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Research Article

A STUDY OF CADIOVASCULAR MORBIDITIES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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A B S T R A C T

Background: Patients with COPD associated with CVD experience high rates of morbidity, including worse quality of life, dyspnea and exercise tolerance. This study has been carried out to highlight the prevalence of cardiac co-morbidities so that future trends of management are directed with keeping them in mind.

Methods: This study was a prospective observational hospital based prevalence study. The diagnosis of COPD was based on symptoms and was confirmed by spirometry.

Results: A Total of 406 patients included, 232 (57.15%) were males and 174(42.85%) were females. The mean age of the patients with standard deviation was 68.62 + /- 9.75. Out of the 406 patients, 270 (66.50%) had stable COPD while the rest 136 (33.49%) came with exacerbations. Cardiovascular co-morbidity was present in 200 cases, out of which, 116 (58%) were males and 84(42%) were females. The different CVS co-morbidities found in this study were: 150 (36.94 %) had hypertension,104 (25.61 %) had right ventricular dysfunction, 128 (31.52 %) had coronary artery disease, 132 (32.51 %) had cardiac arrhythmias and 48 (11.82 %) had heart failure. Different types of arrhythmias found in the study population were atrial fibrillation in 12(9.11%), multifocal atrial tachycardia in 54(40.9%), sustained ventricular tachycardia in 24(18.18%) ,and non-sustained ventricular tachycardia in 42(31.81 %).

Conclusion: COPD is associated with a wide spectrum of cardiovascular co-morbidities. Males and heavy smokers have higher incidence of cardiac co-morbidities. Most of the cases with cardiac co-morbidities were in exacerbation.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by chronic airflow limitation and an increased inflammatory response of the lung [1]. COPD is associated with several comorbidities [2, 3] and can be one of multiple chronic or acute diseases present within one person [4]. Cardiovascular disease (CVD) and COPD share similar risk factors such as ageing, history of cigarette smoking and other exposures and sedentary lifestyle [2, 3, 5]. Patients with comorbid COPD and CVD experience high rates of morbidity, including worse quality of life, dyspnea and exercise tolerance [6], and a higher risk of hospitalisation for COPD and for CVD [7]. In addition, the presence of CVD conditions (such as ischemic heart disease (IHD), heart failure (HF), arrhythmias) increases the risk of frequent exacerbations [8] and mortality [9]. Further, COPD exacerbations and lung function decline are associated with increased CV risk and mortality [10,11]. To minimise the risk of poor outcomes, it is therefore important to ensure that patients with comorbid COPD and CVD are managed effectively. However, drug therapies for COPD could have both beneficial and potential adverse effects on CVD and vice versa.

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Hence it is imperative to recognize and treat them early in the course of the disease. A thorough knowledge of these conditions will create the necessary awareness to look outside lung function limitation alone and help to provide a comprehensive and tailored approach towards management of COPD to contain the overwhelming surge of its medical, social and financial impact. Though recognized for decades, data from this part of the country are very limited. Hence this study has been carried out to highlight the prevalence of cardiac co-morbidities so that future trends of management are directed with keeping them in mind.

MATERIALS AND METHODS

The present study was carried out in the Department of Pulmonary Medicine, Gauhati Medical College and Hospital for a period of one year from September 2016 to August 2018. A consecutive number of 406 COPD patients who met the inclusion criteria were included in the study. This study was a prospective observational hospital based prevalence study. It was approved by the ethical committee of the institute. Diagnosis was based on history, clinical examination, spirometry and other relevant investigation.

Aims and Objectives

1. To estimate the incidence of cardiovascular morbidity in Stable and exacerbation of COPD patients.
2. To determine the strength of association in between the increasing severity of COPD & cardiovascular diseases.

Patients ≥40 years having Cough, sputum or dyspnea for atleast three consecutive months for two years along with a history of exposure to risk factors (Tobacco smoke, biomass fuel etc.) and Spirometry showing post bronchodilator FEV1 /FVC < 0.70 were included in this study. Patients age <40 years patients with active tuberculosis, bronchial asthma, interstitial lung diseases, malignancy, patients not giving consent, patients unable to do spirometry, pregnant and hemodynamically unstable patients were excluded from the study.

