Research Article

Nocturnal Hypoxemia As A Marker Of Disease Severity In Chronic Obstructive Pulmonary Disease: A Cross-Sectional Study

Dr Thirumagal R[1], Dr Elen Ann Abraham[2],Dr.Ghanshyam Verma[3]

[1]Respiratory Medicine Resident, Respiratory Medicine, Sree Balaji Medical College And Hospital
[2]Associate Professor, Sree Balaji medical college and hospital , Chennai
[3]HOD of Respiratory Medicine Department , Sree Balaji Medical College and Hospital

Abstract

Background:
Nocturnal oxygen desaturation (NOD) is a common but underrecognized phenomenon in chronic obstructive pulmonary disease (COPD), contributing to disease progression and adverse clinical outcomes. Its association with disease severity and clinical predictors remains inadequately explored in resource-limited settings.

Methods:
A hospital-based cross-sectional analytical study was conducted from August 2025 to January 2026 among 100 clinically stable COPD patients. Data on demographic and clinical variables were collected, and COPD severity was classified using GOLD criteria. Nocturnal oxygen desaturation was assessed using overnight pulse oximetry, while exercise-induced desaturation was evaluated using the six-minute walk test (6-MWT). Statistical analysis was performed using SPSS version 26.0. Associations were assessed using chi-square test, and predictors were identified using univariate and multivariate logistic regression.

Results:
The prevalence of nocturnal oxygen desaturation was **58%**. NOD increased significantly with COPD severity, from 16.7% in GOLD I to 90.9% in GOLD IV ($p<0.001$). On multivariate analysis, independent predictors of NOD included age >60 years (AOR 1.8, $p=0.03$), smoking (AOR 2.6, $p=0.004$), BMI <18.5 kg/m² (AOR 2.1, $p=0.02$), COPD duration ≥5 years (AOR 1.9, $p=0.04$), GOLD stage III–IV (AOR 3.5, $p<0.001$), and 6-MWT desaturation (AOR 5.2, $p<0.001$).

Conclusion:
Nocturnal oxygen desaturation is highly prevalent in COPD and strongly associated with disease severity and key clinical factors. Early identification using simple screening tools such as pulse oximetry and 6-MWT may facilitate timely intervention and improve clinical outcomes.

Keywords: Chronic Obstructive Pulmonary Disease; Nocturnal Hypoxemia; Oxygen Desaturation; Sleep-Disordered Breathing; Disease Severity; Six-Minute Walk Test.

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory disorder characterized by persistent airflow limitation and chronic inflammatory response of the airways and lung parenchyma. It is increasingly recognized not merely as a pulmonary condition but as a systemic disease with significant extrapulmonary manifestations and comorbidities that influence its clinical course and outcomes [1]. Over the past decade, evolving concepts have emphasized COPD as a complex, heterogeneous syndrome involving multiple pathophysiological pathways rather than a single disease entity [1].

Globally, COPD remains a major public health challenge and is a leading cause of morbidity and mortality. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), COPD contributes substantially to healthcare burden due to frequent exacerbations, hospitalizations, and long-term disability [2]. The World Health Organization estimates that COPD is among the top causes of death worldwide, with a rising trend attributable to aging populations, continued tobacco exposure, and environmental risk factors [3]. In low- and middle-income countries such as India, the burden is even more significant, often described as an “iceberg phenomenon,” where a large proportion of cases remain undiagnosed until advanced stages [4].

A critical aspect of COPD that has gained increasing attention is the role of comorbid conditions in modulating disease severity and prognosis. COPD commonly coexists with cardiovascular diseases, metabolic disorders, and sleep-related breathing disorders, which together contribute to increased morbidity and mortality [5]. Among these, sleep-disordered breathing, particularly obstructive sleep apnea (OSA), has emerged as a clinically significant yet underrecognized comorbidity.

The coexistence of COPD and OSA, referred to as the “overlap syndrome,” was first described by Chaouat et al., who demonstrated that patients with both conditions exhibit more severe nocturnal hypoxemia compared to those with either disorder alone [6]. This overlap leads to additive or even synergistic adverse effects, including worsened gas exchange

abnormalities, pulmonary hypertension, and increased risk of cardiovascular complications [7]. Subsequent studies have reinforced the importance of recognizing overlap syndrome, highlighting its higher prevalence than previously assumed and its significant impact on clinical outcomes [8].

