Cardiac Biomarkers in Exacerbation of Chronic Respiratory Diseases

Rohit K O[1], Reshma Sivanandan A[2]

ABSTRACT

Introduction: Respiratory and cardiac comorbidities can often coexist and during exacerbation it is difficult to distinguish them. In patients with chronic respiratory diseases, during exacerbation cardiac biomarkers are frequently seen elevated.Objectives: To assess the prevalence of elevation of cardiac biomarkers (troponin I & BNP) during exacerbation of chronic respiratory conditions.

Materaila and methods: Patients with chronic respiratory disease exacerbations requiring in hospital treatment was enrolled in our study retrospectively. Troponin I and BNP and disease severity was recorded.

Results: COPD followed by asthma was the moajor respiratory co morbidities. Troponin was positive in 21.6% and BNP in 44.8%. Severity of PAH was in relation to BNP positivity but not with Troponin.

Conclusion: During exacerbation of chronic respiratory diseases, a significant number of patients show elevated cardiac biomarkers. Pulmonary hypertension is directly related to the elevated BNP.

Keywords: Troponin, BNP, Respiratory Diseases, Exacerbations

MeSH Terms: Troponin, Natriuretic Peptide, Pulmonary Disease

INTRODUCTION

Respiratory disease exacerbations accounts for majority of admissions in any medical ward. Major symptoms include dyspnoea, cough and increased sputum production. Worsening of dyspnoea and cough can also be due to associated cardiac comorbities. It is usually difficult to distinguish cardiac and respiratory diseases based on symptomatology alone.[1] Chronic obstructive pulmonary disease (COPD) is the leading respiratory disease and accounts for the third leading cause for mortality worldwide.[2]

Brain natriuretic peptide(BNP) is one of the three major natriuretic peptide involved in circulatory homeostasis. BNP is produced from ventricular myocardium and in pathological states atrial chambers also can produce it. Similar to ANP(Atrial natriuretic peptide) BNP induces natriuresis, diuresis and vasodilation and reduces the cardiac stress from volume overload.[3] It serves as a marker of cardiac pressures and pathological ventricular wall distension.[4] Troponin I is regulatory protein involved in the actin-myosin interaction of cardiac muscle. Rising or falling pattern with at least one value >99th percentile is indicative of myocardial infarction.[5] Numerous other conditions like pulmonary embolism, respiratory failure, COPD exacerbation, sepsis etc. also can elevate troponin level.[3] Even in the absence of acute myocardial infarction, this troponin I elevation is associated with increased risk of mortality.[3,6]

Our objective was to assess the prevalence of elevation of these cardiac markers in chronic respiratory disease exacerbation and its relation with pulmonary hypertension.

MATERIAL AND METHODS

This is a retrospective study done in patients admitted in our centre with exacerbation of respiratory disease. 207 adult patients with chronic respiratory diseases admitted from 2018 March to 2019 February were included. Patients with sepsis, acute or chronic renal failure, acute myocardial infarction, cardiac arrest and acute pulmonary embolism were excluded. Patient's medical history, baseline characteristics, routine blood investigations and chest x ray findings were recorded. Troponin I and BNP levels were done within 24 hours of admission and categorised as normal or elevated based on local reference values. Troponin I >0.02 ng/ml and Brain natriuretic peptide (BNP)>100 pg/ml were taken as positive. Patients Echo findings and X ray features were also noted. Chi square test was used to compare different variables. Mann-Whiteny U test was done for comparing CRP levels with the two cardiac biomarkers.

RESULTS

Data of 207 patients admitted in our centre from 2018 March to 2019 February was analysed retrospectively. Mean age of the population was 69.7±10.6 with male predominance. Baseline characters are shown as in Table 1.

Among primary respiratory problem COPD accounted for 55.6% followed by asthma (19.3%). There were 27 patients with bronchiectasis and 16 with interstitial lung disease. 21 patients were on home oxygen. Only 3.8% patients had associated cardiac problem with left ventricular dysfunction in 5 and hypertrophic obstructive cardiomyopathy (HOCM) in 3 patients.

In our study patients 60 had features of pneumonia causing exacerbation of underlying disease but majority (71%) had no change in X ray chest. 16 patients were having interstitial lung disease based on their CT findings.

Troponin I and BNP was done on the first day of admission

[1]Pulmonologist, Holy Ghost Mission Hospital, Kottayam, Kerala, [2]Assistant Professor, General Medicine, Kottayam, Medical College, Kottayam, Kerala

Corresponding author: Rohit K O, Pulmonologist, Holy Ghost Mission Hospital, Kottayam, Kerala, India

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on 162 and 174 patients respectively. Mean Troponin was 0.03± 0.07. 35 patients (21.6%) were positive. Mean BNP was 238±428.4 and 78 patients (44.8%) were positive.

