Original Article

Prevalence of pulmonary artery hypertension in patients of chronic obstructive pulmonary disease and its correlation with stages of chronic obstructive pulmonary disease, exercising capacity, and quality of life

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Abstract

Background: Pulmonary arterial hypertension (PAH) is a complication of chronic obstructive pulmonary disease (COPD) in advance stages, and its presence indicates poor prognosis. **Aims and Objective:** The present study was design to know the prevalence of PAH in patients with COPD and its correlation with stages of COPD, exercising capacity, and quality of life. **Materials and Methods:** It is a cross-sectional prevalence study over a period of 1 year from August 2015 to July 2016. The study included 109 COPD patients, diagnosed by spirometry, and severity was determined according Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification criteria. Screening two-dimensional echocardiography was done to determine pulmonary arterial hypertension and exercising capacity assessed by 6 min walk test (6MWT) while the quality of life was assessed by St George respiratory Questionnaire for COPD (SGRQ-C) Questionnaires. **Results:** Out of 109 patients, PAH was present in 68 (62.4%) cases consisting of mild grade 41 (37.6%), moderate grade 11 (10.1%), and severe grade 16 (14.7%). In GOLD A stage, there were 20 cases of mild PAH and Stage B included 18 cases of mild and 3 cases of moderate PAH. Stage C had 3 cases of mild and 8 cases of moderate PAH while Stage D had 16 cases of severe PAH. In 6MWT, patients with severe grade PAH fail to perform the test while patients with mild to moderate PAH walked short distance. In SGRQ-C Questionnaires symptom, activity, impact, and total score were high with the severity of PAH. **Conclusion:** The prevalence of PAH in COPD was significant. Therefore, every COPD patient should be evaluated for PAH.

Keywords: 6 min walk test, chronic obstructive pulmonary disease, pulmonary hypertension, St George Respiratory Questionnaire, two-dimensional echocardiography

Introduction

Pulmonary hypertension (PH) is a rare lung disorder, in which the arteries carrying blood from the heart to the lungs become narrowed, making it difficult for blood to flow through the vessels. The features of PH develops if >50% reduction of pulmonary vascular bed (or) >2/3 of lung destruction is present. The more contribution (78.7%) for the development of PH is left heart diseases while 9.7% (second most common) contribution due to lung pathologies. In the lung disorders, more than 50% cases of PAH comes from chronic obstructive pulmonary disease (COPD). The abnormal high pressure strains the right ventricle of the heart, causing it to expand in size. Overworked and enlarged right ventricle gradually becomes weaker and loses its ability to pump enough blood to the lungs leading to the development of right heart failure. PH has been defined

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as an increase in mean pulmonary arterial pressure (MPAP) >25 mmHg at rest or >30 mmHg on exercise.[1,2]

Materials and Methods

This cross-sectional prevalence study enrolled patients attending outdoor and indoor in Medicine department from August 2015 to July 2016. Written consent was taken, and ethical committee was approved this study. The present study included male and female COPD patients diagnosed by spirometry, and severity was determined according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification criteria. Echocardiography was done in all patients to screen PAH with severity. After inclusion and exclusion criteria all patients were examined in detail. Investigations included routine blood examinations, ABG, electrocardiography (ECG), chest X-ray (CXR), NT pro BNP, and echocardiography. Functional assessment was done by 6 min walk test (6MWT) and St George respiratory Questionnaire (SGRQ). Inclusion criteria COPD patients aged 30–70 years of either sex. Exclusion criteria patients having COPD of age <30 years and >70 years, left-sided heart failure, pregnancy, autoimmune disease, HIV disease patient, thyroid disease, rheumatic heart disease, congenital heart disease, ischemic heart disease, renal and liver disease patients.