The diagnosis of COPD was based on symptoms and was confirmed by spirometry. Any subject having history of dyspnea or chronic cough or sputum production for at least three consecutive months in two years, with history of exposure to risk factors (tobacco smoke, environmental tobacco smoke [ETS] , biomass fuel smoke and occupational dusts) along with a post-bronchodilator forced expiratory volume in 1st second/forced vital capacity ratio (FEV_1/FVC)<70% was confirmed as COPD [1]. An exacerbation is defined as an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and / or sputum that is beyond the normal day-to-day variations, is acute in onset and may warrant a change in regular medication in a patient with underlying COPD [1]. On the basis of the post bronchodilator FEV1 % predicted , stable COPD patients were classified into Stage I – Mild COPD (FEV_1 /FVC < 0.70, FEV_1> 80%), Stage II – Moderate COPD (FEV_1 /FVC < 0.70, 50 % ≤ FEV_1< 80%), Stage III – Severe COPD (FEV_1 /FVC < 0.70, 30% ≤ FEV_1< 50%), Stage IV– Very severe COPD (FEV_1 /FVC < 0.70, FEV_1< 30%).

Smokers were asked about whether they were cigarette smokers, bidi smokers or cannabis smokers and duration of smoking. "SMOKING INDEX" was used for QSS (quantified smoking status) and was defined as the number of bidis or cigarettes smoked in a day multiplied by the number of years smoked. Accordingly patients were divided into : Never smokers (SI-0), Light smokers (SI 1 – 100), Moderate smokers (SI 101-300), Heavy smokers (SI> 300) [12].

Those patients were included as having hypertension that had been previously diagnosed by cardiologists/medicine specialists as hypertensive and put on antihypertensive medications. New cases were diagnosed when the average of two or more diastolic BP measurements on atleast two subsequent visits was≥90 mm Hg or when the average of two or more systolic measurements on atleast two subsequent visits was consistently ≥140mm of Hg [13].

Pulmonary hypertension is defined as a mean arterial pressure of ≥25 mmHg as confirmed on right heart catheterisation. Traditionally, the pulmonary arterial systolic pressure has been estimated on echo by utilising the simplified Bernoulli equation from the peak tricuspid regurgitation velocity and adding this to an estimate of right atrial pressure. PAH was classified mild, moderate and severe as systolic pulmonary arterial pressure in between 40-60 mmHg, 60-90 mmHg and >90 mmHg respectively [14].

Right ventricle dimension was measured by M-mode echocardiography, and right ventricular dilation or Cor-Pulmonale was said to be present when it exceeded the normal range of 0.9–2.6 cm. Right ventricle contractility was also noted, and right ventricular systolic dysfunction was said to be present when it was hypokinetic.

Coronary Artery disease (CAD) patients were included as having coronary artery disease who had been previously diagnosed by cardiologists as having CAD, or had a prior history of Myocardial Infarction and on the basis of ST elevation changes on ECG and /or positive cardiac markers (troponin I, troponin T , CPK –MB). Signs on ECG are – ST depression or elevation, T wave inversion (>1mm), Q wave appearance (≥0.04s or ≥25% of R wave amplitude. 2D Echocardiography signs of CAD include left ventricular hypertrophy and/or left ventricular wall motion abnormalities .

Heart failure was diagnosed by using Framingham criteria [15]. Two major OR one major and one minor criteria from the Framingham criteria for Heart failure was used to denote patients as having heart failure.

Descriptive data are presented as frequencies (percentage) for discrete variables and as means (SDs) for continuous variables. For the comparisons between the two groups the Mann-Whitney U test was used. All statistical tests were 2-tailed, and factors were considered statistically significant at $p<0.05$. SPSS version 20 was used for all analysis.

RESULTS AND OBSERVATIONS

A total of 406 patients who fulfilled the inclusion and exclusion criteria were included in the study. A summary of the patient data is provided in Table 1. Out of a total of 406 cases, 232 (57.15%) were males and 174(42.85%) were females and male to female ratio was 1.3:1. In this study it was observed that the highest number of cases (36.95 %) were seen in the age group of 60 – 69 years followed by 34.48% in the age group of 70 -79 years and the lowest number of cases (3.43%) were in the age group of 40-49 years. The mean age of the patients with standard deviation was 68.62 ± 9.75 (Fig:1).

