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Frequency of Pulmonary Hypertension in Chronic Obstructive Pulmonary Disease-A Prospective Study

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ABSTRACT

Introduction: *Pulmonary Hypertension (PH) is one of the common complications of Chronic Obstructive Pulmonary Disease (COPD). Echocardiography is a rapid, non-invasive and accurate method of investigation to diagnose PH. Pulmonary hypertension in COPD adversely affects survival and exercise capacity and is associated with an increased risk of severe acute exacerbation of COPD.* ***Aim:*** *To identify the different grades of pulmonary hypertension in COPD and the correlation between the severity of pulmonary hypertension with the severity of COPD.* ***Materials and Methods:*** *The present cross-sectional observational study was carried out at Veer Surendra Sai Institute of Medical Science & Research, Burla, Odisha, India, from November 2015-October 2017. A total of 40 patients with clinical signs and symptoms of COPD fulfilling inclusion criteria were examined and diagnosed as the case of COPD were included in the study. All cases of COPD are divided into mild, moderate, severe, and very severe as per the GOLD classification of COPD. PH is classified into the mild, moderate, and severe categories as systolic Pulmonary Artery Pressure (sPAP) 30-50, 50-70, >70 mmHg, respectively, and using the Chemla formula, mean pulmonary arterial pressure is calculated, and mean Pulmonary Artery Pressure (mPAP) of 25-35, 35-45, and >45 mmHg is classified as mild, moderate, and severe pulmonary hypertension, respectively. The data were analyzed and a p-value of ≤ 0.05 was considered significant.* ***Results:*** *A total of forty (40) patients, 67.5% were male and 32.5% were female included in this study. The mean age of all patients was 66.42 ± 6.26 years. Half (50%) of patients belong to the age group 60-69 years. Out of 40 patients, 15 (37.5%) patients were found to have pulmonary hypertension. The frequencies of pulmonary hypertension in mild, moderate, severe, and very severe COPD were 0%, 11.76%, 46.15%, and 87.5% respectively. A statistically significant increase in the frequency of PH is noticed as we moved from mild (0%) to moderate (11.76%) to severe COPD (46.15%); similarly between severe COPD (46.15%) and very severe COPD (87.5%).* ***Conclusion:*** *The frequency as well as the severity of pulmonary hypertension increase as the severity of COPD increases and also the frequency of Corpulmonale increases as the severity of COPD increases.*

Keywords: Spirometry, Echocardiography, Pulmonary hypertension, COPD

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable, and treatable disease that is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lungs to noxious particles and gases. COPD is a leading cause of morbidity and mortality worldwide and results in an economic and social burden that is both substantial and increasing [1]. A clinical diagnosis of COPD should be considered in any patient with complaints of dyspnoea, chronic cough or sputum production, history of exposure to risk factors (tobacco smoke, occupational dust, biomass fuels, etc.), and the presence of spirometry with post-bronchodilator finding (FEV1/FVC<0.70) of persistent airflow limitation [1]. Pulmonary Hypertension (PH) is defined as a mean Pulmonary Arterial Pressure (mPAP) >25 mm Hg at rest, measured

during right heart catheterization [2]. It is a complex disorder and may be idiopathic or related to a variety of diseases like idiopathic pulmonary fibrosis, sleep disorder breathing, obesity hypoventilation, and scleroderma interstitial lung disease. In patients with Pulmonary Hypertension (PH), progressive narrowing of the small pulmonary arteries and arterioles results in increased pulmonary vascular resistance, which may ultimately lead to right ventricular failure and death [3]. Pulmonary hypertension is a frequent complication of COPD. PH in COPD is usually mild to moderate with preserved cardiac output and evolves slowly alongside the progression of lung disease and hypoxemia [4]. However, a minority of patients develop severe PH that is out of proportion to underlying COPD [5,6]. Although the true prevalence of PH is unknown, an elevation of pulmonary artery pressure is reported to occur in 5%-40% of patients in a series of selected patients with severe COPD undergoing right heart catheterization [7]. Several studies on severe COPD patients found an incidence of PH up to 91% with most patients having mild to moderate PH (mPAP between 20 mm Hg-35 mm Hg), while 1% to 5% had severe elevations of mPAP above 35 mm Hg or 40 mm Hg, respectively [8,9]. The presence of PH in COPD is associated with shorter survival rates, worse clinical outcomes, and frequent use of health resources. Even in a patient on Long Term Oxygen Therapy (LTOT), the best prognostic factor is not the FEV1, nor the degree of hypoxemia or hypercapnia, but the level of mPAP. The 5-year survival rate is only 36% in patients with initial mPAP >25 mm Hg compared to 62% in those with initial mPAP <25 mm Hg [10]. Given the adverse effects of pulmonary arterial hypertension on morbidity and mortality routine evaluation of PH in patients with COPD may be warranted. The present study was done to identify the different grades of pulmonary hypertension in COPD and the correlation between the severity of pulmonary hypertension and with the severity of COPD.

