ORIGINAL RESEARCH

Screening Parameters for COPD-OSA Overlap Syndrome in COPD Patients: Indian Perspective

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Abstract

Introduction: As Indian patients have different predisposing morphological characteristics, we undertook this study to evaluate the clinical profile of overlap syndrome and compare them with COPD patients to find out the screening tools for obstructive sleep apnea (OSA) in Indian chronic obstructive pulmonary disease (COPD) patients.

Aims and objectives:

- To study the clinical profile of patients with overlap syndrome.
- To compare them with COPD patients.
- To develop screening tools for overlap syndrome in COPD.

Materials and methods: A prospective case-control study was carried out in a tertiary care center. Overnight pulse oximetry was carried out for all COPD patients. Those having snoring or saw-tooth pattern on overnight oximetry were subjected to level 1 polysomnography. About 30 patients of overlap syndrome were compared with 65 COPD patients.

Results: The mean age in overlap syndrome group (56.9 ± 6.86 years) was significantly lower ($p < 0.01$). The daytime PaO_2 and lowest nocturnal saturation were significantly lower in overlap group. $PaCO_2$ and forced expiratory volume at 1 second (FEV1) were significantly higher. For diagnosing overlap syndrome, the positive and the negative predictive values of snoring were 84.42 and 100%; of body mass index (BMI) ≥25 kg/m^2 were 86.67 and 98.88%; and of excessive daytime sleepiness were 37.57 and 97.86%, respectively.

Conclusion: Absence of snoring and BMI <25 kg/m^2 virtually rules out overlap syndrome. The EDS has a high false-positive rate for predicting OSA. Patients having overlap syndrome have poor daytime and nocturnal oxygenation despite good lung functions.

Keywords: Body mass index, Chronic obstructive pulmonary disease, Forced expiratory volume at 1 second, Obstructive sleep apnea, Snoring.

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Abbreviations Used in this Article

AASM = American Academy of Sleep Medicine; ABG = Arterial blood gases; AHI = Apnea hypopnea index; ATS = American Thoracic Society; BMI = Body mass index; BODE = BMI, obstruction, dyspnea, and exercise; COPD = Chronic obstructive pulmonary disease; COPD-OSA = Chronic obstructive pulmonary disease-obstructive sleep apnea; EDS = Excessive daytime sleepiness; ESS = Epworth Sleepiness Scale; FEV1 = Forced expiratory volume at 1 second; FVC = Forced vital capacity; OSA = Obstructive sleep apnea; PSG = Polysomnography.

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Introduction

The co-occurrence of obstructive sleep apnea (OSA) and chronic obstructive pulmonary disease (COPD) in a single patient is termed as "COPD-OSA overlap syndrome" and was first described by Flenley in 1985.[1] Since both the diseases are individually highly prevalent, their co-existence is also very common. This chronic obstructive pulmonary disease has a spectrum of clinical phenotypes ranging from the predominant emphysema to the predominant chronic bronchitis phenotype. The predominant emphysema patients having hyperinflation are less likely to develop OSA.[2] However, higher body mass index (BMI) and the likelihood of right-sided heart failure in the predominant chronic bronchitis phenotype predispose to the development of OSA.[3] Cigarette smoking-associated upper airway inflammation and corticosteroid therapy-associated upper airway muscle dysfunction may also lead to OSA.[4] In practice, most patients with COPD have a mixture of emphysema and chronic bronchitis, and the probability of OSA in COPD will represent the balance of the protective factors of emphysema and promoting factors of chronic bronchitis in an individual patient.

Patients with COPD-OSA overlap syndrome have a worse prognosis compared with COPD or OSA. During sleep, patients with COPD-OSA overlap syndrome suffer more frequent episodes of nocturnal oxygen desaturation. They also have greater daytime hypoxemia and hypercapnia than those who have isolated COPD or OSA.[5,6] These patients are also more prone to develop cardiac

arrhythmias and pulmonary arterial hypertension.[7,8] And COPD-OSA overlap syndrome patients also tend to develop severe respiratory failure requiring a noninvasive ventilator during an acute exacerbation. The life expectancy of untreated COPD-OSA overlap syndrome is much worse than COPD alone with the same lung function.[4] Hence, the diagnosis of COPD-OSA overlap syndrome is important to guide appropriate treatment.

