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ORIGINAL ARTICLE

Predictive Value of NT-PRO-BNP for Morbidity and Mortality among Patients of COPD without Underlying Left Ventricular Dysfunction

HINA KHAN[1], AASIA MAZHAR SHAH[2], RABIA QAYOOM SHAIKH[3], NAILA MASOOD SIDDIQUI[4], IMRAN ALI SHAIKH[5]
[1]*Women Medical Officer, Medical Unit 1, Liaquat University Hospital Hyderabad Sindh, Pakistan*
[2]*Women Medical Officer, Medical Unit 1, Liaquat University Hospital Hyderabad Sindh, Pakistan*
[3]*Postgraduate FCPS, Medical Unit 1 Liaquat University Jamshoro*
[4]*Professor, Liaquat University of Medical and Health Sciences Jamshoro Sindh, Pakistan*
[5]*Professor of Medicine, Liaquat University of Medical and Health Sciences Jamshoro Sindh, Pakistan*
Correspondence to: Dr Imran Ali Shaikh, Email: Imran.shaikh@lumhs.edu.pk

ABSTRACT

Introduction: Elevated pro BNP level is associated with increased morbidity and mortality in various cardiac and pulmonary conditions, also considered a valuable prognostic tool in acute exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) without underlying left ventricular dysfunction and also for prognosis of the disease.

Objective: To assess the predictive value of proBNP for morbidity and mortality among patients with AECOPD patients without underlying left ventricular dysfunction and on follow up.

Study Design: Prospective Cohort

Setting: All Medical Wards & Pulmonology Ward– Liaquat University Hospital Hyderabad.

Duration of Study: Six months, May 2022 –December 2022

Subjects and methods: 217 diagnosed patients of COPD (132 male & 85 female) were enrolled by non-probability consecutive technique. All these patients were followed by measuring estimated NT-pro-BNP levels. The patient was followed up at day 0, 3rd day indoor, and post discharge for 6th month .Patients were excluded from any form of LV dysfunction or other pulmonary diseases.

Results: The mean age was 52.02 ±3.72 years. There were 39.2% females and 60.8% males. COPD stage I was observed in 16 (7.4%), stage II in 81 (37.3%), stage III in 52 (24%), and stage IV in 68 (31.3%) patients. The mean PaO2 was found to be 87.96 ±8.55%. In-hospital morbidity was observed in 77 (35.5%) whereas in-hospital mortality was observed in 54 (24.9%) patients. A significant mean difference of in NT-pro-BNP level was observed in between groups. The mean Pro BNP was significantly higher on 0 day , reduced on 3rd day but after 6month its value again raised, i.e., 142.27 ±11.63,127.56 ±13.67 and 145.68±16.89 respectively (p-value <0.001).

Conclusion: A significantly higher NT-pro BNP was associated with mortality and morbidity despite of normal LV function in indoor patients of COPD. Persistence elevated Pro BNP has been demonstrated positive predicted values.

Keywords: NT-pro-BNP, acute exacerbation of Chronic Obstructive Pulmonary Disease, left ventricular dysfunction.

INTRODUCTION

The chronic bronchitis and emphysema accounts for 5% of mortality all over the globe and more than 60 million people are affected[1]. These two different obstructive lung pattern became leading cause of death after coronary artery disease [2.] A systematic review encompassing 28 developed and developing nations, the worldwide combined prevalence of COPD demonstrated 7.6%.

Research conducted by Finkelstein et al has shown that individuals diagnosed with COPD face a substantially elevated risk of developing various cardiovascular diseases.[3]

Studies have found that more than twenty percent of patients with moderate chronic obstructive disease had undiagnosed heart failure of any class, which emphasized the importance of through investigation of patients .[4]

Few cohort studies shown that high BNP/NT-proBNP levels are a strong predictor for assessing the severity of COPD, predicting mortality from 1 month to 1 year, early symptomatic left ventricular involvement, without overt coronary artery disease.[5]

The Beta natriuretic peptide is released from cardiac cells and sometimes by fibroblasts due to stretch over myocardium. This secretion is a consecutive manner , that is only secreted when ProBNP gene is stimulated .Furthermore, elevated levels of these peptides are also detected in COPD patients even without heart failure and could possibly released from the left and right sides of the heart.[6,]

An increased levels of NT-proBNP is associated with corpulmonale and secondary pulmonary hypertension but low PCO2 is an important etiology for the release of NT-proBNP from the right side of the heart .[7]

Currently that has published, that NT-proBNP is important indicator in many instances, including COPD, where someone correlates its level of severity of disease .[8]

One study suggested that prolonged CO2 retention leads to pulmonary hypertension in COPD patients with increased pulmonary vascular pressure and right heart failure, stimulating increased secretion of NT-proBNP, which is an indicator of poor patient prognosis.[9]

The rationale for researching NT-proBNP levels in acute and stable COPD patients without underlying left ventricular dysfunction is to establish a new sero marker for better diagnostic and prognostic value in managing COPD patients with normal left ventricular function.