MATERIALS AND METHODS

The present cross-sectional observational study was carried out at Veer Surendra Sai Institute of Medical Science & Research, Burla, Odisha, India, from November 2015-October 2017. A total of 40 patients with clinical signs and symptoms of COPD fulfilling inclusion criteria were examined and diagnosed as the case of COPD based on symptoms, history of exposure to risk factors (tobacco smoke, occupational dust, biomass fuels), clinical examination, and Post bronchodilator FEV1/FVC <0.70 in spirometry were included in the study. The patients with other causes of chronic obstructive airway diseases such as Bronchiectasis, Bronchial Asthma, Interstitial Lung Diseases, Cystic Fibrosis, Obstructive sleep apnoea, Tuberculosis, and other causes of pulmonary hypertension were excluded from the study. An informed and written consent was taken from the patient or nearest to the patient. The ethical approval was obtained from the institutional Ethics Committee. The patient's socioeconomic status was classified according to the modified Kuppuswami socioeconomic status scale [11]. The study tool and technique were by using a questionnaire, clinical examination, investigation report, Arterial Blood Gas (ABG) analysis, spirometry with bronchodilator reversibility, chest X-ray PA view, Electrocardiography (ECG), transthoracic Echocardiography (ECHO) with Doppler study, Computed Tomography (CT) thorax. All cases of COPD were divided into mild, moderate and severe, and very severe as per the GOLD classification of COPD [1]. PH is classified into the mild, moderate, and severe categories as sPAP (30-50, 50-70, and >70) mmHg, respectively. The mean Pulmonary Arterial Pressure (mPAP) is calculated using the Chemla formula (mPAP=0.61 sPAP+2 mmHg) and mPAP of 25-35, 35-45, and >45 mmHg is classified as mild, moderate, and severe pulmonary hypertension respectively [12].

Blood flow velocities recorded with Doppler echocardiography were used to determine various intra-cardiac pressures. Tricuspid Regurgitation (TR) velocity reflects the systolic pressure difference between the right ventricle and the right atrium. Therefore, Right Ventricle (RV) systolic pressure can be obtained by adding the estimated Right Arterial (RA) pressure to the 4 × (TR velocity)2 [13-15]. If there is no Right Ventricular Outflow Tract (RVOT) obstruction, pulmonary artery systolic pressure is equal to the calculated RV systolic Pressure, similarly pulmonary regurgitation velocity represents the diastolic pressure difference between the pulmonary artery and the right ventricle. Hence, pulmonary artery end diastolic pressure can be obtained by adding RV end-diastolic pressure (which is equal to RA pressure) to 4 × (pulmonary regurgitation end diastolic velocity)2. The pulmonary artery mean pressure correlates well with the early diastolic pressure difference between the pulmonary artery and right ventricle, hence 4 × (pulmonary regurgitation peak velocity)2. So systolic Pulmonary Artery Pressure, sPAP (mm of Hg)=Right Ventricular Systolic Pressure=Trans-Tricuspid Pressure Gradient (TTPG)+Right Atrial Pressure (RAP), where the trans-tricuspid pressure gradient is 4 V2 (V=peak velocity of tricuspid regurgitation, m/s). RAP is estimated to be 5 mm Hg, 10 mm Hg, or

15 mm of Hg based on the variation of the size of inferior vena cava with inspiration as follows: complete collapse, RAP=5 mm Hg; partial collapse, RAP=10 mm Hg; and no collapse, RAP=15 mm Hg [16]. Mean Pulmonary Artery Pressure can be calculated by using the Chemla formula as follows mPAP (mm of Hg)=0.61 sPAP+2 mm Hg), where sPAP is systolic pulmonary artery pressure [12]. The data were analyzed with the help of SPSS (Statistical Package for the Social Sciences) version 20 for Windows and the Chi-square test was used to determine the associations between categorical variables. A p-value of ≤ 0.05 was considered significant.

