International Journal Dental and Medical Sciences Research
Volume 5, Issue 3, May - June 2023 pp 88-93 www.ijdmsrjournal.com ISSN: 2582-6018

A Study on Cardiac Troponin-I Levels and Its Association with Acute Exacerbation of Chronic Obstructive Pulmonary Disease and In Predicting Morbidity and Mortality

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Date of Submission: 05-05-2023 Date of Acceptance: 15-05-2023

ABSTRACT

INTRODUCTION : Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable disease characterised by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases. Exacerbations and co-morbidities contribute to the overall severity in individual patients.

MATERIALS AND METHODS : This is a cross-sectional study, involved 56 patients of acute exacerbation of chronic obstructive disease satisfying inclusion criteria. Each patient's demographic, clinical, diagnostic and treatment data along with measurement of troponin levels were recorded in the study. The data was analysed using descriptive statistics.

RESULTS : The results depict that 35.71% of the COPD patients were troponin positive. In the present study, Majority of the patients were aged between 61 to 70years, male preponderance was observed. Common symptoms was breathlessness, cough, fever and edema. Increased respiratory rate and pulse rate, along with decreased SPO_2 levels and O_2 had statistically significant associations with troponin elevation group. Duration on NIV, duration on ventilator, duration of ICU stay and duration of hospital stay has statistically significant association with troponin positive group.

CONCLUSION : We conclude that elevated levels of cardiac troponin is common in patients admitted to hospital with exacerbations of COPD. High prevalence of cardiac abnormalities on ECG and echocardiography, duration on NIV, duration on ventilator, duration of ICU stay and duration of hospital stay has statistically significant association with troponin positive group. Troponin elevation has increased risk of mortality.

KEYWORDS : acute exacerbation of chronic obstructive pulmonary disease, troponin

I. INTRODUCTION

COPD has been major leading cause for morbidity and mortality. Chronic obstructive pulmonary disease(COPD) is a persistent airflow limitation which is associated with progressive chronic inflammatory response in airways and lungs to noxious particles or gases.(1) Acute exacerbations indicates progression of the disease leading to decline in lung function and increase in mortality. (2)

Cardiac dysfunction is common in acute exacerbations of COPD, even among patients without clinically suspected cardiac disorders. Cardiac diseases in COPD is rule-out measuring biomarker likeNT-proBNP and cardiac troponin levels. Cardiac troponin is released in response to myocardial injury and NT-proBNP is released due to stretching of cardiac muscles. Abnormal levels of the cardiac biomarkers in acute exacerbations of COPD are associated with a poor prognosis, irrespective of the severity of the exacerbation. (3)

The spectrum of cardiovascular complications commonly associated with COPD are Right ventricular (RV) dysfunction and pulmonary vascular disease and progress with time. Cor pulmonale defined as right ventricular enlargement caused by pulmonary artery hypertension which is a result of disease affecting the structure and function of the lungs. This can progress to right ventricular failure. During acute exacerbations in COPD, patients have an increased cardiac burden. There may be a release of cardiac Troponin-I under these circumstances which could have prognostic implications.(7)

Due to overlapping signs and symptoms of cardiac diseases and COPD, diagnosis becomes challenging. Common diagnostic modalities like ECG and chest radiography may be concealed by pulmonary changes in COPD, leading to difficulty in interpretation. (4)

Cardiac troponin has shown to be a strong predictor of increased mortality in patients with acute coronary syndrome or severe pulmonary embolism. (5) It has been found that elevated levels of cTnT in acute exacerbations is associated with increased heart rate and creatinine.(6)

Despite the substantial burden of COPD on the individual and society, cardiac diseases are

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often undiagnosed and is under-treated. This study is aimed to see if cardiac troponin-I levels play a significant role in prognosis of acute exacerbation of COPD.

II. METHODS

This was a cross sectional study. 56 Patients admitted with signs and symptoms of Acute Exacerbation of COPD to our hospital were enrolled for the study. Patients with chronic illness like chronic renal failure, hypotension, myocardial infarction, sepsis, cardiac arrest before admission, pregnancy and patients with previous history of lung surgeries or genetic disorders like cystic fibrosis, anti trypsin deficiency were excluded. Informed consent was obtained from every patient. Personal data such as age, sex, smoking habits, tobacco use, co-morbid conditions, clinical signs and symptoms patient came with were obtained.

Investigations like arterial blood gas analysis, ECG, ECHO, cardiac Troponin-I were recorded. Duration of hospital stay, requirement of ICU care, ventilator support were also noted. Blood samples for cardiac Troponin-I levels were collected on admission and 24 hours later and levels above 17 ng/L were taken as positive.