Sleep itself introduces physiological changes in respiratory function that predispose individuals with COPD to hypoxemia. During sleep, particularly in rapid eye movement (REM) stages, there is a reduction in ventilatory drive, decreased intercostal muscle activity, and alterations in ventilation-perfusion matching. These changes result in transient hypoventilation and oxygen desaturation, which are exaggerated in patients with compromised pulmonary function [9]. Early studies by Wynne et al. demonstrated that patients with COPD frequently experience significant oxygen desaturation during sleep, even in the absence of daytime hypoxemia [10]. Similarly, Phillipson and Goldstein highlighted the critical influence of sleep on breathing patterns in COPD, emphasizing the vulnerability of these patients to nocturnal respiratory disturbances [11].

Longitudinal observations have further shown that nocturnal desaturation in COPD is not a static phenomenon but may progress over time, correlating with worsening disease severity and functional impairment [12]. Importantly, isolated nocturnal desaturation has been identified in a subset of COPD patients who maintain relatively preserved daytime oxygen levels, suggesting that nocturnal hypoxemia may serve as an early marker of disease progression [13]. This has led to growing interest in the evaluation of overnight oxygen saturation as an adjunct tool in COPD assessment.

The clinical implications of nocturnal hypoxemia are profound. Repeated episodes of oxygen desaturation during sleep can lead to sympathetic activation, oxidative stress, systemic inflammation, and endothelial dysfunction. These pathophysiological mechanisms contribute to the development of pulmonary hypertension, right heart strain, and increased cardiovascular risk. Lacasse et al. emphasized the importance of systematically evaluating nocturnal oxygen desaturation in COPD, given its association with adverse clinical outcomes and potential therapeutic implications [14].

In parallel, there has been increasing recognition of the need for comprehensive assessment tools that capture the multidimensional impact of COPD. The COPD Assessment Test (CAT), developed by Jones et al., provides a standardized measure of symptom burden and health status, facilitating better evaluation of disease severity and treatment response [15]. However, conventional assessment tools may not adequately reflect nocturnal physiological disturbances, underscoring the need for integrating sleep-related parameters into routine evaluation.

Despite growing evidence, nocturnal hypoxemia in COPD remains underdiagnosed and undertreated in clinical practice, particularly in resource-limited settings. Furthermore, the interaction between COPD severity and sleep-related oxygen desaturation is complex and influenced by multiple factors, including comorbid OSA, body habitus, and underlying cardiovascular status. There is also limited data from developing countries, where environmental exposures and healthcare access may further modify disease patterns.

Given these gaps, there is a pressing need to better understand the relationship between nocturnal hypoxemia and COPD severity. Identifying patients at risk of significant nocturnal desaturation may allow for earlier intervention, improved risk stratification, and optimization of therapeutic strategies, including oxygen therapy and management of coexisting sleep disorders.

Therefore, the present study aims to evaluate the association between nocturnal hypoxemia and the severity of COPD, with a focus on identifying clinical correlates and potential implications for disease management. By addressing this critical yet underexplored aspect of COPD, the study seeks to contribute to a more comprehensive understanding of disease burden and improve patient-centered outcomes.

Methodology

A hospital-based cross-sectional analytical study was conducted in the Department of Pulmonary Medicine at a tertiary care center from August 2025 to January 2026, after obtaining approval from the Institutional Ethics Committee. Adult patients diagnosed with chronic obstructive pulmonary disease (COPD) attending both outpatient and inpatient services during the study period were consecutively recruited. COPD was diagnosed based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, and only clinically stable patients were included.

Patients aged 18 years and above who provided informed written consent were enrolled. Patients with acute exacerbation of COPD, previously diagnosed obstructive sleep apnea on treatment, chronic respiratory failure requiring long-term oxygen therapy, or severe comorbid conditions such as advanced cardiac, renal, or neurological diseases were excluded to minimize confounding factors.

A total of 100 patients were included based on feasibility during the study period. Data were collected using a structured proforma, which included demographic variables such as age, gender, smoking status, body mass index (BMI), and duration of COPD. BMI was categorized as <18.5 kg/m², 18.5–24.9 kg/m², and ≥25 kg/m². COPD severity was classified according to GOLD staging (I–IV) based on spirometric findings.

All participants underwent clinical and functional evaluation. Exercise-induced desaturation was assessed using the six-minute walk test (6-MWT). Nocturnal oxygen desaturation (NOD) was assessed using overnight pulse oximetry and was defined as oxygen saturation falling below 90% for a significant duration during sleep.