RESULTS

A total of forty (40) patients were included in this study. Half (50%) belonged to the age group 60-69 years and males and females were 67.5% and 32.5% respectively with M:F=2:1. The mean age was 66.42 ± 6.26 years. The patient's characteristics were shown in Table 1. According to the GOLD classification of COPD, there were two patients in Stage I, 17 patients in Stage II, 13 patients in Stage III, and 8 patients in Stage IV. Among all, 9 (22.5%) patients had a normal chest X-ray. The most common radiological finding was increased translucency in 31 (77.5%) patients followed by the low and flat diaphragm in 24 (60%) and tubular heart in 22 (55%) patients. Increased diameter of the pulmonary artery was seen in 22.5% of cases and the cardiothoracic ratio was >50% in 7.5% of cases. The majority of radiographic changes were seen in stages GOLD III and IV. Chest radiography was normal more frequently in cases of mild and moderate COPD (100% and 29.41% respectively) while it was only 15.38% and 0% in severe and very severe COPD, respectively. Features of hyperinflation like increased translucency, low and flat diaphragm, and tubular heart were seen more frequently in the higher grades of severity of COPD. Increased diameter of Pulmonary Artery was seen in 30.76% of cases of severe COPD and 62.5% of cases of very severe COPD. Cardiothoracic ratio >50% was seen in 37.5% of cases of very severe COPD and absent in other groups (Table 2).

Table 1 Baseline characteristics and demographic profile

Variable		Male	Female
Age in years	50-59	6(15%)	1(2.5%)
	60-69	13(32.5%)	7(17.5%)
	70-79	8(20%)	4(10%)
	80-89	0	1(2.5%)
	Mean age with SD 66.42 ± 6.26 years		
Socio-economical status	Upper	0	0
	Upper Middle	2	0
	Lower Middle	4	2
	Upper Lower	24	8
	Lower	0	0
Occupation	Farmer	12	6
	Daily Labourer	5	3
	Housewife	0	12
	Priest	2	0
Risk factors	Smokers	18	2
	Biomass/dust exposure	1	6
	Non- smokers/no biomass exposure	8	5

Table 2 Distribution of cases according to COPD severity and correlation of severity of COPD and chest radiographic changes

Chest X-ray	COPD severity				p-value
	GOLD I (n=2)	GOLD II (n=17)	GOLD III (n=13)	GOLD IV (n=8)	
Normal	2 (100%)	5 (29.41%)	2 (15.38%)	0	
Increased translucency	0	12 (70.5%)	11 (84.61%)	8 (100%)	0.012
Low and flat diaphragm	0	7 (58.82%)	10 (76.92%)	7 (87.5%)	0.013
Tubular Heart	0	6 (35.29%)	9 (69.23%)	7 (87.5%)	0.012
Increased diameter of pulmonary artery	0	0	4 (30.76%)	5 (62.5%)	0.001
Cardiothoracic ratio >50%	0	0	0	3 (37.5%)	0.013

The most common ECG change was Sinus Tachycardia (40%), followed by P-pulmonale (30%). Right axis deviation was seen in 27.5% of cases and Poor Progression of R wave was seen in 25% of cases. Right ventricular hypertrophy and low QRS complex were seen in 12.5% and 12.5% of cases, respectively. The tachycardia was present in 69.23% of patients who belonged to the GOLD III group and 75% in GOLD IV and only 5.88% of patients in the GOLD II Group. P-pulmonale was present in 30.76% of patients with severe COPD and 87.5% with very severe COPD only 5.88% of patients with moderate COPD. Low QRS Complex and RVH were present in 7.69% of patients with severe COPD and 50% of patients with very severe COPD. RAD was present in 11.76% of patients with Moderate COPD, 30.76% of patients with severe COPD, and 62.5% of patients with very severe COPD. Poor R-wave Progression was present in 38.46% of patients with severe COPD and 62.5% of patients with very severe COPD (Table 3). ECG changes were more marked as the severity of COPD increased.