Statistical analysis

The statistical analysis was done using Statistical Package for Social Sciences (version 15; SPSS Inc. Software, Chicago, IL,USA) statistical analysis software. The values were represented in number (%) and mean ± standard deviation. Statistical formulas such as mean, standard deviation, Chi-square test, analysis of variance (ANOVA), *post hoc* tests (Tukey-HSD), bivariate correlation, and level of significance were used. The level of significance - $P > 0.05$ not significant, $P < 0.05$ significant, $P < 0.01$ highly significant, $P < 0.001$ very highly significant.

Results

Out of 109 cases, 72 were male and 27 were female. The prevalence of patients in GOLD stages A, B, C, and D were as 47 (43.1%), 30 (27.5%), 15 (13.8%), and 17 (15.6%), respectively [Table 1]. Mean age of patients ranged from 55.90 ± 6.97 to 59.88 ± 8.07 years. Mean body weight of patients in normal and mild groups was significantly higher as compared to those in moderate and severe groups ($P < 0.001$). Among 109 cases, 68 (62.4%) had PH which were further distributed as 41 (37.6%) cases of mild PH, 11 (10.1%) cases of moderate, and remaining 16 (14.7%) cases of severe PH [Tables 2 and 3]. Study observed most of cases of normal to mild PH in Stage A and severe PH in Stage D. Thus, PH was significantly increased on deterioration of lung functions ($P < 0.001$). A statistically significant difference among groups was observed for light-headedness, syncope, chest pain, abdominal distension, and bipedal swelling which were seen to be increasing significantly with the increasing severity of PH ($P < 0.001$) and increasing stages of COPD ($P < 0.001$). Icterus was seen in 81.8% of moderate and 50% of severe PH patients only. Edema was seen in 7.3% of mild and all the moderate and severe PH patients. Raised JVP was seen in 2.4% of mild, 81.8% of moderate, and 68.8% severe PH patients while neck vein engorgement was seen in 9.8% of mild, 100% of moderate, and 93.8% of severe PH patients. Icterus, edema, raised JVP, and neck vein engorgement were found to be increasing significantly with increasing stages of COPD ($P < 0.001$). With increasing severity of COPD, a significant increase in proportion of patients with epigastric pulsations, left parasternal heave, loud S2 and S3 was observed ($P < 0.001$). Findings such as pansystolic murmur (tricuspid regurgitation [TR]) and early diastolic murmur were significantly lower in stages A and B as compared to Stages C and D COPD patients ($P < 0.001$). Ascites and hepatomegaly were seen in 2.1% of Stage A, 46.7% of Stage C, and 88.2% of Stage D patients, thus showing presence of these findings in significantly higher proportion of Stage C and D patients as compared to Stage A and B patients ($P < 0.001$). Right axis deviation (RAD) and right bundle-branch block (RBBB) were positive in all the subjects. Supraventricular tachycardia (SVT), atrial fibrillation, and atrial flutter were negative in all the patients. R-wave prominence in V1, right ventricular (RV) hypertrophy and strain, and R/S ratio abnormalities were seen to be significantly increasing with increasing severity of PH ($P < 0.001$) and increasing severity of COPD ($P < 0.001$). All the patients in all the groups had pruning and hyperinflated lung field. Dilated PV was seen in 81.8% of moderate and 100% of severe PH patients ($P < 0.001$). Right atrium (RA)/RV enlargement was seen in none of the normal PH, 2.4% of mild, 63.6% of moderate, and 100% of severe PH patients ($P < 0.001$). Dilated PA and RA/RV enlargement were seen to be increasing significantly with increasing stage of COPD ($P < 0.001$). Patients with GOLD stage D and severe PH were unable to perform 6 MWT. No significant difference in 6MWT findings of different groups was observed for SPO_2, respiratory rate (RR), Pulse rate (PR)-resting and Pulse rate(PR)-mid exercise. However, mean

Table 1: Demographic profile of patients with chronic obstructive pulmonary disease stages