135 patients were evaluated with Echocardiogram during admission and pulmonary hypertension (PAH) was found in 81(60%). Table 3 shows percentage of patients in different group of pulmonary hypertension in relation to BNP and Troponin level. Among patients with Pulmonary hypertension 44 patients (54.3%) had elevated BNP while patients with no pulmonary hypertension 21 (38.8%) had elevated BNP level. Statistical evaluation showed significant (P=<0.001) difference between these two. Table 3 also shows that the percentage of patients with BNP positivity increases with the severity of PAH. However the troponin level were not in relation to the PAH. Troponin was high in 15(22%) and 12(26%) patients in patients with PAH and without PAH respectively. This shows the PAH group had low positivity of Troponin. There was no significant relation of Troponin level with severity of PAH.

There was no significant difference in the number of cases with elevated Troponin and BNP. BNP was significantly high among female patients than males while troponin did not show any gender difference. Higher value of CRP was associated with positivity of troponine and BNP. There was no significant relation between number of days in hospital verses troponin I and BNP level. Only 2 patients were died during hospital admission. A bronchiectasis and COPD patient with infective exacerbation were died and both had negative Troponin and BNP at the time of admission.

Echocardiography showed left ventricular dysfunction in 11(5.3%) patients with severe LV dysfunction in 5, moderate LV dysfunction in 5 and mild LV dysfunction in one patient. 54% of these had elevated BNP and 57% had elevated Troponin. BNP and Troponin elevation was more with severe LV dysfunction.

Features	Number(Percentage)
Males	138 (66.7%)
Females	69 (33.3%)
Mean age	69.7±10.6.
Diabetes	91
Hypertension	103
Coronary disease	53
Mean duration of hospital stay	7.1±3.8
NIV/Ventilator support	66

Table-1: Baseline characteristics

Lung diseases	
Disease	**Number**
COPD	115
CTEPH (Chronic thromboembolic pulmonary hypertension	1
ILD (Interstitial lung disease)	16
Kyphoscoliosis	1
Sarcoidosis	1
ABPA(Allergic bronchopulmonary aspergillosis)	6
Asthma	40
Bronchiectasis	27
Cardiac diseases	
Normal	199
Left ventricular failure	5
HOCM	3

Table-2: Underlying pulmonary and cardiac diseases.

DISCUSSION

Our study showed a significant number of patients with elevated cardiac biomarkers during exacerbation of their underlying respiratory disease. BNP and Troponin was elevated in 44.8% and 21.6% respectively. Even though our study group had low number of patients with cardiac comorbities there was a significant number of patients with elevated cardiac markers. Since exclusion of conditions like acute myocardial infarction, renal failure, sepsis which can alter blood levels of BNP & Troponin were done, our study group could represent respiratory cases mainly. To our knowledge this is the only study which evaluated the relation of both Troponin and BNP during exacerbation of all respiratory diseases. It remains unclear that elevation of these biomarkers is due to direct cardiac involvement or just reflects the severity of respiratory exacerbation. Cardiac troponins are typically elevated in myocardial infarction and congestive cardiac failure. How ever in right ventricular dysfunction, troponin elevation is suspected to be due to right ventricular ischaemia or microinfarction from increased ventricular wall tension, metabolic demand and altered coronary perfusion even without atherosclerosis.[7,8]

A systematic review by Buchan et al shows that there is a link between elevated BNP and increased cardiovascular mortality in patients with acute exacerbation of COPD.[9] A prospective cohort study showed that elevation of Both NT – proBNP and Troponin T at admission was associated with increase in 30 day mortality. Elevation of either of these were associated with 15 fold increased risk of mortality compared with normal levels of these biomarkers.[10] Our study had low number of deaths mainly because we had excluded cases with sepsis, acute myocardial infarction renal failure etc. Like many other studies, our study had lower lumber of patients with positive Troponin when compared with BNP.[10,11] indicates that BNP is a better marker for right ventricular strain.

Our study had significant relation of BNP with the degree of pulmonary hypertension. Level of BNP is significantly high in patients with severe lung disease and with pulmonary

Result %	No PAH	Mild PAH	Moderate PAH	Severe PAH
BNP	38.8%	40.9%	68%	75%
TROP	26%	10.5%	45.5%	12.5%

Table-3: Relation of Pulmonary hypertension with BNP and Troponin

hypertension.[12] Roucco et al study in ILD patients has shown relation with PAH and BNP level.[13] In another study it was found that BNP had 85% sensitivity and 88% specificity for identifying significant pulmonary hypertension.[14] Plasma BNP level have positive correlation with mean pulmonary artery pressure and right ventricular dysfunction.[15,16] but elevation in BNP level is usually seen only if Pulmonary artery pressure is high enough to cause right ventricular strain. So its role as a screening tool for excluding PAH in low risk population is limited. But in certain conditions like systemic sclerosis BNP has proven as a screening test.[17]

In conclusion our study shows that during exacerbation of any underlying chronic respiratory disease a significant number of patients show elevated cardiac markers like Troponin I and BNP even in absence of cardiac ischaemia. This must be in relation to the transient right ventricular strain. The BNP level corresponds with the severity of associated pulmonary hypertension. From our study it is evident that respiratory disease exacerbation can have altered cardiac biomarkers and it may not imply an acute cardiac event.

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