Table 1 Comparison of variables among patients with and without cardiovascular co-morbidity

Variable	With CVS morbidity	Without CVS morbidity	P-Value
Male	104	128	0.158
Female	96	78	
COPD- Stable	96	174	<0.0001
COPD-Exacerbation	104	32	
Non-smoker	98	84	0.511
Smoker	116	108	
Cigarette	40	36	0.7201
Bidi	73	54	0.1719
Cannabis	22	0	0.0016
Light smoker	14	30	0.0556
Moderate smoker	12	64	<0.0001
Heavy smoker	90	14	<0.0001

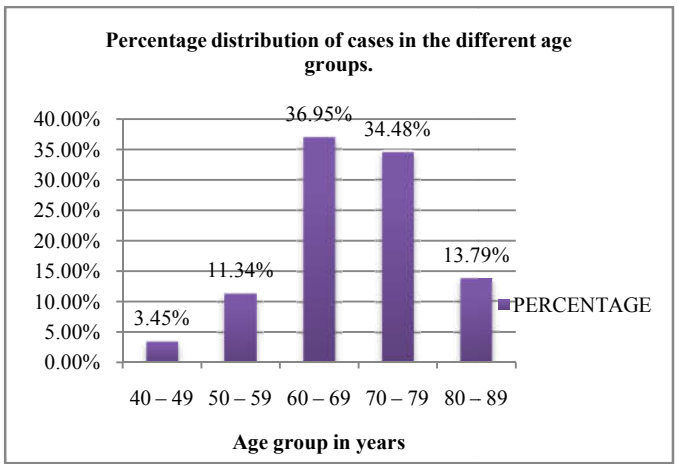

Fig 1 Bar diagram showing percentage distribution of cases in the different age groups.

In this study it was shown that out of the 406 patients, 270 (66.50%) had stable COPD while the rest 136 (33.49%) came with exacerbations. In this study group of 406 patients, 224 (55.18%) cases were smokers. Among non smoker 150 (36.94%) patients had a history of exposure to biomass fuels and 32(7.88%) had history of being exposed to environmental pollutants (Fig:2).

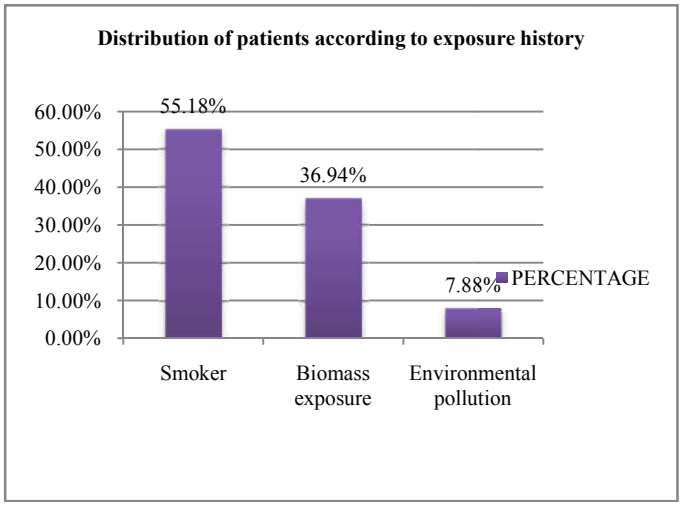

Fig 2 Bar diagram showing distribution of patients according to exposure history.

Out of 224 smoker 126 were bidi smokers, out of which, 100 (79.36%) were males and 26 (20.64%) were females, among 76 cigarette smokers 66 (86.84%) were males and 10 (13.16%) were females. All of the 22 cannabis smokers were males. Most of the patients with biomass exposure were female 122 (81.53%) and male was 28 (18.67%). In the 32 patients with environmental exposure 16 (50%) were males and 16(50%) were females. Thus in all categories of smokers, majority were males. In those with exposure to biomass fuels, majority were females (Tab:2)

Table 2 Table showing gender wise distribution of cases according to exposure history

Type of exposure	Males		Females		Total	
	n	%	n	%	n	%
Bidi	100	79.36%	26	20.64%	126	100%
Cigarette	66	86.84%	10	13.16%	76	100%
Cannabis	22	100%	0	0	22	100%
Biomass Exposure	28	18.67%	122	81.33%	150	100%
Environmental	16	50%	16	50%	32	100%