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0. Categorical variables were expressed as frequencies and percentages. Associations between variables and nocturnal oxygen desaturation were analyzed using the chi-square test. Univariate logistic regression analysis was performed to identify significant predictors, followed by multivariate logistic regression to determine independent predictors. Odds ratios (OR) and adjusted odds ratios (AOR) with 95% confidence intervals (CI) were calculated. A p-value of <0.05 was considered statistically significant.

All ethical standards for research involving human participants were maintained, and confidentiality of patient information was ensured throughout the study.

Results

A hospital-based cross-sectional analytical study was conducted from August 2025 to January 2026 among 100 clinically stable COPD patients to assess nocturnal oxygen desaturation using overnight pulse oximetry and its association with disease severity.

Table 1. Baseline Characteristics (N=100)

Category	**n (%)**
Age	
<50	18 (18.0)
50–60	36 (36.0)
>60	46 (46.0)
Gender	
Male	72 (72.0)
Female	28 (28.0)
Smoking	
Smoker	68 (68.0)
Non-smoker	32 (32.0)
BMI	
<18.5	24 (24.0)
18.5–24.9	52 (52.0)
≥25	24 (24.0)
COPD Duration	
<5 years	40 (40.0)
≥5 years	60 (60.0)

Table 1 shows the baseline demographic and clinical profile of the study population, where the majority of patients were aged >60 years (46%), predominantly male (72%), and smokers (68%), with most having normal BMI (52%) and longer disease duration ≥5 years (60%).

Table 2. Clinical Characteristics (N=100)

Category	**n (%)**
GOLD	
I	12 (12.0)
II	34 (34.0)

III	32 (32.0)
IV	22 (22.0)
NOD	
Present	58 (58.0)
Absent	42 (42.0)
6-MWT Desaturation	
Present	54 (54.0)
Absent	46 (46.0)

Table 2 summarizes the clinical characteristics, demonstrating that most patients belonged to GOLD stage II (34%) and III (32%), with 58% exhibiting nocturnal oxygen desaturation and 54% showing exercise-induced desaturation on 6-MWT.

Table 3. Univariate Logistic Regression Analysis of Factors Associated with NOD (N = 100)

Category	NOD Present n (%) (n=58)	NOD Absent n (%) (n=42)	OR (95% CI)	p-value
Age (in years)				
<50	6 (33.3)	12 (66.7)	1 (Ref)	—
50–60	20 (55.6)	16 (44.4)	2.5 (0.8-7.3)	0.1
>60	32 (69.6)	14 (30.4)	4.6 (1.5-13.5)	0.04
Gender				
Female	12 (42.9)	16 (57.1)	1 (Ref)	0.12
Male	46 (63.9)	26 (36.1)	2.4 (1.0-5.4)	
Smoking Status				
Non-smoker	10 (31.3)	22 (68.7)	1 (Ref)	0.002
Smoker	48 (70.6)	20 (29.4)	5.3 (2.2-12.5)	
BMI (kg/m²)				
18.5–24.9	24 (46.2)	28 (53.8)	1 (Ref)	—
<18.5	18 (75.0)	6 (25.0)	3.5 (1.2-9.8)	0.03
≥25	16 (66.7)	8 (33.3)	2.3 (0.9-6.0)	0.08
COPD Duration				
<5 years	18 (45.0)	22 (55.0)	1 (Ref)	0.01
≥5 years	40 (66.7)	20 (33.3)	2.4 (1.1-5.2)	
GOLD Severity				
I–II	16 (34.8)	30 (65.2)	1 (Ref)	
III–IV	44 (73.3)	16 (26.7)	5.2 (2.3-11.5)	<0.001
6-MWT Desaturation				
Absent	12 (26.1)	34 (73.9)	1 (Ref)	<0.001
Present	46 (85.2)	8 (14.8)	16.3 (6.2-42.5)	

Table 3 presents the univariate logistic regression analysis, showing that advanced age (>60 years), smoking (OR 5.3), low BMI (OR 3.5), longer COPD duration (OR 2.4), higher GOLD stage (OR 5.2), and 6-MWT desaturation (OR 16.3) were significantly associated with nocturnal oxygen desaturation.