All COPD patients need not be evaluated with polysomnography (PSG) routinely. There are many questionnaires available for OSA, but none have been validated specifically for COPD. The presence of OSA in COPD patients causes severe and early symptoms compared with patients having either of them alone; hence screening parameters need to be developed for COPD-OSA overlap syndrome. There are some studies from India on COPD-OSA overlap syndrome but none of the studies has evaluated the screening parameters for it.[9–11] Since Indian patients have different predisposing morphological characteristics for developing OSA compared with Western counterparts, it is important to find out the screening parameters for Indian patients. We aim to study the clinical profile of patients with COPD-OSA overlap syndrome and compare them with COPD alone so that we can find out the screening parameters for OSA in Indian COPD patients.

Aims and Objectives

- To study the clinical profile of patients with COPD-OSA overlap syndrome.
- To compare their BMI, spirometry, pulse oximetry and arterial blood gas (ABG) parameters with patients of COPD alone.
- To find out the screening parameters for COPD-OSA overlap syndrome in COPD.

Materials and Methods

It was a cross-sectional study carried out in a tertiary care center from January 2018 to July 2019 after obtaining institutional ethics committee approval. Clinically stable COPD patients coming to the outpatient department were included in the study after taking their consent. The COPD was diagnosed as per GOLD (2018) guidelines.[12] The spirometry was performed for all the subjects on Medisoft/Morgan Scientific Spiro Airin and was interpreted as per the American Thoracic Society (ATS) guidelines.[13] Forced vital capacity (FVC), forced expiratory volume at 1 second (FEV1), and FEV1/FVC ratio were recorded. The patients were divided into four spirometry grades based on GOLD classification.

History of snoring and BMI was evaluated right at the outset. Snoring history was elicited from the patient as well as close relatives. BODE (BMI, Obstruction, Dyspnea, and Exercise capacity)[14] index is usually the most commonly used tool to predict mortality in COPD patients. The BMI in BODE index has a cut-off value of 21 kg/m^2. Hence, patients with snoring and/or BMI >21 kg/m^2 were subjected to level 1 PSG. Others who did not have snoring or had BMI ≤ 21 kg/m^2 were subjected to only overnight pulse oximetry. A "saw-tooth" pattern on overnight pulse oximetry points toward the presence of OSA.[15] Those who had saw-tooth pattern on overnight pulse oximetry were additionally subjected to level 1 PSG. A level 1 PSG was performed using Philips Alice 5® PSG machine for patients with snoring or saw-tooth pattern on pulse oximetry. Sleep staging and scoring of respiratory events were done. Obstructive sleep apnea was diagnosed as per the American Academy of Sleep Medicine (AASM) guidelines.[16]

Table 1: Inclusion and exclusion criteria for patient recruitment in the study

Inclusion criteria	*Exclusion criteria*
Giving fully informed consent	Unstable vitals with SpO_2 ≤ 92% on room air
Confirmed diagnosis of COPD as per GOLD guidelines	≥1 exacerbation in last 1 year
Clinically stable with regular follow-up	Uncontrolled comorbid conditions like CCF
Duration of disease ≥1 year	Poor mobility
	Neurological or metabolic disorder
	History of psychotropic drug use

The patients were recruited into "COPD alone group" and "COPD-OSA overlap syndrome group" in 2:1 ratio. The inclusion and exclusion criteria are mentioned in Table 1. Patient details were noted which included demographic profile, clinical history and examination. All patients were thoroughly evaluated with respect to their sleep. This included the total duration of sleep; quality of sleep and daytime symptoms. Their Epworth Sleepiness Scale (ESS) score, taken as a marker for excessive daytime sleepiness (EDS), was calculated.[17] The ESS score of 10 or more was considered diagnostic of EDS. All patients were subjected to blood investigations and ABG analysis.

The two groups, COPD alone and COPD-OSA overlap syndrome group were compared based on their symptoms (snoring and EDS), BMI, FEV1 (absolute and % predicted), ABG parameters and lowest nocturnal oxygen saturation. Both the groups were also compared based on these parameters in the respective GOLD grade.