Characteristic	Stage A (*n*=47)	Stage B (*n*=30)	Stage C (*n*=15)	Stage D (*n*=17)	Statistical significance		
					F	χ^2	*P*
Mean age±SD	57.57±6.55 (37-68)	59.10±8.28 (40-69)	57.33±11.02 (38-69)	58.12±5.23 (38-69)	0.295		0.829
Gender, *n* (%)							
Male	34 (72.3)	16 (53.3)	11 (73.3)	11 (64.7)		3.362	0.339
Female	13 (27.7)	14 (46.7)	4 (26.7)	6 (35.3)			
Body weight (mean±SD)	54.38±2.92	53.93±2.72	49.67±4.91	49.24±4.37		14.58	<0.001

SD: Standard deviation

distance, DW, and PR-W showed a significant decline with increasing severity of PH ($P < 0.001$). A significant increase in visual analog scale (VAS) was observed with increasing severity of PH ($P < 0.001$) and increase stage of COPD ($P < 0.001$). With increasing severity of PH, a significant increase in the right ventricular systolic pressure (RVSP), MPAP, right atrial pressure (RAP), and TR velocity was observed whereas with increasing severity a significant decrease in mean TAPSE was observed ($P < 0.001$) None of the cases with normal PH had abnormalities such as RA enlargement, RV enlargement, small left chamber, intravenous (IV) flattening, pericardial effusion, and RV dysfunction. However, proportion of patients with these abnormalities was found to be significantly increasing with increasing severity of PH ($P < 0.001$). Mean RVSP, MPAP, RAP, and TR velocity was seen to be significantly higher in higher stage (Stages C and D) as compared to lower Stages (Stages A and B) ($P < 0.001$) [Table 4]. The prevalence of abnormalities such as RA enlargement, RV enlargement, small left chamber, IV flattening, pericardial effusion, and RV dysfunction also showed a similar trend with higher prevalence in higher Stages of COPD as compared to lower Stages of COPD ($P < 0.001$) [Table 5]. With increasing the severity of PH and increasing stages of COPD, an increase in NT pro-BNP levels was observed ($P < 0.001$). With increasing the severity of PH and increase stage of COPD, a significant increase in all the subscale as well as total scores of SGRQ scale was observed ($P < 0.001$).

Table 2: Prevalence and severity of pulmonary hypertension in chronic obstructive pulmonary disease patients (*n*=109)

Outcome	Number of patients (%)
Normal (no pulmonary hypertension)	41 (37.6)
Pulmonary hypertension	68 (62.4)
Mild	41 (37.6)
Moderate	11 (10.1)
Severe	16 (14.7)

Table 3: Association of pulmonary hypertension with chronic obstructive pulmonary disease stage

COPD stage	Normal (*n*=41), *n* (%)	Mild (*n*=41), *n* (%)	Moderate (*n*=11), *n* (%)	Severe (*n*=16), *n* (%)
A	27 (65.9)	20 (48.8)	0	0
B	9 (22.0)	18 (43.9)	3 (−27.3)	0
C	4 (9.8)	3 (7.3)	8 (72.7)	0
D	1 (2.4)	0	0	16 (100.0)