Out of 406 cases,cardiovascular co-morbidity was present in 200 cases, out of which, 116 (58%)were males and 84(42%) were females. Among those patient 104 (76.47%) were in exacerbation, 52(74.28%) cases were in stage IV , 30 (32.60%) cases were in Stage III, 14 (16.67%) cases in Stage II and none of the cases with stage I disease had cardiovascular co-morbid conditions (Tab:3)

Table 3 Table showing occurrence of cardiovascular co – morbid conditions across different groups of stable COPD

Stages of COPD	CVS morbidity	Total no. of cases	Percentage	p- value
Stage I	0	24	0 %	0.0361
Stage II	14	84	16.67 %	< 0.0001
Stage III	30	92	32.60 %	0.3164
Stage IV	52	70	74.28 %	< 0.0001
Exacerbation	104	136	76.47 %	0.0001

Different CVS co-morbidity found in this study was 150 (36.94 %) had hypertension,104 (25.61 %) had right ventricular dysfunction, 128 (31.52 %) had coronary artery disease, 132 (32.51 %) had cardiac arrhythmias and 48 (11.82 %) had heart failure (Tab:4 & Fig:3).

Table 4 Table showing the different types of cardiovascular co-morbidities

Cvs co-morbidity	Cases	Percentage
Hypertension	150	36.94 %
Pulmonary Hypertension	104	25.61%
Right ventricular dysfunction (PH)	104	25.61 %
Coronary artery disease	128	31.52 %
Cardiac arrhythmias	132	32.51 %
Heart failure	48	11.82 %

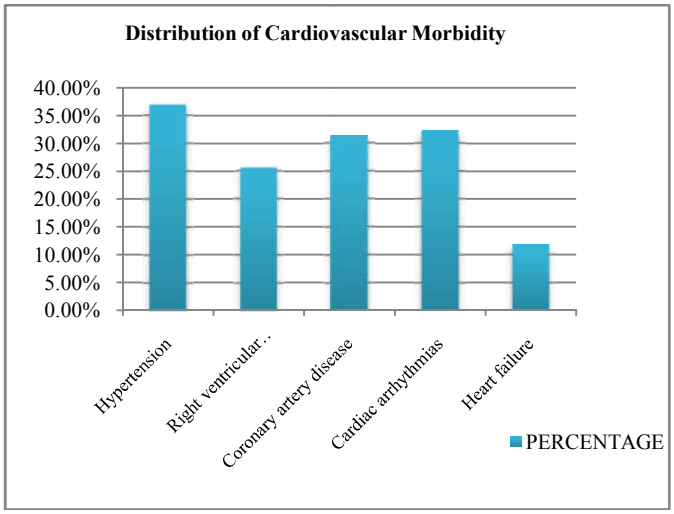

Fig 3 Bar diagram showing distribution of different cardiovascular co- morbid conditions

Among the 104 patients with pulmonary hypertension, 48 (46.15%) were males, and 56(53.85%) were females. But this was not statistically significant. Out of the total cases of PH, majority 62 (60%) were cases of Mild PH, 26(25%) were of Moderate PH and 16(15%) were of Severe PH. Patients having pulmonary hypertension also had right ventricular dysfunction (Tab:5)

Table 5 Table showing gender wise distribution of cases and the number of cases in different grades of PH

cases of ph	no - 104	male (48)	Female (56)	percentage
Mild ph	62	36	26	60%
Moderate ph	26	8	18	25%
Severe ph	16	4	12	15%

In this study CAD was found in 128 (32.52%) cases. Out of them 90 (70.31 %) were males and 38 (29.69 %) were females and P-Value 0.0143. The majority of CAD cases 60 (46.87 %) came in exacerbation, while CAD in the stable COPD cases were 44.12 % in Stage IV, 38.23 % in Stage III, 17.65 % in stage II and no cases were seen in Stage I (Tab:6).