The data were tabulated in MS Excel. Open EPI software was used for statistical analysis. The "Independent t-test" was used to analyze the continuous data between the two groups and "Chi-square test" was used to analyze the categorical data. *p*-value <0.05 was considered to be statistically significant. The positive and negative predictive value was calculated using the standard 2 by 2 table. The sample size was calculated for our primary objective to study the clinical profile of patients with COPD-OSA overlap syndrome. Based on the prevalence of COPD-OSA overlap syndrome from previous studies, using the formula – $(Z_{1-\alpha/2})^{2*}$ $p(1 - p)/d^2$ (assuming a prevalence of 10% and precision of 10%), a minimum sample size of 30 was required.[18]

Results

Figure 1 shows the flow diagram of patient inclusion in our study. A total of 95 patients were enrolled. About 33 patients had a high likelihood of OSA based on the history of snoring and/or BMI >21 kg/m^2 and were subjected to PSG. About 30 patients had apnea-hypopnea index (AHI) of >5/hour and hence were diagnosed as having OSA. About 62 patients underwent overnight pulse oximetry, of which 3 patients showed saw toothing, but none of them had OSA confirmed on PSG. Our study finally consisted of 30 patients with COPD-OSA overlap syndrome and 65 patients with COPD alone. Among the COPD-OSA overlap patient group; 14 (46.67%) patients belonged to "GOLD grade 2" and 13 (43.33%) belonged to "GOLD grade 3." Only 3 (10.00%) patients belonged to "GOLD grade 4" (Table 2). 21 (70%) patients belonged to GOLD A and 9 (30%) patients belonged to GOLD B.

In the COPD alone group, 1 (1.5%) patient belonged to "GOLD grade 1," 23 (35.38%) patients belonged to "GOLD grade 2,"

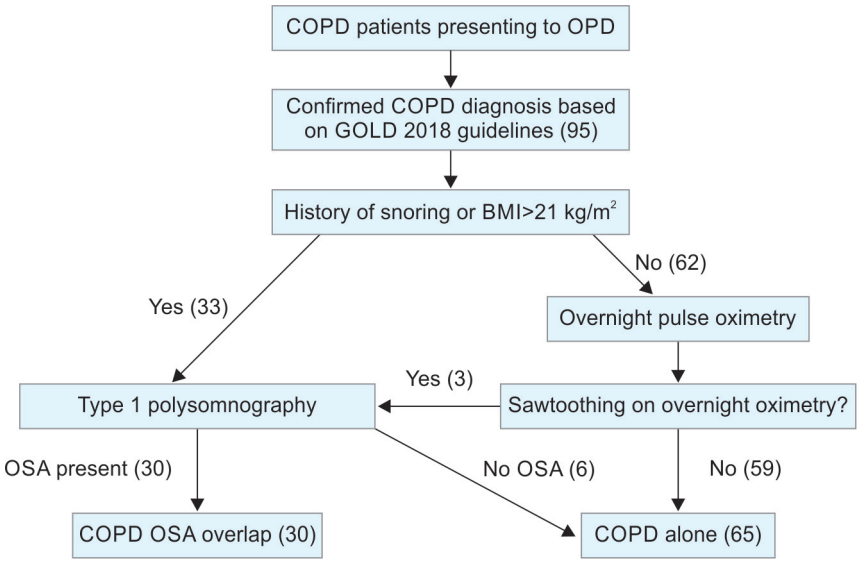

Fig. 1: Flowchart depicting the recruitment and categorization of patients in the study

28 (43.07%) patients were in "GOLD grade 3" and 13 (20%) patients belonged to "GOLD grade 4." And 48 (73.8%) were in GOLD A category and 17 (26.2%) in GOLD B. As the patients with ≥1 exacerbation in the last 1 year were excluded in the study. There were no GOLD C and D category patients. About 36 patients were subjected to level 1 PSG (Fig. 1). The mean AHI in the COPD-OSA overlap group was 22.4/hour. Fifty percent (15 patients) in the COPD-OSA overlap group had mild OSA. And 12 patients had moderate and only 3 patients had severe OSA. The average sleep efficacy was 82.7 %. Snoring was present in 100% of the COPD-OSA overlap patients. The average overnight SpO_2 was 92.3%.

