Original Research Article

Journal of College of Medical Sciences-Nepal, Vol-22, No.2, Apr-Jun 2026

ISSN: 2091-0657 (Print); 2091-0673 (Online) Open Access
DOI: 10.3126/jcms.v22i2.74552

# Prevalence of Pulmonary Hypertension and Its Severity in Patients With Chronic Obstructive Pulmonary Disease

**Rajib Kumar Dey**[1]*, **Ahmed Zooshan**[1], **Gunjan Khadka**[1], **Mohamed Muthuim**[1], **Mohamed Sha**[1], **Hiyan Habeeb**[1], **Ayasha Shrestha**[2]

[1]Department of Internal Medicine, Indira Gandhi Memorial Hospital, Male, Maldives.

[2]Department of Community Medicine, Karuna Foundation, Kathmandu, Nepal.

## ABSTRACT

### Background

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of death and disability worldwide. Pulmonary Hypertension (PH) secondary to COPD significantly contributes to morbidity and mortality. Early identification of this comorbidity may improve prognosis. This study aimed to evaluate the prevalence of PH in COPD patients and assess the association between PH severity and COPD severity using transthoracic echocardiography.

### Methods

An observational cross-sectional study was conducted at Bir Hospital, Kathmandu over six months from August 2019 to January 2020. Sixty-seven patients with spirometry-confirmed COPD were enrolled. PH was assessed using two-dimensional trans-thoracic echocardiography. Doppler echocardiography, defined as systolic pulmonary arterial pressure (sPAP) ≥35 mmHg. COPD severity was classified according to GOLD guidelines.

### Results

The mean age was 68.5±6.7 years; 56.7% were male. The prevalence of PH was 86.6% (58/67 patients). Among these, mild, moderate, and severe PH was observed in 25.4%, 17.9%, and 43.3% of patients, respectively. The frequency of PH increased with COPD severity: 25% in GOLD Grade 1, 80% in Grade 2, 93.1% in Grade 3, and 100% in Grade 4. The association between COPD severity and PH severity was statistically significant ($p<0.001$).

### Conclusions

PH was highly prevalent in this cohort of COPD patients, with both frequency and severity increasing with worsening airflow obstruction. Echocardiography represents a useful non-invasive tool for PH detection in COPD, particularly in patients with advanced disease. However, findings should be interpreted cautiously given study limitations.

**Keywords:** COPD; GOLD staging; Pulmonary hypertension; Echocardiography; Pulmonary artery pressure.

***Correspondence:** Dr. Rajib Kumar Dey, Department of Internal Medicine, Indira Gandhi Memorial Hospital, Male, Maldives. E-mail: dr_rajibdey@yahoo.co.uk, Phone: +960-7980545
**Article received:** 2026-03-05. **Article accepted:** 2026-05-21. **Article published**: 2026-06-30.

## INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of death worldwide, with over 80% of these deaths occurring in low- and middle-income countries.[1] Cardiovascular complication, particularly Pulmonary Hypertension (PH), contribute significantly to COPD related morbidity. [2] PH primarily affects right ventricular function, leading to cor pulmonale, which carries a poor prognosis. Mean pulmonary artery pressure exceeding 20 mmHg significantly predicts five-year survival.[3]

Early detection of PH in COPD patients is therefore essential for reducing morbidity and mortality. Although Right Heart Catheterization remains the gold standard for pulmonary artery pressure assessment, echocardiography is widely preferred due to its non-invasive nature, rapid availability, and lower cost. This study aimed to evaluate the prevalence of PH in COPD patients using echocardiography and to assess the association between PH severity and COPD severity as classified by GOLD guidelines.

## METHODS

### Study Area

This study was conducted at the Bir hospital, Kathmandu, Nepal.

### Study Design

This was an observational cross-sectional, single center study.