χ^2=143.179; *P*<0.001. COPD: Chronic obstructive pulmonary disease

Discussion

All cases were categorized as per GOLD guidelines.[3] On the basis of two-dimensional echocardiography based on Dana point European Society of Cardiology/European Respiratory Society guidelines,[1] the present study revealed the prevalence of PH in 62.4% cases. A previous study found 38.7% cases of PH in 31 patients of COPD.[4] Another study of 215 patients with severe COPD reported PH in 50.2% cases, including moderate PH in 9.8% cases and severe PH in 3.7% cases.[5] The present study found increasing cardiovascular abnormalities with impairment of pulmonary functions ($P < 0.001$). Symptoms and signs of PH may be difficult to recognize because they are nonspecific. Initially, patients present with exertional dyspnea and fatigue. Over the time, patients may eventually develop the signs and symptoms of severe PH with overt RV failure (e.g., exertional chest pain or syncope and congestion, including peripheral edema, ascites, and pleural effusion). The diagnosis is often delayed because the presenting features of PH are frequently attributed incorrectly to age, deconditioning, or a coexisting, or alternate medical condition. As a result, PH is often not suspected until symptoms become severe or serious. It has been estimated that more than 20% of patients have symptoms of PH for longer than 2 years before it is recognized. This is particularly prevalent among patients younger than 36 years and in those with coexisting medical conditions. RAD and RBBB were positive in all the subjects. Nakatsuji *et al.* stated that the R wave amplitude and R/S ratio in the Syn-ECGs were significantly

Table 4: Association of pulmonary hypertension with two-dimensional echocardiography parameters

Finding	Mean±SD				Statistical significance	
	Normal (*n*=41)	Mild (*n*=41)	Moderate (*n*=11)	Severe (*n*=16)	*F*	*P*
RVSP	-	37.5±1.2	48.3±2.0	68.3±4.6	875	<0.001
MPAP	-	24.8±0.6	31.5±1.2	44.0±2.8	953	<0.001
RAP	-	5.3±0.6	10.0±0.0	15.1±0.3	2058	<0.001
TR velocity	-	2.9±0.0	3.1±0.1	3.6±0.2	460	<0.001
TAPSE	1.6±0.2	1.5±0.3	1.0±0.3	0.9±0.1	44.34	<0.001
Finding	***n* (%)**	***n* (%)**	***n* (%)**	***n* (%)**	χ^2	***P***
RA enlargement	0	4 (9.8)	11 (100.0)	16 (100.0)	91.26	<0.001
RV enlargement	0	4 (9.8)	11 (100.0)	16 (100.0)	91.26	<0.001
Small left chamber	0	3 (7.3)	3 (27.3)	13 (81.3)	57.59	<0.001
IV flattening	0	1 (2.4)	3 (27.3)	13 (81.3)	66.50	<0.001
Pericardial effusion	0	0	1 (9.1)	5 (31.3)	25.44	<0.001
RV dysfunction	0	2 (4.9)	6 (54.5)	16 (100.0)	82.04	<0.001

RVSP: Right ventricular systolic pressure; MPAP: Mean pulmonary arterial pressure; RAP: Right atrial pressure; TR: Tricuspid regurgitation; TAPSE: Tricuspid annular plane systolic excursion; RA: Right atrium; RV: Right ventricle; IV: Intravenous; SD: Standard deviation

Table 5: Association of chronic obstructive pulmonary disease stages with two-dimensional echocardiography parameters

Finding	Mean±SD				Statistical significance	
	Stage A (*n*=20)	Stage B (*n*=21)	Stage C (*n*=11)	Stage D (*n*=16)	*F*	*P*
RVSP	37.7±0.7	38.9±4.1	45.4±5.5	68.3±4.6	875	<0.001
MPAP	24.9±0.4	25.7±2.5	29.6±3.4	44.0±2.8	953	<0.001
RAP	5.2±0.5	6.2±1.7	8.6±2.3	15.1±0.3	2058	<0.001
TR velocity	2.9±0.0	2.9±0.1	3.0±0.1	3.6±0.2	460	<0.001
TAPSE	1.5±0.3	1.6±0.2	1.2±0.5	0.9±0.2	44.34	<0.001
Finding	**Grade A (*n*=47), *n* (%)**	**Grade B (*n*=30), *n* (%)**	**Grade C (*n*=15), *n* (%)**	**Grade D (*n*=17), *n* (%)**	χ^2	*P*
RA enlargement	3 (6.4)	3 (10.0)	9 (60.0)	16 (94.1)	59.62	<0.001
RV enlargement	3 (6.4)	3 (10.0)	9 (60.0)	16 (94.1)	59.62	<0.001
Small left chamber	3 (6.4)	0	3 (20.0)	13 (76.5)	51.56	<0.001
IV flattening	1 (2.1)	0	3 (20.0)	13 (76.5)	51.56	<0.001
Pericardial effusion	0	0	1 (6.7)	5 (29.4)	23.20	<0.001
RV dysfunction	2 (4.3)	0	6 (40.0)	16 (94.1)	71.40	<0.001