The comparison between the two groups is given in Table 2. The mean age of patients in COPD-OSA overlap syndrome group was 56.9 ± 6.86 years, which was significantly less ($p = 0.01$) than the COPD alone group (60.6 ± 7.25 years). The mean BMI was 30.78 ± 4.63 kg/m^2, which was significantly higher ($p < 0.001$) than the COPD alone group (21.29 ± 2.71). Other anthropometric parameters, such as neck circumference, waist circumference, and Mallampati score were compared between both the groups. There was no statistical difference except for higher Mallampati grade in COPD-OSA overlap syndrome patients compared with COPD alone (Table 2). The presence of EDS was seen in 83.33% of the COPD-OSA overlap patients, which was significantly higher ($p < 0.001$) than that in the COPD alone group (15.3%). The mean SpO_2, the mean PaO_2, and the mean lowest nocturnal saturation were significantly lower in the COPD-OSA overlap group. The mean FEV1, FEV1% predicted, $PaCO_2$, and HCO_3 levels were significantly higher in the COPD-OSA overlap group. Among the comorbidities, the prevalence of pulmonary hypertension was 30% in COPD-OSA overlap group compared with 7.69% in COPD alone group, the difference being statistically significant (Table 3).

A comparison among the two groups in individual GOLD stages is given in Table 3. In all the respective grades, patients with COPD-OSA overlap syndrome had significantly higher BMI, FEV1, $PaCO_2$, and HCO_3 but the daytime PaO_2 and minimum value of nocturnal saturation were significantly lower. Thus, despite having better lung functions, they had worse daytime and nocturnal hypoxia. And this persisted irrespective of the COPD grade.

All the 30 patients in the COPD-OSA overlap syndrome group had snoring. However, only 3 out of the 65 patients with COPD alone had snoring. About 25 out of 30 (83%) patients with COPD-OSA overlap syndrome reported that they had EDS. But even in COPD alone patients, 10 (15.3%) patients had EDS. In COPD-OSA overlap syndrome group, only 3 out of 30 patients had BMI < 25 kg/m^2. On the contrary, only 1 out of 65 patients in COPD alone group had BMI of more than 25 ≥ kg/m^2. The negative predictive value of the presence of snoring is 100% and the positive predictive value is 84.42% for the detection of COPD-OSA overlap syndrome. The negative predictive value of the presence of BMI ≥ 25 kg/m^2 is 98.88% and the positive predictive value is 86.67%. The negative predictive value for the presence of EDS is 97.86% and the positive predictive value is 37.57%. So, the presence of snoring, BMI ≥ 25 kg/m^2, preserved FEV1, and daytime hypoxia should alert the physician to evaluate the patient for COPD-OSA overlap syndrome in COPD. Excessive daytime sleepiness can be present even in COPD alone without OSA.

Discussion

Chronic obstructive pulmonary disease is a debilitating disease in itself and the co-occurrence of OSA further increases morbidity and mortality. Patients with COPD-OSA overlap have increased nocturnal oxygen desaturation, daytime hypoxemia, and hypercapnia compared with either disease alone thereby increasing the risk of pulmonary hypertension and respiratory failure. The presence of the COPD-OSA overlap syndrome is also associated with a higher frequency of COPD exacerbations, severe respiratory symptoms, and poor quality of life. Early identification of COPD-OSA overlap syndrome in COPD has important clinical consequences. The treatment of the OSA component by continuous positive airway pressure has been shown to improve the mortality in COPD-OSA overlap syndrome. It is also effective in reducing the COPD exacerbations.[5,19] Owing to the improved clinical outcome with early intervention in COPD-OSA overlap syndrome, it is important for clinicians to screen patients with COPD for detecting OSA.

There are few studies which have found screening methods for OSA in patients with COPD. While PSG is the gold standard to detect

Table 2: Comparison of different clinical, spirometry and blood gas parameters among the COPD-OSA group vs COPD group