### Sample size and sampling

No formal sample size calculation was performed; the final sample of 67 patients reflects the number of eligible participants who met inclusion criteria: Male or female subjects, aged above 40 years. Patient already diagnosed with COPD for at least 1 year, with spirometry test done within the past 1 year showing a (post-bronchodilator) FEV1 <80% of predicted normal and a baseline (post-bronchodilator) FEV1/FVC ratio <70%. Two-dimensional transthoracic echocardiography done within 6 months of last spirometry test, with a left ventricular ejection fraction (LVEF) >50%. Exclusion criteria: Patient has a known respiratory disorder other than COPD (e.g.: lung cancer, sarcoidosis, tuberculosis, lung fibrosis, cystic fibrosis). Patients with PH due to groups 1, 2, 4 and 5 as per the 6th World Symposium on Pulmonary Hypertension.[4] Patients having undergone lung surgery (e.g. lung reduction, lung transplant) were excluded from the study. The study utilized a convenience sample of all eligible COPD patients presenting to the hospital during the six-month study period.

### Data Collection

The study was conducted over the period of six-month from August 2019 to January 2020 after taking approval from the Institutional Review Board of the National Academy of Medical Sciences, Bir Hospital (Ref. No:1075/076/077). Data were collected from eligible COPD patients who completed both spirometry and echocardiography within the specified timeframe.

A pulmonary function test (PFT) was performed, and all the necessary measures were calculated: FEV1, FVC, FEV1/FVC ratio, VC, PEF, FEF and IVC. The main parameters utilized to stage COPD patients according to GOLD guidelines were post-bronchodilator FEV1, FVC, and the FEV1/FVC ratio. For those with FEV1/FVC ratio less than 0.7, the post-bronchodilator FEV1 values were used to stage the severity of COPD as per GOLD guidelines as given in (Table 1).[5]

**Table 1: COPD GOLD Grading**

| In patients with FEV1/FVC < 0.70 | | |
|---|---|---|
| **GOLD Grade** | **Severity** | **FEV1 (% predicted)** |
| 1 | Mild | ≥80% |
| 2 | Moderate | ≥50% to <80% |
| 3 | Severe | ≥30% to < 50% |
| 4 | Very Severe | <30% |

Two-dimensional transthoracic Doppler echocardiography was done on all patients by cardiologists. Tricuspid regurgitant flow was measured using color flow Doppler, and peak jet velocity was quantified using continuous wave Doppler without intravenous contrast. All echocardiographic examinations were performed by

experienced cardiologists using standard parasternal, apical, and subcostal views. The modified Bernoulli equation was employed to determine right ventricular systolic pressure (RVSP), which was deemed to be equal to systolic pulmonary arterial pressure (sPAP) in the absence of right ventricular outflow obstruction.

RVSP = trans-tricuspid pressure gradient (TTPG) + right atrial pressure (RAP) = sPAP (mmHg)

$RVSP = 4Vmax^2 + RAP$

Where trans-tricuspid pressure gradient is $4Vmax^2$ (V= peak velocity of tricuspid regurgitation in m/s). PH was defined as sPAP ≥35 mmHg at rest, consistent with echocardiographic criteria commonly used in clinical practice and prior studies when right heart catheterization is not performed.[3, 6] It should be noted that the current hemodynamic definition of PH established by the 6th World Symposium on Pulmonary Hypertension uses mean pulmonary arterial pressure (mPAP) >20 mmHg measured by right heart catheterization.[4] The sPAP ≥35 mmHg threshold corresponds approximately to an mPAP >20-25 mmHg, though echocardiographic estimation tends to overestimate pressures compared to invasive measurement.[7, 8] This definition was selected to maintain comparability with existing echocardiography-based studies in COPD populations. PH was categorized as mild, moderate, or severe based on sPAP values of 35-50, 50-70, and >70 mmHg, respectively.[6]

**Data Analysis**

The collected data was entered in MS-Excel Sheet and analyzed as per study objectives. The statistical analysis was performed using SPSS version 21. Fisher exact test was used to assess the association between GOLD grades and PH severity categories, as some cells had expected frequencies less than 5, meeting the assumptions for this test. A p-value <0.05 was considered statistically significant. Descriptive statistics are presented as frequencies with percentages and 95% confidence intervals calculated using the Wilson score method for proportions.

## RESULTS

A total of 67 patients were enrolled. The mean age ± standard deviation was 68.5±6.7 years. Among the 67 patients, 38 (56.7%) were males and 29 (43.3%) were females. Seven patients (10.4%) were aged less than 60 years, 30 patients (44.8%) were aged 60 to 70 years, and 30 patients (44.8%) were aged more than or equal to 70 years. The age distribution of patients is shown in (Figure 1).