RVSP: Right ventricular systolic pressure; MPAP: Mean pulmonary arterial pressure; RAP: Right atrial pressure; TR: Tricuspid regurgitation; TAPSE: Tricuspid annular plane systolic excursion; RA: Right atrium; RV: Right ventricle; IV: Intravenous; SD: Standard deviation

greater in patients with PH than in the controls ($P < 0.01$) while the R wave amplitude in the Syn-ECGs exhibited a significant and better correlation with the PASP than lead V1.[6] There was statistically significant dilated PA or RA/RV enlargement in 81.8% of moderate and 100% of severe PH ($P < 0.001$). Patients of severe PH and Stage D COPD were failed to perform 6MWT. However, mean distance, DW, and PR-W showed a significant decline with increasing severity of PH and increasing stage of COPD A significant increase in VAS was observed with increasing severity of PH ($P < 0.001$) and increasing Stages of COPD ($P < 0.001$). Durheim *et al.* reported that physical function declined over time in GOLD group D but remained stable in Groups A, B, and C. GOLD classification was associated with time to death or first COPD-related hospitalization. Baseline 6 min walk distance was more strongly associated with time to death or first COPD-related hospitalization (hazard ratio, 0.50 [95% confidence interval, 0.34–0.73] per 150 m, $P = 0.0003$) than GOLD 2011 classification.[7] With increasing severity of PH, a significant increase in RVSP, MPAP, RAP, and TR velocity was observed whereas with increasing severity, a significant decrease in mean TAPSE was observed ($P < 0.001$). None of the cases with normal PH had abnormalities such as RA enlargement, RV enlargement, small left chamber, IV flattening, pericardial effusion, and RV dysfunction. However, proportion of patients with these abnormalities was found to be significantly increasing with increasing severity of PH ($P < 0.001$). Mean RVSP, MPAP, RAP, and TR velocity was seen to be significantly higher in higher Stages (Stages C and D) as compared to lower stages (Stages A and B) ($P < 0.001$). The prevalence of abnormalities such as RA enlargement, RV enlargement, small left chamber, IV flattening, pericardial effusion, and RV dysfunction also showed a similar trend with higher prevalence in higher Stages of COPD as compared to lower Stages of COPD ($P < 0.001$). A study using echocardiographic evaluation of COPD had observed measurable TR in 27/40 (67.5%) cases and PH (defined as sPAP >30 mmHg) in 17/27 (63%) cases.[8] The frequencies of PH in mild, moderate, severe, and very severe COPD were 16.67%, 54.55%, 60.00%, and 83.33%, respectively. RAP was 10 mmHg in 82.5% cases and 15 mmHg in 17.5% cases. Cor pulmonale was observed in 7/17 (41.17%) case. With increasing severity of PH and increase stages of COPD, a significant increase in all the subscales as well as total scores of SGRQ scale were observed ($P < 0.001$). These findings support a previous study revealing SGRQ scores (total and domain) had been increased progressively for individual components with the decrease in airflow limitation (<0.05), body mass index (<0.002), and 6MWT (<0.05).[9] Therefore, further studies involving larger sample size are needed to understand better clinical and biochemical profile of COPD patients.

Conclusion

The study concluded that PH is highly prevalent in advanced COPD and associated with a significant high risk for mortality and morbidity. Our study put emphasis on early cardiac screening of all COPD patients which will be helpful in the assessment of prognosis, morbidity, and mortality.

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Conflicts of interest

There are no conflicts of interest.

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