	COPD-OSA (30)	*COPD (65)*	*p-value*
Age (years)	56.9 ± 6.86	60.6 ± 7.25	0.01
M: F	28:2	61:4	
BMI (kg/m^2)	30.78 ± 4.63	21.29 ± 2.71	<0.001
Neck circumference	40.2 ± 3.8	38.8 ±3.76	0.096
Waist circumference	108.2 ±14.86	102.08 ±14.90	0.065
Mallampati score	2.24 ± 1.01	0.98 ± 1.2	<0.001
Snoring	30	3	<0.001
EDS	25	10	<0.001
Insomnia	8	26	0.104
Comorbidity			
• Diabetes	19 (63.34%)	40 (61.54%)	0.867
• Hypertension	22 (73.34%)	34 (52.30%)	0.052
• Pulmonary hypertension	9 (30%)	5 (7.69%)	0.004
• Heart disease	8 (26.67%)	12 (18.46%)	0.361
• Hypothyroidism	8 (26.67%)	13 (20%)	0.467
SpO_2 (%)	89.72 ± 18.39	96.3 ± 2.17	0.002
FEV1 (L)	1.33 ± 0.45	0.89 ± 0.31	<0.001
FEV1% PREDICTED	50.16 ± 15.83	45.3 ± 16.8	0.17
GOLD Spirometric severity			
Grade I (*n*)	0	1 (1.5%)	
Grade II	14 (46.67%)	23 (35.38%)	
Grade III	13 (26.67%)	28 (43.07%)	
Grade IV	3 (10.66%)	13 (20%)	
GOLD group A	21 (70%)	48 (73.8%)	
GOLD group B	9 (30%)	17 (26.2%)	
PaO_2 (mm Hg)	65.49 ± 20.91	75.70 ± 8.38	<0.001
$PaCO_2$ (mm Hg)	42.58 ± 10.26	35.71 ± 4.8	<0.001
HCO_3 (mEq/L)	29.99 ± 3.09	26.36 ± 8.48	0.02
Lowest nocturnal saturation (%)	73.16 ± 12.39	87.86 ± 5.71	<0.001

Table 3: Comparison of BMI, FEV1, blood gas parameter and nocturnal saturation among patients with COPD-OSA group and COPD group in individual GOLD spirometry grades (1 and 2)

	GOLD grade 2			*GOLD grade 3*			*GOLD grade 4*		
	COPD-OSA (14)	*COPD (23)*	*p-value*	*COPD-OSA (13)*	*COPD (28)*	*p-value*	*COPD-OSA (3)*	*COPD (13)*	*p-value*
BMI (kg/m^2)	29.89 ± 5.1	22.68 ± 2.13	<0.05	31.84 ± 4.33	21.08 ± 2.71	<0.05	30.33 ± 4.05	21.5 ± 1.83	<0.05
FEV1	1.72 ± 0.23	1.14 ± 0.19	<0.05	1.08 ± 0.2	0.83 ± 0.18	<0.05	0.65 ± 0.1	0.50 ± 0.15	0.12
FEV1 (%Pred)	64.57 ± 6.67	61.13 ± 6.9	0.14	40.5 ± 6.9	40.64 ± 5.8	0.94	24.66 ± 4.72	22.7 ± 5.11	0.56
SpO_2 (%)	96.7 ± 2.55	95.43 ± 3.07	0.2	95.23 ± 3.65	95.89 ± 1.37	0.40	95.66 ± 2.51	96.15 ± 1.99	0.71
PaO_2 (mm Hg)	60.96 ± 10.04	78.6 ± 10.1	<0.05	63.56 ± 10.28	72.96 ± 7.14	<0.05	61.66 ± 3.5	75.9 ± 5.5	<0.05
$PaCO_2$ (mm Hg)	41.27 ± 12.3	35.37 ± 5.33	<0.05	42.33 ± 7.7	36.66 ± 4.4	<0.05	42.36 ± 2.8	32.96 ± 4.7	<0.05
HCO_3 (mEq/L)	28 ± 2.1	24.76 ± 3.15	<0.05	28.02 ± 2.92	25.65 ± 2.5	<0.05	29.3 ± 2.9	25.28 ± 2.67	<0.05
Lowest nocturnal SpO_2 (%)	69.78 ± 12.7	87.17 ± 4.85	<0.05	77.69 ± 10.49	87.03 ± 7.31	<0.05	69.33 ± 16.6	89.6 ± 4.55	<0.05