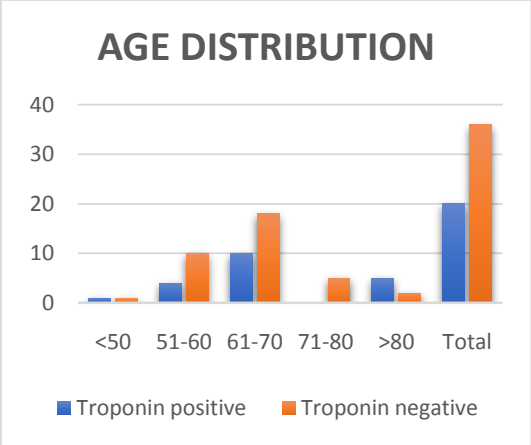
III. STATISTICALANALYSIS

Chi square test will be used as and when required for finding the correlation between Cardiac Troponin-I levels and its significance in prognosis of Acute exacerbation of COPD.

IV. RESULTS

Among the 56 patients included in the study, cardiac troponin was positive among 20 patients, which corresponds to 35.71% of the population, remaining 64.28% were cardiac troponin negative. Majority of the patients in troponin positive group and troponin negative group were between 61 to 70 years. In the study, cTnI positive group had 5% patients <50 years, 20% between 51 to 60 years, 50% were 61 to 70 years and remaining 25% were above 80years. In the cTnI negative group, 2.8% patients were <50 years, 27.8% were between 51 to 60 years, 50% were 61 to 70 years, 1.9% were between 71 to 80 years and rest 5.6% were above 80 years.

Majority of the patients were males, with 85% males in cTnI positive group and 86.1% in cTnI negative group. Mean duration of symptoms in cTnI positive group was 7.9 days of breathlessness and 4.1 days of breathlessness and cough.



Mean duration of symptoms in cTnI negative group was 0.56 days of fever, 9 days of breathlessness, 6.6 days of breathlessness and cough, and 1.22 days of edema. We observed symptoms being more in cTnI negative group compared to cTnI positive group.

Patients in cTnI positive group had a mean SPO_2 of 79.2 and patients in cTnI negative group had a mean SPO_2 of 82.82. There was statistically significant association of reduction in SPO_2 in cTnI positive group compared to in cTnI negative group.

Mean Arterial blood gas analysis shows less PCO_2 levels are higher in entire study population. There was no statistical difference between the groups. Mean Arterial blood gas analysis shows less PO_2 levels than normal in entire study population.

More do-morbidities were observed in cTnI positive group, common being IHD (15%), atrial fibrillation (15%).

On ECHO, Larger patients in cTnI positive group had Dilated right atrium/right ventricle and left atrial dysfunction. Sinus tachycardia (75%), P-pulmonale (10%) and multifocal atrial fibrillation(10%) were common in cTnI positive group. Whereas, right atrial enlargement (60.8%), Sinus tachycardia (24.2%) and left ventricular hypertrophy(8.3%) were common in cTnI negative group.

Mean duration of requirement of NIV was more in cTnI positive group. Mean duration of patients on ventilator and ICU stay were significantly longer among cTnI positive group compared to cTnI negative group.

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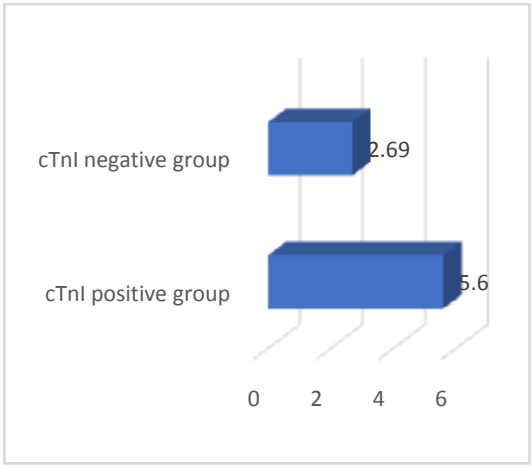
Co-morbidity	cTnI positive group		cTnI negative group	
	Frequency	Percent	Frequency	Percent
AF	3	15.0	0	0
DM	1	5.0	3	8.3
DM, HTN	2	10.0	9	25.0
HTN	1	5.0	7	19.4
HTN, IHD	1	5.0	0	0
IHD	3	15.0	1	2.8
Nil	9	5.0	16	44.4
Total	20	100.0	36	100.0



Duration of ICU stay among cTnI positive group and cTnI negative group

The mean troponin 1 levels in cTnI group was 0.1±0.3ng/ml and in cTnI negative group was 0.02ng/ml. The mean troponin 2 levels in cTnI group was 0.05±0.229ng/ml and in cTnI negative group was 0.2ng/ml. There was no statistical difference between the group in terms of PEFR and FEV1/FVC.

