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Frequency of Pulmonary Hypertension in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT

Introduction: Chronic obstructive pulmonary disease (COPD) is frequently associated with pulmonary hypertension, which significantly impacts patient outcomes. This study aimed to determine the frequency of pulmonary hypertension in patients with COPD. **Methodology:** This descriptive cross-sectional study was conducted at the Department of Pulmonology, Liaquat National Hospital, Karachi. A total of 162 COPD patients aged 18-80 years were enrolled using non-probability consecutive sampling. Pulmonary hypertension was diagnosed via echocardiography when pulmonary artery systolic pressure was >35 mmHg and tricuspid regurgitant velocity was >3.4. Data was analyzed using SPSS v25.0. **Results:** Among 162 patients, 92 (56.8%) were males and 70 (43.2%) were females with a mean age of 46.17±14.27 years. Pulmonary hypertension was found in 44 (27.2%) patients. Significant associations were observed between pulmonary hypertension and diabetes mellitus (p=0.001), smoking (p=0.001), and COPD duration (p=0.001). No significant associations were found with gender, age groups, or BMI categories. **Conclusion:** Pulmonary hypertension was present in more than one-fourth of COPD patients. Diabetes mellitus, smoking history, and longer COPD duration were significantly associated with the development of pulmonary hypertension in these patients.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) globally leads to chronic health issues and death. Acute exacerbation signifies a sudden and lasting deterioration in a patient's stable condition with notable electrolyte imbalances. Limited awareness of triggers and prognosis indicators contributes to poor outcomes in COPD exacerbations.[1-2] A previous study revealed that 7.9% of intensive care unit admissions were COPD patients.[3] COPD is associated with various morbidities and complications, indicating a poor prognosis if left untreated. Pulmonary hypertension is a common complication among COPD patients, highlighting the need for timely management to improve outcomes.[4-5]

Pulmonary hypertension in COPD is common, ranging from mild to severe. Approximately 5–10% of end-stage COPD patients develop severe pulmonary hypertension leading to right heart failure. This condition belongs to group 3 in the WHO classification. Patients with this complication have a higher risk of acute exacerbations, mortalities, and morbidities. The prevalence of pulmonary hypertension in stable COPD can vary widely depending on the severity of COPD and the method used to measure pulmonary artery pressure.[6-7]

In a study, pulmonary hypertension was found in 45.4% of COPD patients.[8] In another study, pulmonary HTN was observed in 40% of the COPD cases.[9] In another study, prevalence of pulmonary hypertension in chronic obstructive pulmonary disease came out to be 29.03%.[10] In another study, pulmonary HTN was seen in 62.86% COPD cases.[11] In COPD patients, pulmonary hypertension is a common complication that can complicate their condition. It's important to screen all COPD patients for pulmonary hypertension to manage it early and improve their quality of life.

METHODOLOGY

The study, conducted at the Department of Pulmonology, Liaquat National Hospital in Karachi, utilized a descriptive cross-sectional design with non-probability consecutive sampling over six months. A total of 162 cases meeting selection criteria provided written consent and received approval from the hospital's Ethical Committee. Demographic information (name, age, address) was collected. The sample size of 162 was determined with a

7% margin of error, 95% confidence level, and 29.03% prevalence of pulmonary hypertension.[10]

Patients aged 18-80 with COPD were included, excluding those with left heart failure, asthma, pulmonary embolus, lung cancer, acute or chronic renal failure, or pregnancy. Pulmonary hypertension was confirmed by echocardiography showing PASP >35 mmHg and TRV > 3.4 at rest.

Bias control was achieved through exclusion. Researcher collected all data using a specified form. Data entry and analysis were done on SPSS v25.0. Mean±S.D calculated for age, weight, height, BMI, and COPD duration. Median (IQR) calculated if variables were not normally distributed. Shapiro-Wilk test used for normality assessment. Frequency and percentage calculated for gender, pulmonary hypertension, smoking, and diabetes. Data was stratified for effect modifiers like age, gender, BMI, COPD duration, smoking (>5 pack/year), and diabetes (FBS>126mg/dl). Chi-square test applied post-stratification with p-value ≤0.05 as significant threshold.

