Original article:

Study to assess the correlation of severity of airflow obstruction & pulmonary hypertension in chronic obstructive pulmonary disease patients based on spirometry and 2d resting echo-cardiography in tertiary care centre, Bikaner

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ABSTRACT:

Background: Chronic obstructive pulmonary disease (COPD) is the common cause of secondary pulmonary hypertension (PH). Echocardiography is the first screening method for PH in patients with COPD and it can also appreciate the cardiac consequences of PH, especially on the right ventricle.

Objective: To estimate prevalence of pulmonary hypertension and to find correlation between severity of airflow limitation and pulmonary hypertension in COPD patients.

Methodology: A hospital based cross-sectional study was carried out to estimate prevalence of pulmonary hypertension and to find correlation between severity of airflow limitation and PH in 100 randomly selected COPD patients reporting to Dept. of respiratory medicine in S. P. Medical College Bikaner in from July 2016 to June 2017.

Right axis deviation, P-pulmonale, Low voltage complex and Poor R wave progression reliably predicted Result: 100 COPD patients participated in the study. Majority (80%)of them were male and Majority (53%) of them were from the 50-59 yr age group. Frequency of PHTN increased with the severity of airflow obstruction. 48.6% of severe and 58.7% of very severe air flow obstruction patients had PHTN. Patients with PHTN had a 2.16± 0.67 mean number of exacerbation of COPD compared to 0.67 ± 0.69 in without PHTN and the difference was statistically significant. the presence PHTN.

Conclusion: PHTN are common in COPD patients. The frequency of PHTN increased with severity of airflow obstruction. Echo-Cardiography can be used to detect, assess and manage PHTN timely to prevent further complication like corpulmonale and CHF and early mortality in the PHTN.

Keywords: PHTN, COPD, Echo-cardiography

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) represents an important public health challenge and is a major cause of chronic morbidity and mortality throughout the world. COPD is currently the fourth leading cause of death in the world[1], but is projected to be the 3rd leading cause of death by 2020. More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally. Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population[2].

In India the prevalence rate of COPD in males varies from 2.12% to 9.4% & 1.4% to 4.08% and in females varies from 1.33% to 1.49% & 1.2% to 2.55% in studies conducted from North India and South India respectively[3]. As per GOLD guidelines 2017, Chronic Obstructive Pulmonary Disease (COPD) is a common,

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preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. The chronic airflow limitation that is characteristic of COPD is caused by a mixture of small airways disease (e.g., obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person[4].

Worldwide, the most commonly encountered risk factor for COPD is tobacco smoking. COPD is the result of a complex interplay of long-term cumulative exposure to noxious gases and particles, combined with a variety of host factors including genetics, airway hyper-responsiveness and poor lung growth during childhood.[5-7]

COPD is associated with many comorbid diseases, which may be pulmonary or extrapulmonary (coronary vascular disease, congestive heart failure, pulmonary hypertension, diabetes mellitus, metabolic syndrome, obstructive sleep apnea, skeletal muscle dysfunction, cachexia, osteoporosis, depression, lung cancer).[8-10] Comorbid diseases in COPD are independently associated with a higher risk of hospitalization and mortality.[11]

Cardiovascular disease is a major comorbidity in COPD & probably both the most frequent & most important comorbidity coexistent with COPD.[12] The cardiovascular comorbidities of COPD are ischemic heart diseases, heart failure, atrial fibrillation, systemic hypertension & pulmonary hypertension (PHTN).

PHTN is a well-recognized complication of COPD. In patients with COPD, whether mild or more severe, the presence of PHTN is associated with an increase in hospitalization & a poorer prognosis.[13] Indeed in some studies the degree of PHTN is more powerful indicator of prognosis than the measure of airflow limitation. [14] Abnormal right ventricular function is also associated with poorer prognosis in patients with COPD.[15]

PH is defined as an increase in mean pulmonary arterial pressure (PAPm) ≥25 mmHg at rest as assessed by right heart catheterization (RHC).[16] Although the severity of PH tends to correlate with degree of airflow obstruction & the degree of severity of hypoxemia, the degree of PH tends to be mild to moderate.