METHODS

217 indoor patients were selected from Liaquat university hospitals Hyderabad and Jamshoro Sindh Pakistan branches by nonprobability consecutive sampling after approval of the research from Ethical Review Committee, LUMHS, letter no LUMHS/REC/ 78 20.04.2021.

All patients presenting to the study were included after taking written informed consent. Data was collected using a well-structured questionnaire, which contained basic bio data, socio-demographic details, disease history, presenting complaints, GOLDs classification and smoking status. Patient s NT-pro-BNP levels were monitored and the clinical condition at days 0 &3 in-hospital morbidity and mortality, then patients were followed for 6 month after discharge. NT-Pro-BNP was measured 3 times ,0 at time of admission, on the 3rd day and 6th month.

For NT-pro-BNP 3cc blood sample was obtained from main vein aseptically and was sent to the Diagnostics & Research Lab, LUMHS. Alere NT-pro-BNP for Alinity I reagent kit, Ref 04S7920 was used.

ABGs were done by taking arterial sample from the radial or femoral artery which was easily accessed after explaining whole procedure to patient and obtaining permission, around 2cc sample were taken aseptically and placed on ABG machine SSIEMENS RAPID Lab 348EX model No.10844678.Ꭻ-stat method used to calculate.

The cost of the test was bear by authors. The anonymity and confidentiality of the patients was protected by assigning codes to the data set, instead of names and keeping the data password protected.

INCLUSION CRITERIA

- Diagnosed Cases of COPD either Sex
- Consenting patients
- Aged > 40 Years
- Presenting with AECOPD

EXCLUSION CRITERIA

- Non-consenting patients.
- Patients with Occupational Lung Diseases & Lungs Vascular Diseases
- Patients with underlying left ventricular dysfunction
- Patients with tuberculosis, lung malignancy, pulmonary fibrosis, pulmonary embolism, Interstitial Lung Disease, Myocardial Infarction or valvular heart diseases.

Statically analysis: The statically analysis was done on SPSS version 22. Quantitative data (weight, Age, height, BMI, sex, COPD stages. PaO2& NT-pro-BNP levels were expressed as mean & standard deviation (X ± SD). Chi square test was used for categorical data analysis to assess the significance of the eventual association. INOVA was used to determine the association between altered NT-pro-BNP levels with 0 day, 3 day in-hospital, morbidity and mortality. Student T Test was applied on Pre & Post discharge ProBNP levels. P value ≤ 0.05 was considered statistically significant.

RESULTS

The mean age of the patients was 52.02 ±3.72 years. (Table 1). Gender distribution showed that 85 (39.2%) patients were females and 132 (60.8%) were males. The patients were divided into < 52 years and > 52 years (Chart 1). The BMI of the patients was 26.63 ±5.11 kg/m^2 respectively. (Tables 2) COPD stage I was observed in 16 (7.4%), stage II in 81 (37.3%), stage III in 52 (24%), and stage IV in 68 (31.3%) patients. (Chart 2) The mean PaO2 was found to be 87.96 ±8.55%. (Table 3) A significant mean difference of NT-pro-BNP level was observed in between groups. The mean was significantly higher on time of admission but on 3rd day it declined, i.e., 142.27 ±11.63 and 127.56 ±13.67 respectively but again it raised after 6 month 145.68±16.89 (p-value <0.001), as shown in (Table 4). The p-value of Pro BNP was <0.001 indicated a highly significant difference from a baseline or control value at morbidity and mortality at time of admission and increased after 6 months.(Table 5 & 6)

Table 1: Mean age of the patients, years (n=217)

Mean ±SD	Minimum	Maximum
52.02 ±3.72	40	69

Table 2: Mean BMI of the patients, kg/m^2 (n=217)

Mean ±SD	Minimum	Maximum
26.63 ±5.11	18.70	33.00

Table 3: Mean PaO2 of the patients, % (n=217)

Mean ±SD	Minimum	Maximum
87.96 ±8.55	65	105

Table 4: Mean difference of NT-pro-BNP and P-value (n=217)