RESULTS

Out of 162 patients, 92 (56.8%) were males and 70 (43.2%) were females. The age distribution showed that 31 (19.1%) of patients were between 18-30 years, 52 (32.1%) were between 31-45 years, and 79 (48.8%) were above 45 years of age. The mean age of the participants was 46.17±14.27 years. Regarding BMI classification, 57 (35.2%) had normal BMI, 77 (47.5%) were overweight, and 28 (17.3%) were obese, with a mean BMI of 27.8±2.35 kg/m^2. Diabetes mellitus was present in 29 (17.9%) of the patients. Smoking history was positive in 34 (21.0%) of patients.

The duration of COPD was ≤3 months in 85 (52.5%) of patients and >3 months in 77 (47.5%), with a mean duration of 3.2±1.65 months. Pulmonary hypertension was found in 44 (27.2%) of the patients. Statistically significant associations were observed with diabetes mellitus (p=0.001), smoking (p=0.001), and COPD duration (p=0.001). No significant associations were found with gender (p=0.283), age groups (p=0.116), or BMI categories (p=0.753).

Table 1

Frequency distribution of different variables (n=162)

Variables		Frequency	Percent
Gender	Male	92	56.8
	Female	70	43.2
Age groups	18-30 years	31	19.1
	31-45 years	52	32.1
	>45 years	79	48.8
	Mean age (years)	46.17±14.27	
BMI	Normal	57	35.2
	Overweight	77	47.5
	Obese	28	17.3
	Mean BMI (kg/m^2)	27.8±2.35	
Diabetes mellitus	Yes	29	17.9
	No	133	82.1
Smoking	Yes	34	21.0
	No	128	79.0
Duration of COPD	≤3 months	85	52.5
	>3 months	77	47.5
	Mean duration of COPD (months)	3.2±1.65	
Pulmonary hypertension	Yes	44	27.2
	No	118	72.8

Table 2

Stratification of pulmonary hypertension with respect to different variables

Variables		Pulmonary hypertension		p-value
		Yes	No	
Gender	Male	28(30.4%)	64(69.6%)	0.283
	Female	16(22.9%)	54(77.1%)	
Age groups	18-30 years	5(16.1%)	26(83.9%)	0.116
	31-45 years	12(23.1%)	40(76.9%)	
	>45 years	27(34.2%)	52(65.8%)	
BMI	Normal	16(28.1%)	41(71.9%)	0.753
	Overweight	22(28.6%)	55(71.4%)	
	Obese	6(21.4%)	22(78.6%)	
Diabetes mellitus	Yes	15(51.7%)	14(48.3%)	0.001
	No	29(21.8%)	104(78.2%)	
Smoking	Yes	17(50.0%)	17(50.0%)	0.001
	No	27(21.1%)	101(78.9%)	
Duration of COPD	≤3 months	14(16.5%)	71(83.5%)	0.001
	>3 months	30(39.0%)	47(61.0%)	

DISCUSSION

Our study found that the frequency of pulmonary hypertension in COPD patients was 27.2%, consistent with previous research by Chaouat et al. who reported rates ranging from 20-35%, and Andersen et al. who found approximately 30% in their cohort study. Variations in prevalence may stem from differences in patient populations, disease severity, and diagnostic criteria.[12-13] In their systematic review, Shujaat et al. found that prevalence rates of pulmonary hypertension vary widely (20% to 91%) based on COPD severity and diagnostic methods used.[14]

Our findings showed no significant gender association with pulmonary hypertension (p=0.283), but a slightly higher occurrence in males (30.4%) than females (22.9%). This aligns with Seeger et al.'s observation of male COPD patients possibly having a slightly higher risk of pulmonary vascular issues. Lack of statistical significance in our study could stem from sample size limitations or the complex nature of pulmonary hypertension in COPD.[15]

Age distribution analysis revealed an increasing trend of pulmonary hypertension with age (16.1% in 18-30 years, 23.1% in 31-45 years, 34.2% in >45 years), albeit not statistically significant (p=0.116). This aligns with Thabut et al.'s findings that age-related vascular changes might contribute to pulmonary hypertension in COPD. The progressive nature of COPD and vascular remodeling with aging likely explains this observed trend.[16] Weitzenblum et al. observed that pulmonary hypertension becomes more common as COPD patients age, possibly because of continued exposure to risk factors and ongoing vascular changes.[17]