OSA in patients with COPD, it is limited by cost and availability. Overnight pulse oximetry has been used as a simple screening test to detect nocturnal hypoxia during sleep. A saw-tooth pattern on overnight oximetry indicates the presence of OSA, and this should be confirmed by PSG studies.[5] We have used this method in our study to screen for OSA in those with low clinical probability. As per BODE[14] index, patients with COPD with BMI ≤ 21 kg/m^2 have a poor prognosis. Hence, a BMI cut-off value of 21 kg/m^2 was taken for subjecting the patients to PSG. Ours is the first Indian study which has attempted to find out the screening parameters for the presence of COPD-OSA overlap syndrome in COPD patients. Our study also brings out a relatively less known fact that the patients having COPD-OSA overlap syndrome in spite of preserved lung functions have poor days as well as nocturnal oxygenation. About 30 patients diagnosed with COPD-OSA overlap syndrome were compared with 65 stable patients who have COPD. We observed that the mean age was significantly lower in the COPD-OSA overlap syndrome group. A similar finding was observed in a study done by Schreiber et al.[20] Higher age is one of the risk factors of OSA in the general population.[21] So, questionnaires like "STOPBang" which

includes high age as risk factors are possibly unreliable screening tools for COPD-OSA overlap syndrome. The lower mean age of COPD-OSA overlap syndrome patients in our study can be explained by the fact that these patients present the syndrome at younger age owing to the severity of symptoms.

We found that the presence of snoring and/or BMI ≥ 25 kg/m^2 be taken as a screening parameter to evaluate for OSA in Indian patients with COPD. The presence of snoring is considered a risk factor for OSA without COPD too.[22] In our study, all 30 patients with OSA had snoring. Eliciting snoring history in the evaluation of patients with COPD may result in early detection of OSA. Only 3 out of 65 patients in the COPD alone group had snoring. The BMI is considered one of the predictors of COPD-OSA overlap syndrome as per the study by Steveling et al.[23] But the cut-off value to evaluate for OSA in Indian OSA patients was never evaluated earlier in patients with COPD. The Asia-Pacific guidelines define obesity as the BMI of 25 kg/m^2 or more.[24] A Korean study suggested that the Asia-Pacific BMI classification was more appropriate in reflecting the correlation between obesity and the manifestation of COPD in Asian patients when compared with the WHO classification system.[25] Hence, we had chosen a BMI cut-off of 25 kg/m^2 to find out if the BMI cut-off of 25 kg/m^2 helps in identifying OSA in patients with COPD. In COPD-OSA overlap syndrome group, only 3 out of 30 patients had BMI <25 kg/m^2. On the contrary, only 1 out of 65 patients in the COPD alone group had a BMI of ≥ 25 kg/m^2. Even when patients were compared in their respective GOLD grades, patients of COPD-OSA overlap syndrome had a higher BMI. Some earlier studies had also compared the morphological differences among Asian versus Caucasian patients regarding the development of OSA. They found that the Asian patients with OSA had lower BMI and different cephalometric parameters.[26–28]

Patients with OSA commonly have EDS. But EDS cannot be taken as a predictor of OSA in COPD. This is because 15.3% of patients in the COPD alone group had EDS, and 17% of the COPD-OSA overlap group did not have EDS, though EDS was significantly higher in the COPD-OSA overlap group. Insomnia, restless leg syndrome, and cough/breathlessness at night are important contributors to the poor sleep quality in patients with COPD. This probably makes EDS an unreliable predictor for OSA in patients with COPD. In a Swiss study by Steveling et al. it was found that EDS cannot be used to identify the presence of possible COPD-OSA overlap syndrome.[23] The essence of our study is to highlight the fact that classical clinical features of OSA like obesity and EDS may not be evidently present in patients with COPD-OSA overlap syndrome. This may result in missing the diagnosis of COPD-OSA overlap syndrome in COPD patients. Thereby the history of snoring should always be asked in COPD patients and high index of suspicion should be kept in those who are overweight to look for COPD-OSA overlap syndrome. We observed that patients with COPD-OSA overlap syndrome had less severe airway obstruction as compared with patients with COPD alone with respect to both absolute FEV1 and FEV1% predicted. Previous studies have also supported this finding.[20,23] Thus, poor lung function is protective against OSA in Indian COPD patients too. This is because patients with COPD having poor lung functions have low BMI due to the systemic effects of COPD, and hence this low BMI has a protective influence on the development of OSA. Also, in COPD, hyperinflation causes reduced upper airway collapsibility by lowering the critical closing pressure.[2] Majority of the COPD-OSA overlap syndrome patients belonged to the GOLD spirometry "grade 2" and "grade 3" but only 3 out of 30 patients belonged to "grade 4." Hence, a lower FEV1 can be regarded as a negative predictor of COPD-OSA overlap syndrome.