NT-pro-BNP	Mean ±SD	p-value	95% CI
On Admission	142.27 ±11.63	<0.001	13.46 to 15.94
On 3rd day	127.56 ±13.67		
After 6 Month	145.68±16.89		

Table 5: In-hospital morbidity & mean of NT-pro-BNP on 0 day, 3rd day after 6 months (n=77)

NT-pro-BNP	Mean ±SD	p-value	95% CI
On Admission	141.29 ±10.50	<0.001	11.72 to 13.38
On 3rd day	127.53 ±13.44		
After 6 Month	147.07±16.7		

Table 6: No In-hospital mortality & mean of NT-pro-BNP on 0 day, 3rd day, after 6 months (n=163)

NT-pro-BNP	Mean ±SD	p-value	95% CI
On Admission	142.65 ±11.59	<0.001	13.17 to 16.08
On 3rd day	128.02 ±13.65		
After 6 Month	147.09±16.00		

Chart 1: Age wise distribution

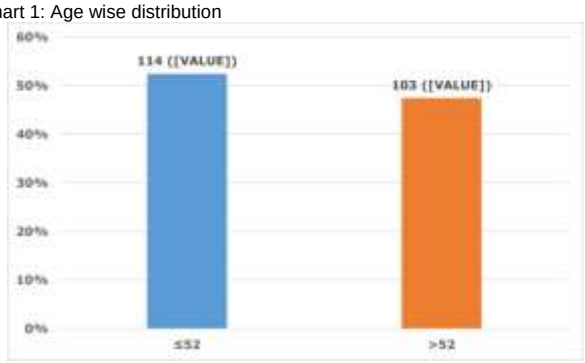
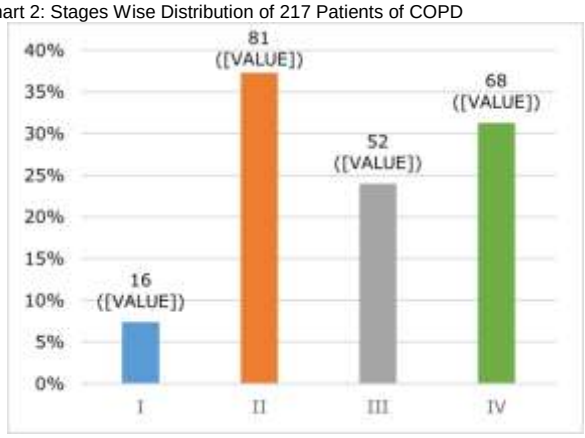


Chart 2: Stages Wise Distribution of 217 Patients of COPD



DISCUSSION

This study was conducted to assess the levels of NT-pro-BNP at three different time points. The findings suggested that there was a measurable and statistically significant change in the levels of NT-pro-BNP between three time points, which could indicate that the intervention or treatment had an impact on the heart's function.

Medina et al [10]conducted a prior study to an evaluate the prognostic significance of NT-pro-BNP in patients experiencing acute exacerbation of COPD.

In another study, notable connections were observed between elevated seromarker BNP levels, systolic pressure, along with left ventricular dysfunction in patients with asymptomatic chronic lung disease.[11]

According to the current study, the in-hospital mortality rate is 35.5%, while a different study by Connors et al. reported a rate of 24.9%.[12]

One publication shown that NT-proBN was a very good marker for assessment of severity of COPD with pulmonary hypertension as compared to patients with normal pulmonary pressure. Increased NT-proBNP values were found to be in 16–60% patients with acute deterioration of COPD without heart involvement, and remained elevated in more than half patients after discharge.[13]

Some researchers have observed a significant increase in NT-proBNP levels in COPD patients with normal heart function, which is match able to our study showed high BNP levels after 6 months of hospital admission for acute exacerbation of COPD.[14]

In our study, patients were classified in to four stages of GOLD criteria and showed higher Pro BNP with an advanced

stage which is match able to one study demonstrated plasma levels of pro BNP correlated with the severity of GOLD class .[15]

The findings of our study should be considered with certain limitations, such as being conducted in a single center with a limited number of samples. Additionally, certain crucial predictor variables were not reported in this study.

Nevertheless, despite these limitations, the study has presented significant findings from one of the largest public sector hospitals in Hyderabad. Our study invites other researches for elaborate further by doing large scale cohort.

CONCLUSION

A significant mean of seromarker NT-pro-BNP level was observed at 0 day, at 3rd day after 6 months suggested that there was a measurable difference the levels of NT-pro-BNP that conclude morbidity and mortality impact. This will need large studies for incorporation into the guidelines.

This study concluded that NT-Pro-BNP level should include in the diagnostic workup of the COPD patients with normal LV function findings

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