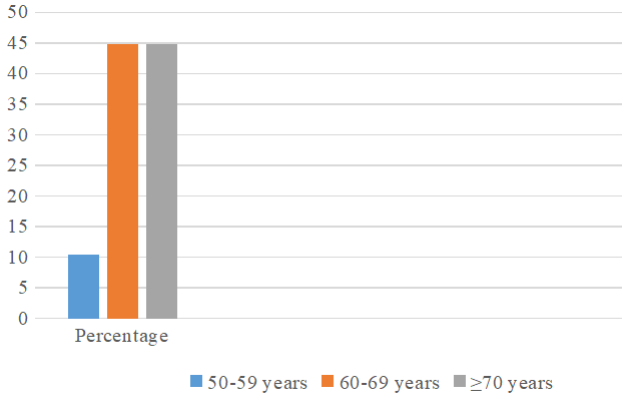


**Figure 1: Age distribution of patients (n=67)**

This study showed that maximum number of patients belonged to GOLD Grade 3 (43.3%), while the minimum number of patients belonged to GOLD Grade 1 (6%). There were 20 patients (29.8%) in GOLD Grade 2, while 14 patients (20.9%) were present in GOLD Grade 4.

The prevalence of PH in COPD patients enrolled in this study was 86.6%.

In our study, most of the patients (43.3%) has severe PH. Nine patients (13.4%) demonstrated normal sPAP on echocardiography, while 25.4% and 17.9% patients demonstrated mild and moderate PH respectively as shown in (Table 2).

**Table 2: Severity of pulmonary hypertension (n=67).**

| Severity of PH | Frequency n (%) | 95% CI(%) |
|---|---|---|
| Normal | 9 (13.4 ) | 7.2-23.6 |
| Mild | 17 (25.4) | 16.4-37.1 |
| Moderate | 12 (17.9) | 10.5-28.9 |
| Severe | 29 (43.3) | 32.0-54.5 |

The following Table 3 illustrates the frequency of PH in various grades of COPD. It shows that the

frequency increases with increasing GOLD Grade. The frequencies of PH in GOLD Grades 1, 2, 3 and 4 were 25%, 80%, 93.1%, and 100% respectively.

**Table 3: Frequency of PH in Grades of COPD (n=67)**

| GOLD Grade | Frequency of PH (%) | 95% CI |
|---|---|---|
| 1 | 1 (25.0) | 4.0-6.0 |
| 2 | 16 (80.0) | 57.8-92.3 |
| 3 | 27 (93.1) | 77.6-98.3 |
| 4 | 14 (100) | 77.6-100 |

The severity of PH in COPD increased with increasing GOLD Grade, as shown in Table 4

In GOLD Grade 1, there were a total number of 4 patients, with 3 patients had normal sPAP. The remaining 1 patient had mildly elevated sPAP, hence mild PH.

In GOLD Grade 2, there were a total number of 20 patients, with 16 patients had elevated sPAP (80%), and out of which 12 (60%) and 4 (20%) patients had mild and moderate PH respectively. No patients were detected to have severe PH in this Grade.

In GOLD Grade 3, there were a total number of 29 patients, with 27 patients had elevated sPAP (93.1%). Out of this, 4 patients (13.8%) 7 patients (24.1%) and 16 patients (55.2%) had mild PH, moderate and severe PH respectively.

In GOLD Grade 4, out of 14 patients, 1 patient (7.1%) had moderate PH, and 13 patients (92.9%) had severe PH.

**Table 4: Association of severity of PH with Grades of COPD (n=67).**

| GOLD Grade | Severity of pulmonary hypertension | | | |
|---|---|---|---|---|
| | Normal (%) | Mild (%) | Moderate (%) | Severe (%) |
| 1 | 3 (75) | 1 (25) | 0 | 0 |
| 2 | 4 (20) | 12 (60) | 4 (20) | 0 |
| 3 | 2 (6.9) | 4 (13.8) | 7 (24.1) | 16 (55.2) |
| 4 | 0 | 0 | 1 (7.1) | 13 (92.9) |

Fisher exact test was applied to these data, demonstrating that as the GOLD Grade increases, the severity of the PH also increases ($p < 0.001$). The stacked bars illustrate the absolute number of patients in each PH severity category (Normal, Mild, Moderate, Severe) within each GOLD grade.