Majority of the patients in the study did undergo discharge but there is high percentage of mortality, though statistically significant. In patients with cTnI positive group, 20% had death and 80% were discharged. In patients with cTnI negative group, 8.3% had death and 91.7% were discharged.

V. DISCUSSION

COPD is a progressive airflow obstruction that is not fully reversible. Thus, airflow modification is used a prognostic factor in determining the effects of management of disease. Acute exacerbations are common with disease progression. These patients also present with extra-pulmonary effects, which becomes complicated for disease management. Cardiac dysfunction is also common in repeated acute exacerbations, even when there is no clinical suspicion of cardiac disorders. (2,3)

Cardiac troponins are established markers of myocardial damage, and were included in the diagnostic criteria for myocardial infarction in 2000.(8) Additionally, cardiac troponin elevation is also seen in a variety of conditions not directly related to flow-limiting coronary stenosis or occlusion of the coronary arteries, such as pulmonary embolism, septic shock, heart failure and stroke.

An exacerbation of COPD may be defined as "an acute worsening of respiratory symptoms that results in additional therapy." The triggering factors of AECOPD include infectious and noninfectious precipitants. Common respiratory symptoms in COPD are dyspnoea, cough and/or sputum, these are more than usual day-to-day variations observed in acute exacerbations requiring change in medications. Dyspnea is the most bothersome COPD symptom for many patients.

In the present study, we found that 35.71% patients were positive for elevation of troponin and 64.28% were negative for elevation of troponin. A study Brekke PH et al, 12 patients (27%) of the COPD experienced elevated cardiac troponin levels. (9) This suggests that cardiac injury exists in patients with acute exacerbation of COPD.

Abroug et al studied the accuracy of cardiac biomarkers in the diagnosis of left ventricular dysfunction in AECOPD, and troponin T was shown to have a significant value in ruling in/out left ventricular dysfunction during exacerbations of COPD. (10) Shafuddin et al,(3) revealed that cardiac biomarkers are helpful diagnostic tools for the detection of acute cardiac dysfunction during COPD exacerbations.

The present study shows similar results with the mean age of study population of 64.69 years. Patients in cTnI positive mean age was 65.15 years and cTnI negative patients was 64.69 years. As both troponin positive and negative group showed statistical significance in the current study, the overall study population shows no difference with respect to age. Although more men are diagnosed as having chronic obstructive pulmonary disease (COPD), its prevalence is increasing among women. Little is known about gender differences

in exacerbations of COPD, gender did not show any associations with elevated troponin levels.

In the present study, major presenting symptom is sudden onset breathlessness. We observed symptom duration being more in cTnI negative group compared to cTnI positive group, this could be because of the intensity of the disease being mild, these patients took time before reaching hospital. However, sudden onset breathlessness is intense and requires urgent management. As the breathlessness in patients with elevated troponin levels could be attributed to cardiac disease. These patients seeked medical support early with short duration of history.

In the present study respiratory rate was was significantly higher in cTnI positive group compared to cTnI negative group. In patients with flared by symptoms of COPD there are various factors that suggests increase in respiratory rate like pulmonary infection, airflow limitations due to allergens or disease as such requires extra efforts from the patients leading to increased respiratory rate.

Studies have shown that Patients with COPD have low levels of oxygen in their blood. Oxygen levels might be low all the time, or only at night when breathing slows during sleep. Some people use bottled oxygen through the night at home, to try and improve their breathing. The review of trials found that when people with COPD and low levels of blood oxygen did this for the long term, their survival rates improved. However, it did not lengthen survival of people whose oxygen levels were only moderately low, or only low at night. In our study there was statistically significant reduction in saturation in cTnI positive group compared to in cTnI negative group.

Brekke P et al study showed no association of blood pressure with elevated troponin levels in COPD. (9) Our study also showed similar results with no statistical difference among the group with respect to systolic blood pressure.

A study by Cukic V et al, study on blood gas analysis in COPD confirms that there is statistically significant decrease of PaO2 ($p < 0.01$) and pH, ($p < 0.05$) and an increase in PaCO2 ($p < 0.01$). It also showed that in follow up patients who received regular medications had decrease of pH and PaO_2 and increase of $PaCO_2$ in phases of exacerbations of illness.(31) Our study we found that, there was significantly less PO_2 levels in cTnI positive group compared to cTnI negative group.