Clinical symptoms & physical signs of PH may be difficult to identify in patients of COPD. Echocardiography is the best screening tool for assessment of PH. Transthoracic echocardiography provides several variables which correlate with right heart hemodynamics including PAP & should always be performed in a case of suspected PH[17]. Echocardiography provides a non-invasive method to evaluate cardiac status like - right ventricular (RV) function, RV filling pressure, tricuspid regurgitation and left ventricular function[18]. Many studies have confirmed that echocardiographically derived estimates of pulmonary artery pressure (PAP) correlate closely with those derived by cardiac catheterization[18,19].

AIMS AND OBJECTIVES

1) To estimate prevalence of pulmonary hypertension in COPD patients reporting to tertiary care center.
2) To know correlation between severity of airflow limitation and pulmonary hypertension in COPD patients.

MATERIAL AND METHODS

Material and Methods

This cross-sectional study was carried out among 100 randomly selected COPD cases who attended OPD or got admitted in the department of pulmonary medicine, S P Medical College, Bikaner and Informed consent was taken. The diagnosis of COPD was based on clinical criteria suggested by GOLD [2017] guidelines respectively.

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Inclusion Criteria

1. Diagnosis of COPD consistent with recommendations of GOLD
2. A stable clinical state
3. Acceptable performance of spirometry as recommended by ATS
4. FEV_1/ FVC ratio≤ 0.7
5. Chest radiograph PA showing no evidence of acute infection or any other pulmonary disease and compatible with a diagnosis of COPD.

Exclusion Criteria

1. Coronary artery disease.
2. Congenital heart disease
3. Valvular heart diseases.
4. Systemic hypertension.
5. Old pulmonary tuberculosis.
6. Interstitial lung disease
7. Psychiatric illnesses
8. Patients who lost follow up/ died during study

In all these patients detailed history, clinical examination & investigations (Sputum for acid fast bacilli ,Fasting blood sugar level, Digital chest X-ray PA view, 2D resting echocardiography and spirometry) was done.

Patients included in the study was subjected for pulmonary function tests by spirometry. Spirometric indices FEV_1, FEV_1/FVC were included in the study. The staging will be done as per the GOLD criteria (2017).

Echocardiography was done to assess the pericardium, valvular anatomy and function, left and right side chamber size and cardiac function. Tricuspid regurgitant flow will be identified by color flow Doppler technique and the maximum jet velocity will be measured by continuous wave Doppler without the use of intravenous contrast. Pulmonary hypertension (PHTN) was defined in this study as sPAP ≥ 30 mmHg. PHTN was classified into mild, moderate, and severe category as sPAP 30–50, 51–70, >70 mmHg, respectively (using Chemla formula, mean pulmonary arterial pressure (MPAP) =0.61 PASP + 2 mmHg and putting value of 25–35, 36–45, and>45 mmHg of MPAP for mild, moderate, and severe pulmonary hypertension, respectively).

Right ventricle dimension will be measured by M-Mode echo and right ventricular dilation or cor-pulmonale will be said to be present when it exceeded the normal range of 0.9–2.6 cm. Right ventricle contractility will be also noted and right ventricular systolic dysfunction will be said to be present when it will be hypokinetic.

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RESULT

Table 1 Showing Clinical profile of COPD patients

Age group (In years)	**No of patient**	**Percentage**
40-49	25	25%
50-59	53	53%
>60	22	22%
Total	100	100.00%
Duration (in Years)		
< 10	78	78%
>10	22	22%
Total	100	100%
Classification according to GOLD stage		
Mild	17	17%
Moderate	22	22%
Severe	35	35%
Very severe	26	26%
Total	100	100.00%
2D Echocardiographic findings		
Measurable TR	42	42%
Pulmonary hypertension	38	38%
Cor-pulmonale	20	20%

In this study out of 100 patients 80 were males (80%) and rest 20 were females (20 %). Mean age of the patients was 54.57 ± 5.96 years. Majority (53%) were in the 50-59 years age group. The mean duration of illness was 7.40±3.05 years. Maximum number of patients (78%) had symptoms for less than 10 years and (22%) of patients had symptoms for≥ 10 years. According to GOLD staging the frequency of mild, moderate, severe and very severe disease was 17%, 22%, 35% and 26 % respectively. Nearly 2/3rdof the patients had severe and very severe disease. Tricuspid regurgitation was measurable in 42(42%) patients. Pulmonary hypertension was observed in 38 (38 %) and cor-pulmonale in 20 (20%) patients.