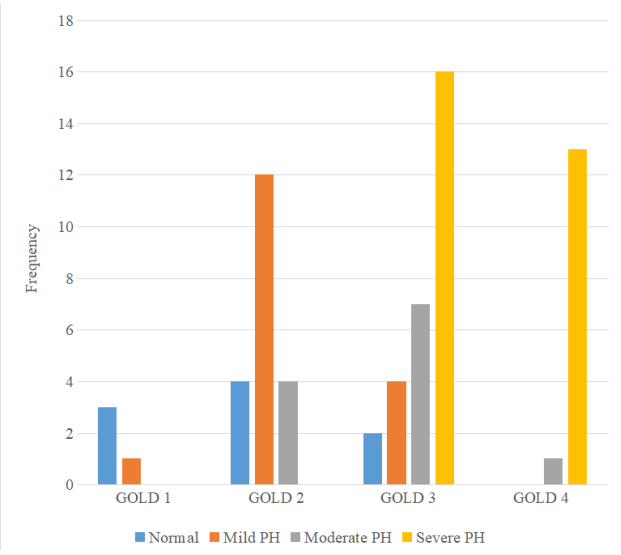


**Figure 2: Frequency of PH in different GOLD Grades (n=67).**

The proportion of patients with PH increases progressively from GOLD Grade 1 (25%) to Grade 4 (100%), with severe PH predominantly observed in Grades 3 and 4 ($p<0.001$, Fisher's exact test).

## DISCUSSION

COPD is associated with extra pulmonary effects among which cardiovascular complications are more frequent. Right ventricular dysfunction and significant structural changes in the pulmonary circulation affect the clinical course of COPD and is inversely related to survival. Chronic hypoxia triggers cellular phenotypic alterations including increased proliferation and migration of vascular smooth muscle cells, as well as synthesis of extracellular matrix proteins that remodel lung vasculature. Remodeling of vessels increases the risk of PH and eventually right heart failure.[7] When measured by right heart catheterization, elevated pulmonary arterial pressure occurs in approximately 20%-30% of patients with COPD.[8] Several studies have shown that the severity of PH has a prognostic

value in COPD patients. In one of these studies, the 5-year survival rates were 50% in patients with mild PH, 30% in those with moderate to severe PH, and none in the small group of patients with very severe PH, indicating that PH severity is directly proportional to the poor outcome in patients with COPD with or without long-term oxygen therapy. [9]

Our study reveals 86.6% patients of various severity of COPD had findings of PH, which is similar in prevalence to previous studies. The frequencies of PH in COPD Grade 1, 2, 3 and 4 were 25%, 80%, 93.1%, and 100%, respectively. In this study it was observed that normal to mild PH was present mainly in GOLD Grades 1 and 2, while moderate to severe PH was present mostly in GOLD Grades 3 and 4 COPD. Among patients with grade 3 COPD, 55.2 % had severe PH, while 92.9% of patients in Grade 4 COPD had severe PH. Thus, the severity of PH was significantly increased with deterioration of lung function. ($P<0.001$).

In a study done by Gupta et al. on 40 COPD patients, PH was found in 42.5% of cases with mild, moderate, and severe PH with prevalence rates of 25%, 10%, and 7.5%, respectively.[3] Our findings were comparable to this study. They concluded that prevalence and severity of PH increase with the severity of COPD. Similar conclusions were made by Scharf et al. where the severity of PH tends to correlate with the degree of airflow obstruction. Our study results also showed a similar correlation.

*Higham et al.,* concluded that echocardiography can efficiently and reliably detect the presence and severity of PH in the COPD patients and given the negative effects of PH on morbidity and mortality, routine echocardiography in patients with severe COPD should be done.[10-12]

A critical distinction between our study and previous work relates to the method of PH assessment. Our echocardiographic approach yielded higher prevalence estimates than the 42.5% reported by *Gupta et al.,*[3] who used similar echocardiographic criteria but studied a smaller cohort with a different COPD severity distribution. Studies employing right heart catheterization have consistently reported lower PH prevalence (20-30%),[8, 13-15] underscoring the methodological contribution to prevalence estimation.