Table 6 Table showing Stage wise distribution of CAD:

	Exacerbation	Stable copd (68)			
	(60)	Stage I	Stage II	Stage III	stage IV
CAD cases	60	0	12	26	30
percentage	46.87 %	0	17.65 %	38.23 %	44.12 %
P - value	0.0101	0.0368 *	0.0561	0.6761	0.0071

Cardiac arrhythmia in this study was seen in 132 (32.51%) cases, out of which 76 (57.58 %) were males and 56 (42.42%) were females. In exacerbation of COPD arrhythmia was found in 70(51.47%) cases. Cardiac arrhythmia was found in different stages of stable COPD were 45.71% stage IV, 26.08% of Stage III, 4.76% of Stage II, and none in stage I had arrhythmia. Statistically significant correlation was observed in stage II, stage IV and exacerbation cases (Tab:7).

Table 7 Stage wise distribution of the Arrhythmia cases

Stages	Number	Percentage	P value
Stage I (24)	0	0 %	0.0678
Stage II (84)	5	4.76%	0.0007
Stage III (92)	24	26.08 %	0.5135
Stage IV (70)	33	45.71 %	0.0003
Exacerbation (136)	70	51.47 %	< 0.0001

Different types of arrhythmias was found in the study population were atrial fibrillation in 12(9.11%), multifocal atrial tachycardia in 54(40.9%), sustained ventricular tachycardia in 24(18.18%) ,and non-sustained ventricular tachycardia in 42(31.81 %) (Tab:8).

Table 8 Table showing types of arrhythmia

Types of arrhythmia	Number	%
Atrial fibrillation	12	9.11%
Multifocal atrial tachycardia	54	40.9%
Sustained ventricular tachycardia	24	18.18%
Nonsustained ventricular tachycardia	42	31.81%
Total	132	100 %

Heart failure was seen in 48 (11.8%) cases of a total of 406 COPD cases. Out of those 30 (62.5%) were males and 18 (37.5 %) were females. In exacerbation 19.11 % of patients had heart failure and also 14.28% stage IV, 8.88 % of Stage III, 4.76% of Stage II , and none in stage I had heart failure. Statistically significant correlation was noted in heart failure in exacerbation cases (Tab:9)

Table 9 Showing stage wise distribution of heart failure cases

Stages	Number of cases	Percentage	p-value
Stage I (24)	0	0 %	0.5977
Stage II (84)	4	4.76 %	0.5018
Stage III (92)	8	8.88 %	1.0000
Stage IV (70)	10	14.28 %	0.1523
Exacerbation (136)	26	19.11 %	0.0361

In this study combine cardiovascular co-morbidities like hypertension, arrhythmia and right heart dysfunction found in 40 (20%) of COPD patients followed by combine hypertension, coronary arterial disease, arrhythmia, and right heart dysfunction in 36 (18%) of COPD patients (Tab:10).

Table 10 Showing different co-existing cardiovascular co-morbidities in the patients.

Cardiovascular co-morbidities	Numbers	Percentage
HTN + RVD+ CAD + Arr + HF	8	4%
RVD + CAD + Arr	12	6%
HTN + CAD + Arry + HF	36	18%
HTN + CAD + Arry	20	10%
HTN + CAD + RVF	16	8%
HTN + Arr + RVD	40	20%
HTN + CAD + HF	4	2%
RVF + Arr	14	7%
HTN + CAD	22	11%
HTN	4	2%
CAD	10	5%
RVF	14	7%
TOTAL	200	100%

HTN – Hypertension, RVD - Right ventricular dysfunction, CAD - Coronary artery disease,Arr– Arrhythmia
HF – Heart failure

DISCUSSION

In this study the total sample size was 408 out of which 232 (57.15%) were males and 174 (42.85%) were females. The male to female ratio was 1.3: 1. The mean age of the patients with standard deviation was 68.62+/- 9.75. The finding in our study is comparable to the previous multi-centric study by S K Jindal *et al*, where male to female ratio of 1.56: 1 [16]

In this study, 270 (66.50%) had stable COPD while the rest 136 (33.49%) came with exacerbations. Of the stable COPD cases, 24(8.89%) cases were classified as mild, 84 (31.12%) as moderate, 92 (34.07%) as severe and 70 (25.92%) as very severe COPD. Highest number of cases (34.07%) belonged to stage III or severe COPD. In a study done by Kornmannn *et al*, based on GOLD criteria, 37% had stage 0, 5% had stage I, 46% had stage II and 12% had stage III COPD [17]. Whereas in our study 8.89% had stage I, 65.19% had stage II, and 25.92% had stage III COPD. In the OLIN (Obstructive Lung disease in Northern Sweden) study by Lindberg *et al* , 8.2% had mild COPD, 5.3% had moderate COPD, 0.7% had severe and 0.1% had very severe COPD [18]