Table 2 Showing Severity of PHTN in relation to Severity of airflow obstruction

Severity of airflow obstruction	**Severity of PHTN**			
	Mild	**Moderate**	**Severe**	**Total**
Mild (17)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0.00% (0)
Moderate (22)	5 (83.33%)	1 (16.67%)	0 (0.00%)	27.27% (6)
Severe (35)	7 (41.18%)	7 (41.18%)	3 (17.65%)	48.57% (17)
Very severe(26)	1 (6.67%)	8 (53.33%)	6 (40.00%)	57.69% (15)

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None of the patients with mild airflow obstruction had PHTN. The number of patients with moderate, severe and very severe airflow obstruction who had PHTN were 6, 17 and 15 respectively. Majority (32 out of 38 patients) had severe and very severe airflow obstruction. As the severity of airflow obstruction increases frequency of PHTN also increases.

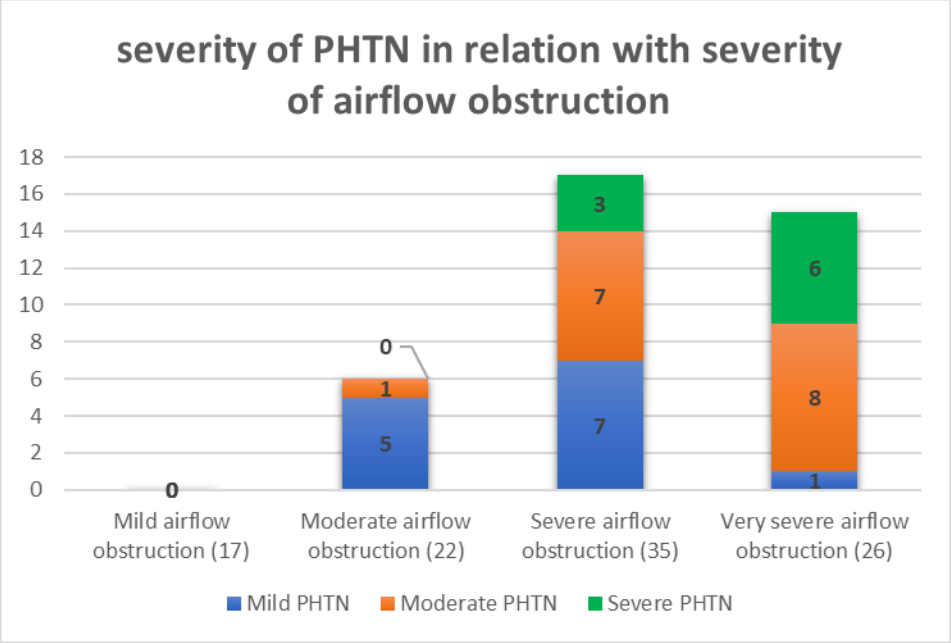

Table 3 showing Frequency of Corpulmonale with Severity of PHTN:

Severity of PHTN	% of patient with Cor- Pulmonale
Mild (13)	15.38% (2)
Moderate (16)	62.50% (10)
Severe (9)	88.89% (8)

Majority (88.98 %) of patient with severe PHTN had cor-pulmonale while corpulmonal in mild and moderate PHTN was 15 % and 62.5% respectively. Frequency of Cor-pulmonale increased with the severity of PHTN.

Table 4 showing Frequency of Cor-pulmonale with Severity of airflow obstruction:

Severity of airflow obstruction	% of patient with Cor-Pulmonale
Mild (17)	0.00% (0)
Moderate (22)	0.00% (0)
Severe (35)	31.43% (11)
Very severe (26)	34.61% (9)

Patient with mild and moderate COPD did not have cor-pulmonale while 31.43 % of patients with severe COPD and 34.61 % of patents with very severe COPD had cor-pulmonale. The frequency of Cor-pulmonale increased with severity of airflow obstruction.

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Table 5 showing Duration of disease in relation to PHTN:

Duration of illness in years	PHTN		p value
	Present [n=38]	Absent [n=62]	
Mean ± SD	9.92 ± 1.56	5.85 ± 2.69	<0.001

The mean duration of illness in subjects with PHTN was 9.92 ± 1.56 years, whereas the duration in those without PHTN was 5.85 ± 2.69 years. The subjects with PHTN had significantly longer duration of the illness ($p < 0.001$).

DISCUSSION

The study included 100 subjects with COPD of which 80 were males (80%) and 20 were females (20%). The male to female ratio was 4 : 1.The higher incidence of COPD in males can be attributed to smoking. The male-female distribution in this study is in line with that of JC Banergea[20], who reported 80% male population. Chappel A.G[21], also showed 81.25% male distribution in a study on chronic bronchitis and emphysema.