On evaluating the ABG in both the groups, the mean daytime PaO_2 and oxygen saturation were low in the COPD-OSA overlap group compared with COPD alone group. The $PaCO_2$ was higher in COPD-OSA overlap group compared with COPD alone group. Also, the lowest nocturnal saturation was significantly lower in the COPD-OSA overlap syndrome group. Even the GOLD spirometry grade-wise comparison of the two groups suggested that patients with COPD-OSA overlap syndrome had a significantly lower PaO_2 and lowest nocturnal saturation and higher $PaCO_2$ and bicarbonate levels. Several studies have previously demonstrated that patients with COPD-OSA overlap syndrome have profound nocturnal desaturation as compared with patients with either disease alone.[29] Nocturnal desaturation is associated with surges in systemic and pulmonary blood flow and cardiac arrhythmias.[4] Patients with COPD-OSA overlap syndrome have an increased risk of pulmonary hypertension, and right heart failure resulting from the underlying nocturnal desaturation, daytime hypoxemia, and hypercapnia as compared with either disease alone.[5] Our findings of a significantly higher prevalence of pulmonary hypertension in the COPD-OSA overlap group compared with COPD alone is in line with earlier studies.

Conclusion

Patients with COPD-OSA overlap syndrome have poor daytime oxygenation and greater nocturnal desaturation as compared with COPD alone despite having better lung functions. Early identification of the associated hypoxemia, which is easily reversible with positive airway pressure therapy, may prevent the associated cardiovascular complications. Snoring, BMI ≥ 25 kg/m^2, and lower daytime PaO_2 despite having preserved FEV1 may be regarded as the pointers to COPD-OSA overlap syndrome in Indian COPD patients. Evaluating these patients with PSG may help in the early detection of the COPD-OSA overlap syndrome.

Limitations of the Study

Although our study highlights the important characteristics of COPD-OSA overlap syndrome and brings out the differences between patients of COPD-OSA overlap syndrome and COPD alone, it has certain limitations. The small sample size in our study limits its use for greater population. Conducting the study with a higher sample size and statistical use of multivariate analysis will increase the accuracy of predictors. Because of logistic issues, we could not perform PSG on all the COPD patients. Though the presence of saw-tooth pattern on pulse oximetry is a very sensitive tool for the detection of OSA, there was a rare possibility of missing out on OSA based on pulse oximetry.[15] Although the study was carried out in a tertiary care center, there were limited resources for carrying out such a study; hence more such studies are needed which can include more variables of the patients for a better validation of screening parameters.

References

1. Flenley DC. Sleep in chronic obstructive lung disease. Clin Chest Med 1985;6:651–661. PMID: 2935359.
2. Krachman SL, Tiwari R, Vega ME, et al. Effect of emphysema severity on the apnea-hypopnea index in smokers with obstructive sleep apnea. Ann Am Thorac Soc 2016;13(7):1129–1135. DOI: 10.1513/AnnalsATS.201511-765OC.