BMI classification did not significantly correlate with developing pulmonary hypertension (p=0.753), differing from prior research like Maor et al. which hinted at a link between obesity and pulmonary hypertension in COPD patients. Our results suggest that in COPD, respiratory factors may have a stronger impact on the pathophysiological mechanisms leading to pulmonary hypertension compared to body mass.[18]

Our study found significant links between pulmonary hypertension and diabetes mellitus, smoking, and COPD duration (all p=0.001). Diabetes mellitus is associated with a higher risk of pulmonary hypertension, supporting Makarevich et al.'s suggestion that diabetes complications

may worsen pulmonary vascular remodeling in COPD. Endothelial dysfunction is a common factor that likely contributes to both conditions.[19] Suleman et al. in Pakistan linked diabetes to pulmonary hypertension in COPD patients.[20]

The strong link between smoking and pulmonary hypertension (50.0% in smokers versus 21.1% in non-smokers) aligns with Seimetz et al.'s findings showing tobacco smoke exposure directly influences pulmonary vascular cells, leading to proliferation and remodeling regardless of hypoxia. This emphasizes the significance of quitting smoking to prevent pulmonary hypertension in COPD patients.[21] **Wright et al.** also documented the direct toxic effects of cigarette smoke on pulmonary vasculature, leading to endothelial dysfunction and vascular remodeling.[22]

The relationship between COPD duration and the development of pulmonary hypertension reflects the progressive vascular remodeling seen in chronic respiratory diseases. Prolonged exposure to hypoxemia and inflammatory mediators in COPD causes irreversible changes in pulmonary vasculature, emphasizing the need for early intervention in COPD management.[17] In their longitudinal study, Kessler et al. found that pulmonary artery pressure in COPD patients increases by an average of 0.6 mmHg annually.[23]

Aziz et al. reported a higher rate of pulmonary hypertension (45.4%) in COPD patients in Pakistan compared to similar studies, possibly due to differences in patient selection criteria and disease severity. Similarly, Gupta et al. in India found a significant increase in pulmonary hypertension rates (38.02%) with worsening COPD severity.[24-25]

The development of pulmonary hypertension in COPD involves a complex interplay of factors. Hypoxic pulmonary vasoconstriction, key in early stages, results from chronic hypoxia, leading to vascular remodeling. Inflammation and oxidative stress also drive progression. Peinado et al.'s research highlights the presence of inflammatory elements in COPD patients' pulmonary arteries from the disease's onset.[26-27]

Managing pulmonary hypertension in COPD is a challenge. Long-term oxygen therapy benefits survival in hypoxemic COPD patients but has limited impact on pulmonary hypertension. Continuous oxygen therapy has shown improved survival over nocturnal oxygen therapy alone without significant effect on pulmonary hypertension. The use of pulmonary vasodilators like phosphodiesterase-5 inhibitors or endothelin receptor antagonists has yielded variable outcomes in COPD-related pulmonary hypertension.[28] Prins et al.'s systematic review found that although the agents may enhance hemodynamics, their effect on clinical outcomes is unclear.[29]

Our study findings have important clinical implications. The link between diabetes and pulmonary hypertension implies diabetic COPD patients may benefit from increased screening for vascular complications. Additionally, the strong tie to smoking emphasizes the need for cessation programs in COPD care. Disease duration association underlines the potential benefits of early interventions to prevent pulmonary vascular changes.

Several limitations should be acknowledged, including the cross-sectional design that inhibits establishing causal relationships. While echocardiography is clinically practical, it may not be as precise as right heart catheterization for assessing pulmonary pressure. Kovacs et al. highlighted that right heart catheterization is the primary method for diagnosing pulmonary hypertension, with echocardiography serving as a useful screening tool.[30] Future longitudinal studies incorporating more detailed hemodynamic assessments would provide valuable insights into the temporal progression of pulmonary hypertension in COPD.

CONCLUSION

Pulmonary hypertension is a significant issue in COPD patients, seen in over 25% of the study group. The strong links to diabetes, smoking, and disease duration suggest potential areas for prevention strategies. It emphasizes the need for holistic COPD management covering both respiratory and vascular aspects. Timely intervention and improved outcomes can result from early detection of pulmonary hypertension in high-risk patients through regular screening.

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