Table 4. Multivariate Logistic Regression Analysis for Predictors of NOD (N = 100)

Category	AOR (95% CI)	p-value
Age (in years)		
<50	1 (Ref)	—
50–60	1.3 (0.6-2.8)	0.48
>60	1.8 (1.1-3.9)	0.03
Gender		

Female	1 (Ref)	
Male	1.4 (0.7-2.9)	0.30
Smoking Status		
Non-smoker	1 (Ref)	0.004
Smoker	2.6 (1.3-5.2)	
BMI (kg/m²)		
18.5–24.9	1 (Ref)	—
<18.5	2.1 (1.1-4.8)	0.02
≥25	1.2 (0.5-2.6)	0.62
COPD Duration		
<5 years	1 (Ref)	0.04
≥5 years	1.9 (1.0-3.6)	
GOLD Severity		
I–II	1 (Ref)	<0.001
III–IV	3.5 (1.8-6.8)	
6-MWT Desaturation		
Absent	1 (Ref)	<0.001
Present	5.2 (2.4-10.9)	

Table 4 depicts the multivariate logistic regression analysis, identifying age >60 years (AOR 1.8), smoking (AOR 2.6), low BMI (AOR 2.1), longer disease duration (AOR 1.9), severe COPD (AOR 3.5), and 6-MWT desaturation (AOR 5.2) as independent predictors of nocturnal oxygen desaturation.

Table 5. Association Between GOLD Severity and NOD

GOLD Stage	NOD Present n (%) (n=58)	NOD Absent n (%) (n=42)	Total n (%)	% with NOD	p value
I	2 (3.4)	10 (23.8)	12 (12.0)	16.7	<0.001
II	14 (24.1)	20 (47.6)	34 (34.0)	41.2	
III	22 (37.9)	10 (23.8)	32 (32.0)	68.8	
IV	20 (34.5)	2 (4.8)	22 (22.0)	90.9	
Total	58 (100)	42 (100)	100 (100)		

Table 5 illustrates the association between COPD severity and nocturnal oxygen desaturation, showing a significant progressive increase in NOD prevalence from 16.7% in GOLD I to 90.9% in GOLD IV (p<0.001).

Discussion

In the present study, nocturnal oxygen desaturation (NOD) was observed in 58% of COPD patients, indicating a high prevalence of sleep-related hypoxemia. Similarly, Raman et al. [16] reported that more than half of COPD patients exhibited nocturnal hypoxemia, with significantly higher prevalence in moderate-to-severe COPD compared to mild disease. They demonstrated a statistically significant association between COPD severity and nocturnal desaturation (p<0.05). This similarity in prevalence suggests that nocturnal hypoxemia is a common and clinically significant feature of COPD across different populations.

In our study, NOD prevalence increased progressively from 16.7% in GOLD I to 41.2% in GOLD II, 68.8% in GOLD III, and 90.9% in GOLD IV (p<0.001). Raman et al. [16] also demonstrated a graded increase in nocturnal hypoxemia with advancing GOLD stages, showing significantly higher desaturation indices in severe COPD groups. Furthermore, Jain et al. [17] reported that patients with COPD-OSA-PLMS overlap had significantly higher oxygen desaturation index (ODI) and longer duration of hypoxemia compared to isolated COPD, highlighting an additive effect. These findings support that both disease severity and comorbid sleep disorders contribute synergistically to nocturnal hypoxemia.

In the present study, patients with GOLD III–IV disease had significantly higher odds of NOD (OR 5.2; AOR 3.5, p<0.001). Donovan et al. [18] reported that COPD patients at high risk for undiagnosed OSA had significantly worse clinical outcomes, including higher hospitalization rates and mortality, although exact percentages of hypoxemia were not quantified. Their findings indicate that overlap syndrome contributes to increased disease burden, which aligns with our observation that severe COPD is strongly associated with nocturnal hypoxemia.

Smoking was a major determinant in our study, with 70.6% of smokers having NOD compared to 31.3% of non-smokers (OR 5.3; AOR 2.6, p=0.004). Zeng et al. [19] found that polycythemia was significantly more prevalent in COPD patients with OSA (approximately 10–15%) compared to those without OSA, indicating chronic hypoxic exposure. This supports our finding that smoking, by worsening airway inflammation and gas exchange, contributes to sustained nocturnal hypoxemia and its systemic consequences.

Age also showed a strong association, with 69.6% of patients aged >60 years exhibiting NOD compared to 33.3% in <50 years (OR 4.6; AOR 1.8, p=0.03). Donovan et al. [18] observed that older patients had a higher probability of undiagnosed OSA and worse outcomes, although exact prevalence was not specified. This suggests that age-related decline in respiratory mechanics and ventilatory control contributes to increased nocturnal hypoxemia.