3. Kim V, Han MK, Vance GB, et al. The chronic bronchitic phenotype of COPD: an analysis of the COPDGene Study. Chest 2011;140(3):626–633. DOI: 10.1378/chest.10-2948.
4. Owens RL, Malhotra A. Sleep-disordered breathing and COPD: the overlap syndrome. Respir Care 2010;55(10):1333–1346. PMID: 20875160.
5. Singh S, Kaur H, Sigh S, et al. The overlap syndrome. Cureus 2018;10(10):e3453. DOI: 10.7759/cureus.3453.
6. Chaouat A, Weitzenblum E, Krieger J, et al. Association of chronic obstructive pulmonary disease and sleep apnea syndrome. Am J Respir Crit Care Med 1995;151(1):82–86. DOI: 10.1164/ajrccm.151.1.7812577.
7. Shepard JW, Garrison MW, Grither DA, et al. Relationship of ventricular ectopy to nocturnal oxygen desaturation in patients with chronic obstructive pulmonary disease. Am JMed 1985;78(1):28–34. DOI: 10.1016/0002-9343(85)90457-7.
8. Bradley TD, Rutherford R, Grossman RF, et al. Role of daytime hypoxemia in the pathogenesis of right heart failure in the obstructive sleep apnea syndrome. Am Rev Respir Dis 1985;131(6):835-839. DOI: 10.1164/arrd.1985.131.6.835.
9. Sanjay S. COPD-OSA "The Overlap syndrome". Indian J Appl Res 2018;8(7):1–3. DOI: 10.36106/ijar.
10. Grover H, Janmeja AK, Aggarwal D. Obstructive sleep apnea in chronic obstructive pulmonary disease – overlap syndrome in a tertiary care center in Northern India. Chest 2015;148(4):1048A. DOI: 10.1378/chest.2263675.
11. Halkanche GV, Mhaisekar DG. Study of correlation between obstructive sleep apnea and obstructive airway disease. MedPulse Int Med J 2017;4(2):217–221. DOI: 18 February 2017.
12. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for diagnosis, management, and prevention of COPD, 2018. Accessed on 21 Nov, 2019. Available from: http://goldcopd.org.
13. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry "ATS/ERS task force: standardisation of lung function testing." Eur Respir J 2005;26(2): 319–338. DOI: 10.1183/09031936.05.00034805.
14. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med 2004;350(10):1005–1012. DOI: 10.1056/NEJMoa021322.
15. Netzer N, Eliasson A, Netzer C, et al. Overnight pulse oximetry for sleep-disordered breathing in adults. Chest 2001;120(2):625–633. DOI: 10.1378/chest.120.2.625.
16. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the scoring of sleep and associated events. deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. J Clin Sleep Med 2012;8(5):597–619. DOI: 10.5664/jcsm.2172.
17. Johns MW. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. Sleep 1991;14:540–545. DOI: 10.1093/sleep/14.6.540.
18. Charan J, Biswas T. How to calculate sample size for different study designs in medical research? Indian J Psychol Med. 2013;35(2):121–126. DOI: 10.4103/0253-7176.116232.
19. McNicholas WT. Chronic obstructive pulmonary disease and obstructive sleep apnoea—the overlap syndrome. J Thorac Dis 2016;8(2):236–242. DOI: 10.3978/j.issn.2072-1439.2016.01.52.
20. Schreiber A, Cemmi F, Ambrosino N, et al. Prevalence and predictors of obstructive sleep apnea in patients with chronic obstructive pulmonary disease undergoing inpatient pulmonary rehabilitation. COPD 2018;15(3):265–270. DOI: 10.1080/15412555.2018.1500533.
21. Chung F, Abdullah HR, Liao P. STOP-Bang questionnaire: a practical approach to screen for obstructive sleep apnea. Chest 2016;149(3):631–638. DOI: 10.1378/chest.15-0903.
22. Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. Anesthesiology 2008;108(5):812–821. DOI: 10.1097/ALN.0b013e31816d83e4.
23. Steveling EH, Christian F, Clarenbach CF, et al. Predictors of the overlap syndrome and its association with comorbidities in patients with chronic obstructive pulmonary disease. Respiration 2014;88(6): 451–457. DOI: 10.1159/000368615.
24. Pan WH, Yeh WT. How to define obesity? Evidence-based multiple action points for public awareness, screening, and treatment: an extension of Asian-Pacific recommendations. Asia Pac J Clin Nutr 2008;17(3):370–374. PMID: 18818155.
25. Lim JU, Lee JH, Kim JS, et al. Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients Int J COPD 2017:12 2465–2475. DOI: 10.2147/COPD.S141295.
26. Yu X, Fujimoto K, Urushibata K, et al. Cephalometric analysis in obese and nonobese patients with obstructive sleep apnea syndrome. Chest 2003;124(1):212–218. DOI: 10.1378/chest.124.1.212.
27. Akashiba T, Kawahara S, Kosaka N, et al. Determinants of chronic hypercapnia in Japanese men with obstructive sleep apnea syndrome. Chest 2002;121(2):415–421. DOI: 10.1378/chest.121.2.415.
28. Patro M, Gothi D, Ojha UC, et al. Predictors of obesity hypoventilation syndrome among patients with sleep-disordered breathing in India. Lung India 2019;36(6):499–505. DOI: 10.4103/lungindia.lungindia_61_19.
29. Sanders MH, Newman AB, Haggerty CL, et al. Sleep and sleep-disordered breathing in adults with predominantly mild obstructive airway disease. Am J Respir Crit Care Med 2003;167(1):7–14. DOI: 10.1164/rccm.2203046.