The cross-sectional design of this study permits identification of associations but does not establish causality. While COPD severity and PH severity were significantly associated in our cohort, we cannot determine whether this relationship reflects a direct causal pathway, shared risk factors, or confounding by unmeasured variables.

## Limitations

Several limitations of this study should be acknowledged. First, this was a single-center investigation with a modest sample size (n=67) and no a priori power calculation, which together limit statistical power and the generalizability of the findings to broader COPD populations. Second, PH was defined using echocardiographic estimation of sPAP (≥35 mmHg) rather than the gold standard right heart catheterization (mPAP >20 mmHg); since echocardiography can overestimate pulmonary pressures, particularly in patients with hyperinflated lungs, this may have contributed to the high PH prevalence observed and introduced misclassification bias. Third, the statistical analysis was restricted to descriptive and bivariate comparisons using Fisher's exact test; multivariable analysis controlling for potential confounders such as age, sex, body mass index, smoking history, and comorbidities could not be performed due to the limited sample size. Consequently, residual confounding cannot be excluded, and the reported associations should be interpreted as unadjusted relationships. Fourth, the interval between spirometry and echocardiography extended up to six months in some cases, and although all patients were clinically stable at the time of echocardiography, disease progression or regression during this period could have influenced the correlation between COPD and PH severity. Additionally, inter-observer variability for echocardiographic measurements was not formally assessed, which may have introduced measurement error. Finally, recruitment was conducted at a tertiary

care referral hospital, which likely resulted in overrepresentation of patients with advanced COPD (64.2% in GOLD Grades 3-4). This referral bias limits the applicability of our prevalence estimates to primary care or community-based settings where milder disease predominates, and may have inflated the observed strength of association between COPD severity and PH.

## Conclusions

In conclusion, our echocardiographic findings showed that PH was progressively more prevalent in higher GOLD stages of COPD, with a statistically significant association. Echocardiography appears to be a practical, non-invasive tool for detecting PH in this population.

## Abbreviations

COPD- Chronic Obstructive Pulmonary Disease
FEF- Forced Expiratory Flow
FEV1- Forced Expiratory Volume in one second
FVC- Force Vital Capacity
GOLD- Global initiative for chronic Obstructive Lung Disease
IVC- Inspiratory Vital Capacity
PEF- Peak Expiratory Flow
PH- Pulmonary Hypertension
RAP- Right Atrial Pressure
RVSP- Right Ventricular Systolic Pressure
sPAP- systolic Pulmonary Artery Pressure
TTPG- trans-tricuspid pressure gradient
VC- Vital Capacity

**Ethics approval:** This research was approved by the Institutional Review Board of the National Academy of Medical Sciences, Bir Hospital, Kathmandu, Nepal (Ref. No.:1075/076/077). All methods were performed in accordance with the relevant guidelines and regulations. Written consent was taken from all the participants.

**Acknowledgement:** The authors are sincerely grateful to the patients who participated in this study.

**Conflict of interest:** The author declares no conflict of interest.

**Funding:** No funding was received from any agency for conducting this study.

**Availability of data and materials:** The datasets used in this study are available on reasonable request from the corresponding author. The data is not publicly available to ensure the privacy of the study participants.

## Author contributions

**Conceptualization:** Rajib Kumar Dey, Ahmed Zooshan, Gunjan Khadka

**Data curation:** Ahmed Zooshan, Gunjan Khadka, Mohamed Muthuim, Mohamed Sham, Hiyan Habeeb, Ayasha Shrestha

**Formal analysis:** Rajib Kumar Dey, Ahmed Zooshan, Ayasha Shrestha

**Methodology:** Rajib Kumar Dey, Ahmed Zooshan, Gunjan Khadka

**Supervision:** Rajib Kumar Dey, Ahmed Zooshan, Gunjan Khadka

**Writing-original draft:** Rajib Kumar Dey, Ahmed Zooshan, Gunjan Khadka

**Writing-review & editing:** Rajib Kumar Dey, Ahmed Zooshan, Gunjan Khadka, Ayasha Shrestha

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**Citation:** Dey RK, Zooshan A, Khadka G, Muthuim M, Sham M, Habeeb H, et al. Prevalence of Pulmonary Hypertension and Its Severity in Patients With Chronic Obstructive Pulmonary Disease. J Coll Med Sci-Nepal. 2026 Jun. 30;22(2):117-23.