Table 3 Association of the severity of COPD with ECG changes

ECG changes	GOLD I (n=2)	GOLD II (n=17)	GOLD III (n=13)	GOLD IV (n=8)	p-value
Tachycardia	0	1 (5.88%)	9 (69.23%)	6 (75%)	0.00
P-pulmonale	0	1 (5.88%)	4 (30.76%)	7 (87.5%)	0.00
Low QRS	0	0	1 (7.69%)	4 (50%)	0.007
RAD	0	2 (11.76%)	4 (30.76%)	5 (62.5%)	0.04
Poor R-wave progression	0	0	5 (38.46%)	5 (62.5%)	0.001
RVH	0	0	1 (7.69%)	4 (50%)	0.007
RAD: Right Axis Deviation; RVH: Right Ventricular Hypertrophy					

The most common echocardiographic abnormality noticed was PH, seen in 15 (37.5%) patients, and 13 (32.5%) patients had RV dilatation as cardiac abnormality followed by low EF and low FS (7.5% each). The corpulmonale was found in 46.15% of patients with severe COPD and 87.5% of patients with very severe COPD. Low EF and FS were found only in patients with very severe COPD (37.5%). PAH was found in 11.7% of patients with moderate COPD, 46.15% of patients with severe COPD, and 87.5% with very severe COPD respectively. Statistical analysis of this study showed that the difference in the presence of PH in different groups was statistically significant (p-value<0.05) (Table 4).

Table 4 Association of severity of COPD and Echocardiographic parameters

Echocardiography	GOLD I (n=2)	GOLD II (n=17)	GOLD III (n=13)	GOLD IV (n=8)	p-value
RV dilatation (n=13)	0	0	6 (46.15%)	7 (87.5%)	0.00
Low EF (n=3)	0	0	0	3 (37.5%)	0.01
Low FS (n=3)	0	0	0	3 (37.5%)	0.01
PH (n=15)	0	2 (11.7%)	6 (46.15%)	7 (87.5%)	0.00
RV: Right Ventricle; EF: Ejection Fraction; FS: Fractional Shortening; PAH: Pulmonary Hypertension					

Pulmonary hypertension was observed in 15 (37.5%) patients in the total study population. Out of the which 3 (20%) patients were having mild pulmonary hypertension, 2 of which belonged to GOLD III and 1 belonged to GOLD II. 7 (46.67%) patients were having moderate pulmonary hypertension, 1 of which belonged to moderate COPD, 3 were having severe and 3 were very severe COPD. Out of 15 patients with pulmonary hypertension 5 (33.3%) patients were having severe pulmonary hypertension. Among those 5 patients, 1 patient was having severe COPD and 4 patients were having very severe COPD (Table 5).

Table 5 Correlation of severity of pulmonary hypertension with the severity of COPD

The severity of Pulmonary Hypertension (PH)	Severity of COPD			
	GOLD I (n=2)	GOLD II (n=17)	GOLD III (n=13)	GOLD IV (n=8)
Mild (mPAP 25 mmHg-35 mmHg) (n=3)	0	1 (5.88%)	2 (15.38%)	0
Moderate (mPAP 35 mmHg-45 mmHg) (n=7)	0	1 (5.88%)	3 (23.07%)	3 (37.5%)
Severe (mPAP >45 mmHg) (n=5)	0	0	1 (7.69%)	4 (50%)
mPAP: means Pulmonary Artery Pressure				