In order to understand the disease as such, understanding about the risk factors and associated co-morbidities are important. keeping that in mind we considered the presence of co-morbidities while comparing the troponin levels among the groups. Our study we did not find any statistical difference among the two groups in terms of comorbidities. A study by Brekke PH et al(9), compared the co-morbidities among troponin elevated and non-elevated group. They found that prior cardiac disease like myocardial infraction, heart failure and diabetes had significant association with elevated troponin group. As we did not find any difference, it prevents the possible bias that could be attributed to co-morbidities.

ECHO is the primary test to detect associated cardiac abnormalities in COPD patients. LV Dysfunction assessed in Abroung F et al (11) study showed no association of LV dysfunction with acute COPD exacerbation. In the present study patients with elevated troponin levels had Dilated right atrium/right ventricle and left atrial dysfunction. Whereas, patients with negative troponin levels had Dilated right atrium / right ventricle(25%), left ventricular dysfunction (2.8%), left ventricular hypertrophy(8.3%) and right ventricular dysfunction(5.6%). These changes could also be due to co-morbidities like hypertension. Our findings also highlight that an accurate interpretation of ECG and chest radiographs in the setting of COPD exacerbations is difficult.

The use of non-invasive ventilation has been shown to decrease the in-hospital mortality rate among patients with COPD. Our study mean duration of patients on NIV was higher among cTnI positive group compared to cTnI negative group. Patients with COPD are prone to develop acute exacerbations, which pushes them into acute respiratory failure. A number of well conducted studies support the fact that non-invasive positive pressure ventilation (NIPPV) in these circumstances reduces rates of intubation, mortality, complications and duration of hospital stay.(12,13)

Majority of the patients in cTnI group required hospitalizations due to complications and due to need for monitoring. mean duration of hospital stay were significantly longer among cTnI positive group compared to cTnI negative group. Majority of the patients in cTnI group required hospitalizations due to complications and due to need for monitoring.

We observed that mean duration of patients in ICU were significantly longer among cTnI positive group compared to cTnI negative group. Our study mean duration of patients on ventilator were significantly longer among cTnI positive group compared to cTnI negative group.

Pulmonary complications affect up to 40% of patients, and their occurrence is associated with an increased duration of hospital stay.

In our study, positive group the mean troponin 1 level was 0.1ng/ml and troponin 2 levels were 0.05ng/ml. Elevated levels were associated with severity of the disease.

The 2011 Global Initiative for Obstructive Lung Disease (GOLD) guidelines emphasise the role of symptom assessments and exacerbation frequency, in addition to the degree of spirometric obstruction in determining the severity of COPD; this is important because patients at similar levels of FEV1 /FVC may have widely varying clinical presentations. (2,14)

Most studies in COPD have not been sufficiently powered to detect a survival benefit from the intervention, so the lack of a demonstrable effect on mortality does not necessarily mean it is not present. It can be assessed using BODE index and the inspiratory capacity to total lung capacity ratio. (31) In a historic cohort study of patients hospitalised for COPD exacerbation, found that patients with cardiac troponin T (cTnT) $\geq$ 0.04 µg/l had a mortality rate nearly twice as high as patients with no measurable cTnT in the first year after discharge.(2) Our study showed higher death rate among cTnI positive groups compared to cTnI negative group, though not statistically significant.

Our study is in par with various studies where elevation of troponin is associated with increase in mortality. It is also described that treatment of associated cardiac failure would be supported by evidence suggesting that it is a major cause of early death in patients hospitalised with COPD. Early identification of risk with the help of biomarker like troponin among COPD patients could reduced the mortality risk among these patients.

VI. CONCLUSION

In the present study, Majority of the patients were aged between 61 to 70 years, male preponderance was observed. Common symptoms was breathlessness, cough, fever and edema. Increased respiratory rate and pulse rate, along with decreased SPO_2 levels and O_2 had statistically significant associations with troponin elevation group. Common ECHO findings in troponin positive group was Dilated right atrium/right ventricle and left atrial dysfunction.

Duration on NIV, duration on ventilator, duration of ICU stay and duration of hospital stay has statistically significant association with troponin positive group. Mortality rate was higher in troponin positive group. Whereas discharge rate was higher in troponin negative group. Hence, we could conclude that early detection of troponin levels could be predicting factor in COPD prognosis.

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