In this study group of 406 patients, 224 (55.18%) cases were smokers. The smoker to non- smoker ratio was 1.23: 1. One hundred fifty (36.94%) patients had a history of exposure to biomass fuels and 32(7.88%) patients had history of being exposed to environmental pollutants. This is comparable to a study conducted by Mahmood T *et al*. in his study 200 COPD patients where 113 (56.5%) cases were non- smokers. The

smoker to non-smoker ratio was 1:1.29. Biomass exposure was present in 30% and environmental and occupational exposure was present in 7.5% cases. 5.75% cases had a history of both smoke and biomass fuel exposure [19]. In the multicentric study funded by ICMR and carried out by SK Jindal *et al*, the smoker: nonsmoker ratio in COPD patients was 2.65: 1. Out of the smokers, 33.93 % smoked cigarettes whereas 56.25% smoked bidis. 9.82 % gave history of smoking cannabis [20]. In another study by Jindal *et al*, 19.08% smoked cigarettes , and 74.62% cases smoked bidis. History of smoking hookah was given by 6.3% cases [15].

Out of 406 study cases, cardiovascular co-morbidity was present in 200 (49.26%) cases out of which 104 (52%) were males and 96 (48 %) were females. According to the article "Systemic Manifestations of COPD" by Murali Mohan BV *et al*, cardiovascular disease and systemic hypertension was present 40.3% cases of COPD [21]. In our study population different CVS morbidities found was, 150 (36.94%) had hypertension,104(25.61%) had pulmonary hypertension, 104(25.61 %) had right ventricular dysfunction , 128 (31.52 %) had coronary artery disease, 132(32.51 %) had cardiac arrhythmias and 48 (11.82 %) had heart failure.

In this study 150 (36.94%) cases had hypertension. According to the article "Systemic Manifestations of COPD" by Murali Mohan BV *et al*, cardiovascular systemic hypertension was present 20.2 % cases of COPD [21]. In this study there were 25.61% cases with pulmonary hypertension. Majority of the patients (59.61 %) had mild Pulmonary Hypertension, 25 % had moderate PH and 15.38 % had severe PH. In the study done by Mohit K *et al*, 48% had pulmonary hypertension out of which 66.66% had mild, 8.33% had moderate and 25% had severe Pulmonary Hypertension [22].

In our study Coronary artery disease was found in 128 (32.52%) cases. In a study by Mapel D W *et al*, prevalence of Coronary artery disease in COPD was found to be 33.6% which is comparable to our study [23]. In a similar study by Jeremy Falk *et al*, 12.7% cases of COPD were reported to have coronary artery disease 24].

In this study it was seen that there were 132 (32.51%) cases of cardiac arrhythmias. Out of them, Atrial fibrillation was seen in 9.11% case, sustained ventricular tachycardia in 18.18%, non-sustained ventricular tachycardia in 31.81% and multifocal atrial tachycardia in 40.9% cases. In the study by Hanrahan JP *et al*, around 40% patients had cardiac arrhythmias. Different type of arrhythmia in his study was sustained ventricular tachycardia in 0.3%, non-sustained ventricular tachycardia in 3.1% and multifocal atrial tachycardia in 41.8 % cases [25]. In a similar study by Zaghla H *et al*, Atrial fibrillation was seen in 4% cases and non-sustained ventricular tachycardia in 28% [26]. Heart failure was seen in 48 (11.8%) cases of the total 406 COPD cases in our study. In a study by McCullough *et al*, the incidence of heart failure in COPD patient was 21% [27].

CONCLUSION

COPD is associated with a wide spectrum of cardiovascular co-morbidities and patients may be affected by more than one cardiac disease. Males and smokers, especially heavy smokers have higher incidence of cardiac co-morbidities. Most of the cases with cardiac co-morbidities were in exacerbation. Cardiovascular co-morbidities in COPD are common and may influence the outcome and management of COPD. Hence they should be actively sought for and treatment of COPD should include concurrent management of co-morbid conditions as well.

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