DISCUSSION

Chronic Obstructive Pulmonary Disease (COPD) has considerable effects on cardiac function, including those of the right ventricle, left ventricle, and pulmonary blood vessels. Most of the increased mortality associated with COPD is due to cardiac involvement. Electrocardiography and echocardiography provide a rapid, non-invasive, and accurate method to evaluate cardiac changes. Based on GOLD staging, the majority of patients (42.5%) belonged to moderate followed by 32.5% to severe and 20% to very severe COPD. This is not following the study by Gupta NK, et al., where the majority of patients (45%) were of mild disease [17]. This may be due to the health awareness or health-seeking behavior of the patients. In a study done by Kaur, et al., the majority of patients (58%) were of severe COPD followed by 28% were of moderate COPD [18]. The discrepancy may be due to delayed presentation as the mild disease is usually neglected by the patients. Among all, 22.5% of patients had a normal chest X-ray. The most common radiographic abnormality noticed was increased translucency (77.5%) followed by the low and flat diaphragm (60%). Chest radiographic abnormalities tend to be more frequent in more severe degrees of COPD. The most common ECG changes observed were sinus tachycardia (40%) followed by P-pulmonale 30%, right axis deviation 27.5%, and poor progression of R-wave was seen in 25% of cases. Low voltage QRS complex and RVH were seen in 12.5% and 12.5% of cases respectively. Agrawal RL, et al. reported sinus tachycardia in 28.6% and P-pulmonale in 35.7% cases [19]. Carid and Wicken found an incidence of P-pulmonale in 15.5% while Scott, et al. and Piano, et al. recorded the same incidence of 32.7% in their studies [20-22]. P-pulmonale, Low QRS complex, RAD, and RVH were seen with significantly higher frequency in very severe COPD compared to severe COPD (p-values<0.05). Because as the disease progresses, more burden on the right heart further increases which reflects as p-pulmonale, RAD, right ventricular strain, and RVH.

Right atrial pressure was measured to be 15 mm Hg in three patients and 10 mm Hg in the rest of the patients. Pulmonary hypertension was observed in 37.5% of the total study population. The frequencies of Pulmonary hypertension in mild,

moderate, severe, and very severe COPD were 0%, 11.76%, 46.15%, and 87.5% respectively. Statistically significant increased frequency of PH is noticed as we moved from GOLD stage I to GOLD stage IV and similar findings have been observed by Gupta NK, et al. [17]. Statistical analysis of this study showed that the difference in the presence of PH in different groups was statistically significant (p-value<0.05) and there is a positive correlation between the severity of COPD and PH i.e. with an increase in severity of COPD, incidence of PH increases. Thus the incidence of PH is directly proportional to the severity of COPD. Patients with a severe and very severe form of COPD must be undergone cardiological evaluation for early detection of PH and to prevent morbidity and mortality associated with it. Patients with Pulmonary hypertension in moderate COPD were having mild or moderate PH, while the majority of patients with Pulmonary hypertension with severe COPD were with moderate PH and the majority of patients with PH with very severe COPD were with severe PH. So we can see that as the severity of COPD increases the frequency as well as the severity of PH increases. In the study conducted by Fazli Maula, PH was present in 61.5% of patients, and mild, moderate, and severe PH was seen in 29.4%, 44.1%, and 32.7% respectively [23]. In this study, it was 20%, 46.67%and 33.3% respectively. In this study, the percentage of corpulmonale among the total study population is 32.5% and the percentage of corpulmonale in patients with severe and very severe COPD was 46.15% and 87.5% respectively, and absent in other groups. Thus a statistically significant increase in the frequency of corpulmonale is seen in very severe COPD compared to severe COPD (p-value<0.05). In the study conducted by Fazli Maula, corpulmonale was found in 32.4% of COPD [23]. In a study by Gupta NK, et al. corpulmonale was observed in 17.5% and they did not find any correlation between corpulmonale and severity of COPD [17]. In the study conducted by Kaur, et al., corpulmonale was found in 46% of COPD where frequencies of corpulmonale in mild, moderate, severe, and very severe COPD were 0%, 28.6%, 48.3%, and 100% [18]. Tiwari, et al. found that corplumonale was present in 23.7% of COPD patients, and prevalence in mild, moderate, severe, and very severe patients was 12%, 15%, 40%, and 44% respectively [24].

Limitations

The study population is small, so for a definite conclusion more cases to be included. Right heart catheterization was not done in our patients as it would have further helped in the detection of more cases.

CONCLUSION

The frequency, as well as the severity of pulmonary hypertension, increased as the severity of COPD increased and the frequency of corpulmonale increased as the severity of COPD increased. So screening of all COPD patients for cardiac complications is suggested. This would contribute to the proper assessment of prognosis in these patients and assist in identifying individuals likely to suffer increased mortality and morbidity warranting close monitoring and intense treatment.

DECLARATIONS

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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