In our study, underweight patients (BMI <18.5 kg/m²) had a NOD prevalence of 75% compared to 46.2% in normal BMI (OR 3.5; AOR 2.1, p=0.02). Hornyak et al. [22] reported that PLMS and sleep disturbances are associated with altered physiological states including metabolic imbalance and autonomic dysfunction, which can influence oxygenation. This indicates that poor nutritional status in COPD may impair respiratory muscle strength and worsen hypoxemia.

A key finding in the present study was that 85.2% of patients with 6-MWT desaturation had NOD compared to only 26.1% without desaturation (OR 16.3; AOR 5.2, p<0.001). Although direct comparative percentages are limited, Budhiraja et al. [20] reported that PLMS persisted in a significant proportion of OSA patients even after CPAP therapy, indicating that hypoxemia may be influenced by multiple physiological mechanisms beyond airway obstruction. This supports our finding that exercise-induced desaturation is a strong clinical predictor of nocturnal hypoxemia.

Regarding PLMS, Budhiraja et al. [20] reported that periodic limb movements were present in a substantial proportion of OSA patients and persisted despite treatment, suggesting independent physiological significance. Al-Alawi et al. [21] found that PLMS was associated with increased prevalence of hypertension and daytime sleepiness, indicating systemic impact. These findings suggest that PLMS contributes to sleep fragmentation and physiological stress, potentially worsening hypoxemia.

Hornyak et al. [22] further reported that PLMS is associated with frequent arousals and autonomic activation, while Charokopos et al. [23] demonstrated that PLMS occurs in COPD patients and may interact with respiratory disturbances during sleep. These findings support the hypothesis that PLMS may act as an additional burden in COPD patients, exacerbating nocturnal hypoxemia.

Mirza et al. [24] showed that patients with frequent PLMS had a significantly increased risk of atrial fibrillation, while Sforza et al. [25] demonstrated increased cardiovascular variability and autonomic dysfunction associated with PLMS. These findings indicate that PLMS has important cardiovascular implications, which may be mediated through recurrent hypoxemia and sympathetic activation.

Murase et al. [26] reported that patients with OSA and PLMS had significantly higher inflammatory markers compared to those without PLMS, while Murase et al. [27] further demonstrated that PLMS was associated with elevated plasma fibrinogen levels, indicating increased cardiovascular risk. These findings suggest that PLMS contributes to systemic inflammation, which may further aggravate hypoxemia and disease severity.

DelRosso et al. [28] reported that higher periodic limb movement index was significantly associated with hypoxemia, demonstrating a direct link between PLMS and oxygen desaturation. Additionally, DelRosso et al. [29] found that residual PLMS after CPAP therapy remained associated with persistent hypoxemia, indicating that treatment of OSA alone may not fully resolve nocturnal oxygen abnormalities.

Finally, Jung et al. [30] reported that nocturnal hypoxemia and PLMS were independent predictors of mortality, with significantly higher mortality rates in patients exhibiting both conditions. This highlights the prognostic importance of sleep-related disturbances and supports our findings that nocturnal hypoxemia is not merely a physiological observation but a clinically significant marker of disease severity.

Conclusion

The present study demonstrates that nocturnal hypoxemia is highly prevalent (58%) among COPD patients and shows a strong, statistically significant association with disease severity, with prevalence rising sharply to 90.9% in GOLD stage IV. In addition, factors such as smoking (70.6%), low BMI (75%), advanced age (>60 years: 69.6%), and exercise-induced desaturation (85.2%) were identified as significant predictors of nocturnal oxygen desaturation. These findings highlight that nocturnal hypoxemia is not an isolated phenomenon but closely linked to both pulmonary impairment and systemic clinical parameters.

When interpreted in the context of existing evidence, nocturnal hypoxemia appears to result from a complex interplay between

airflow limitation, impaired gas exchange, systemic inflammation, and coexisting sleep-related disorders such as obstructive sleep apnea and periodic limb movements. This multifactorial mechanism contributes to worsening disease severity, increased cardiovascular risk, and poorer clinical outcomes.

Therefore, early identification of patients at risk of nocturnal hypoxemia—particularly those with severe COPD, smoking history, low BMI, and exercise desaturation—is crucial. Incorporating simple screening tools such as overnight pulse oximetry and 6-minute walk test into routine clinical practice may facilitate timely detection. Targeted interventions, including optimization of COPD management, evaluation for overlap syndromes, and appropriate oxygen therapy, may significantly reduce morbidity and improve quality of life.

In conclusion, nocturnal hypoxemia represents an important, yet underrecognized clinical dimension of COPD, and its systematic evaluation should be integrated into comprehensive disease assessment strategies to improve long-term outcomes.

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