21	
Severe	22	352.93 46.47	
Very Severe	16	462.6 76.15	

**Table 2:- Association of NT -PRO BNP Level with number of Exacerbation Per Year among AECOPD patients**

No of Exacerbation Per Year	No. of patients	NT -PRO BNP Level (Mean SD)	Percentage
1	5	213.2 64.27	<0.0001***
2	10	213.2 62.03	
3	19	333.95 85.62	
4	15	412.47 90.28	
5	11	386.73 71.35	

**Table 3:- Association of NT -PRO BNP Level with duration of stay in hospital (days) among AECOPD patients**

Duration of stay in hospital (days)	No. of patients	NT -PRO BNP Level (Mean SD)	Percentage
3 days	29	325.07 122.71	0.0480
4 days - 6 days	26	339.73 97.95	
>6 days	5	344.8 78.65	

**Table 4:- Association of NT -PRO BNP Level with hypoxemia in AECOPD patients**

SPO2% level	No. of patients	NT -PRO BNP Level (Mean SD)	Percentage
60%	5	484.0 20.15	<0.0001***
61%-70%	7	379.57 85.15	
71%-80%	14	399 90.15	
81% - 90%	27	289.96 82.82	
90%	7	213.14 57.73	

**Table 5:- Association of NT -PRO BNP Level with pH level of blood in AECOPD patients**

Blood pH	No. of patients	NT -PRO BNP Level Mean SD	P-value
7-7.24	15	451.53 82.15	<0.0001***
7.24	45	293.58 84.57	

**DISCUSSION**

Our study showed the mean values of NT -PRO BNP level was 462.6 76.15 pg/ml in very severe AECOPD patients and 213.2 60.44 pg/ml in mild cases of AECOPD. The comparison of NT -PRO BNP level was statistically significant (P<0.0001\*\*\*) in between severity of AECOPD in our study. A similar results were obtained by Sin DD et al<sup>(6)</sup> who found COPD to be an independent risk factor for increased NT-proBNP levels, and the levels increased with the severity of COPD. A single study in 170 patients reported the proportion of patients with elevated BNP stratified by COPD severity [30]. NT-proBNP was elevated in GOLD stages I to IV in 21, 21, 23 and 28% of patients, respectively (p = 0.87).

Our study showed that majority of AECOPD patients (19/60, 31.66%) had 3 exacerbations per year in our study. The association of NT -PRO BNP level was higher with increased number of exacerbations per year. The comparison of NT -PRO BNP level was statistically significant (P<0.0001\*\*\*) in between no. of exacerbations per year. A similar study done by Farnoosh Ebrahimzadeh et al<sup>(7)</sup> found that there was a significant relationship between the mean serum level of NT-pro BNP and number of exacerbations per year(P=0.009).

Our study showed that majority of the patients (29/60, 48.33%) had duration of hospital stay of less than 3 days followed by 26 (43.34%) patients with duration of hospital stay between 4 days to 6 days and only 5 patients had duration of hospital stay of more than 6 days. The association of NT -PRO BNP level was higher with increased duration of hospital stay of AECOPD patients and is statistically significant (P=0.04). However a similar study done by Farnoosh Ebrahimzadeh et al<sup>(7)</sup> found that there was no significant relationship between the mean serum level of NT-pro BNP and the length of stay in hospital (P=0.1). Another study done by Muhammad Adrish et al<sup>(8)</sup> found Patients with elevated NT-pro-BNP levels were more likely to require intensive care (63% vs 43%; P=0.0207) and had a longer hospital length of stay (P=0.0052).

Our study showed that levels of NT -PRO BNP were seen lower with higher SPO2% levels in AECOPD patients in our study. The comparison of NT -PRO BNP level was statistically significant (P<0.0001\*\*\*) in between various SPO2% levels. A similar study done by Farnoosh Ebrahimzadeh et al<sup>(7)</sup> observed that there was a significant relationship between mean serum level of NT-pro BNP and hypoxemia, and the mean serum level of NT-pro BNP was higher in patients with hypoxemia (SpO2<90%). Hypoxia causes natriuretic peptides secretion by two mechanisms: the first mechanism suggests that hypoxia is the most important factor in the development of pulmonary hypertension and right ventricular wall stretch or tension by induction of pulmonary vasoconstriction, the second mechanism suggests that hypoxia causes direct release of BNP from myocardium<sup>(9)</sup>

Our study showed that majority of cases (75%) had more than 7.24 blood pH and 25% cases had blood pH between 7-7.24. We found inverse correlation between blood pH and N-terminal pro BNP level. The comparison of NT-PRO BNP level was statistically significant (P<0.0001\*\*\*) in between blood pH levels. A similar study done by Farnoosh Ebrahimzadeh et al<sup>(7)</sup> who observed that there was a significant relationship between the mean serum level of NT-pro BNP and blood pH(P=0.001). The serum level of NT-pro BNP was higher in patients with blood pH under 7.25 and 7.25-7.30. A similar results found with Hatem El Mallawany et al<sup>(10)</sup> who reported significant inverse correlation between pH and N-terminal pro BNP level.

**CONCLUSION**

Patients with AECOPD who had elevated Serum NT-pro BNP levels had higher likelihood of ICU admission and longer hospital stay. Thus elevated NT-pro BNP levels warrants the need of intensive care for early and better management of COPD patients.

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