Mean age of the subjects was (54.57 ± 5.96) years. Majority of the subjects (53%) were in the 50-59 years age group. A similar observation was made by Burrows et al[22], who reported a mean age of 56.5 ± 7.4 years. In a study by Gupta et al[23], the mean age was 55± 10 years. Dave L et al[24]also showed the mean age of 57.76 ± 7.90 years.

The mean duration of illness was (7.40 ±3.05) years. Maximum number of subjects (78%) had symptoms for less than 10 years and (22%) of them were symptomatic for ≥ 10 years. In a study by Gupta et al[23], the mean duration of symptoms was 8.9 ± 4.9 years. In a study by Dave L et al[24]the mean duration of symptoms was 6.78 ±3.81 years, correlates with the findings of present study.

The frequency of mild, moderate, severe and very severe airflow obstruction by GOLD classification was seen in 17%, 22%, 35% and 26% subjects respectively. In a study by Gupta et al[25], the frequency of mild, moderate, severe and very severe COPD was 45%, 27.5%, 12.5% and 15% respectively. The present study had more patients with severe and very severe disease (nearly 2/3rd). In a study by Daveet al[26], the frequency of mild, moderate, severe and very severe COPD was 12%, 19%, 31% and 38% respectively. In a study by Sachin D et al[27], the frequency of mild, moderate, severe and very severe COPD was 8%, 22%, 44% and 26% respectively.

All the 100 patients underwent echocardiography examination. Prakash[28] found in their study that ECG had a sensitivity and specificity of 31% and 85%, whereas echo had 93% sensitivity and 95% specificity in detecting RV dysfunction Tricuspid regurgitation was measurable in 42 (42%) subjects. Pulmonary hypertension was observed in (38%) patients. 4 patients had measurable Tricuspid regurgitation but pulmonary hypertension was not found. 13 patients (34.21%) had mild PHTN.16 patients (42.10%) had moderate PHTN. Severe PHTN was observed in 9 (23.68%) subjects. The level of PHTN has a prognostic value in COPD. This has been demonstrated by several studies. In a study by Weitzenalum E. et al [29], the 5-year survival rates were

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50% in mild PHTN, 30% in those with moderate to severe PHTN, and 8% in very severe PHTN. Thus a high degree of PHTN bears poor prognosis.

The incidence of corpulmonale was 20% (20 patients) in our study as evidence by RV dilatation (more than 2.6 cm.). Gupta N K et al[25]reported corpulmonale in 17.5% of patients. Alexander et al[217]reported corpulmonale in 25% of patients. D. Radha Krishnan[30] reported corpulmonale in 20% of patients.

The incidence of PHTN increases with the advancing age. Subjects with PHTN had a mean age of 59.31± 4.18 years. Where as the mean age in patients without PHTN was 51.66± 4.94 years. This difference was statistically significant ($p < 0.001$). The patients with PHTN were relatively older. There was no statistically significant difference in the gender distribution of PHTN ($p = 0.3$).

Usually the patients with COPD develop PHTN late in the course of the disease. So the longer the duration of illness, more the incidence of PHTN. In this study the mean duration of illness in subjects with PHTN was 9.92±1.56 years, whereas the duration in those without PHTN was 5.85± 2.69 years. This difference was statistically significant ($p < 0.001$).

As the severity of COPD progresses, so does the cardiovascular comorbidity. PHTN usually present in those with severe disease. In this study none of the subjects with mild COPD had PHTN. Majority of the patients with PHTN (32 of 38 patients; 84.21%) had severe and very severe COPD. Only six of them (15.79%) had moderate disease.

CONCLUSION

- From the results of the present study it can be concluded that pulmonary hypertension are common in COPD patients and as the severity of airflow obstruction increases frequency of PHTN also increases.
- Although clinical assessment often helps to suspect associated cardiac dysfunction in COPD patients, ECG may further help to detect PHTN & Cor-Pulmonale in more number of patients suspected on clinical ground, however; Echo-Cardiography is useful for accurate assessment of cardiac status in COPD patients in routine clinical practice. Therefore Echo-Cardiography should always be considered in the routine assessment of patient to detect, assess and manage pulmonary hypertension in these patient timely to prevent further complication like corpulmonale and CHF and early mortality in the pulmonary hypertension.

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