



PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN INDIA

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ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease as well as Obstructive Sleep Apnea are two chronic, common respiratory diseases with significant morbidity and mortality; each having increased socio-economic burden; hampering the development of a nation independently. However, the concomitant occurrence of both known as “overlap syndrome” further complicates the scenario and makes it quite difficult to handle. At present, the prevalence of Overlap syndrome varies from 0.2%-28% globally. Data on overlap syndrome are sparse; perhaps because of failure to diagnose and report OSA on time. **Aims and Objectives:** In order to diagnose early a case of OSA among COPD patients and to find-out any correlation between Apnea –Hypopnea index (AHI) and Body Mass Index(BMI) with severity of COPD alone and Overlap syndrome in Indian population. **Method and materials:** We performed a cross sectional comparative study to evaluate OSA in diagnosed COPD patients who attended the outpatient department of our Hospital. All patients included in this study underwent evaluation of overnight polysomnography (cut off value of AHI for OSA was >5), ESS, mMRC scale, CAT score. **Results:** We evaluated 64 patients of COPD between 40 to 80 years of age group. Out of 64 patients, 11 (17.19%) had overlap syndrome with mean value of BMI 27.57 ± 3.54 ($p=0.000$), AHI 26.03 ± 6.41 ($p<0.001$), BPD 90.73 ± 5.38 and nocturnal saturation 87.73 ± 1.95 ($p=0.000$). **Conclusion:** OSA was common among patients with COPD than general population with a prevalence of 17.19 in our study. The early recognition of co-existing OSA in COPD patients is of utmost clinically importance in the management of overlap syndrome and to decrease the burden of the fatal disease and to improve the quality of life. Patients with overlap syndrome have a greater risk of morbidity and mortality than either COPD or OSA alone.

INTRODUCTION

GOLD 2018 defines COPD as “Chronic Obstructive Pulmonary Disease (COPD) is a common preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.”^[1]

At present, COPD is the fourth leading cause of death in the world^[2] but is projected to be the third most common cause of death worldwide by 2020. More than 3 million people died of COPD in 2012 (up from 2.4 million deaths in 1990) accounting for 6% of all death globally. COPD affects 329 million people or nearly 5 percent of the global population. It typically occurs in people over the age of 40. More than 90% of these deaths occur in the developing world. The number of deaths is projected to increase further because of higher smoking rates and an aging population in many countries. In the European Union, the total direct costs of Respiratory diseases are

estimated to be about 6% of the total health care budget, with COPD accounting for 56% (38.6 billion Euros) of the cost of respiratory diseases.^[3] In the United States, the estimated direct costs of COPD are \$32billion and the indirect costs \$20.4 billion.^[4] It resulted in an estimated economic cost of \$2.1 trillion in 2010.

It has been estimated that the average prevalence of COPD is 6.2% in Asia and almost one-fifth of identified subjects are categorized as having severe COPD.^[15] WHO estimates suggest that 90% of COPD-related deaths occur in low and middle income countries. India and China constitute 33% of the total human population and account for 66% of the global COPD mortality.^[5] Further, it has been estimated that COPD associated mortality is likely to grow by 160% in the Southeast Asian region in the coming decades.^[6] Globally the increase in the burden of COPD has been attributed to cigarette smoking among men and

women, longer survival of populations, and high levels of air pollution, particularly in developing countries.^[12]

India is a large country comprising of people with varying sociodemographic profiles, cultural practices and ethnicities. Hence the risk factors for COPD are also likely to be different across various Indian states and regions.

Sleep apnea is a type of a breathing disorder that takes place during sleep. The breathing may partially or completely stop when an individual is sleeping and it can last for ten seconds or more. There are three types of sleep apnea namely obstructive sleep apnea, central sleep apnea and mixed sleep apnea. Obstructive sleep apnea is caused by obstruction of the upper respiratory tract during sleep. Central sleep apnea caused by a disturbance of central respiratory control, there is no respiratory movements taking place during this type. Mixed sleep apnea is a combination of obstructive sleep apnea and central sleep apnea, in this the initial event is central sleep apnea later obstructive apnea predominates (Black and Hawks, 2005).

Obstructive sleep apnea (OSA) is the most common type of sleep-disordered breathing and is characterized by recurrent episodes of upper airway collapse during sleep. These episodes are associated with recurrent oxyhemoglobin desaturations and arousals from sleep.

OSA that is associated with excessive daytime sleepiness is commonly called obstructive sleep apnea syndrome also referred to as obstructive sleep apnea-hypopnea syndrome (OSAS).

Sleep-disordered breathing (mainly obstructive sleep apnea [OSA]) and COPD are among the most common pulmonary diseases, so a great number of patients have both disorders. The possibility that COPD may predispose to OSA and OSA to COPD has been explored in many studies over past two to three decades.

The combination of chronic obstructive pulmonary disease and sleep apnea-hypopnea syndrome has been denominated "overlap syndrome" by the late David Flenley. This "overlap syndrome" causes more severe nocturnal hypoxemia than either disease alone.

This common combination of OSA and COPD has important implications for diagnosis, treatment, and outcome. Specifically, patients with COPD and OSA have a substantially greater risk of morbidity and mortality, compared to those with either COPD or OSA alone. Only now are the interactions between these two systemic diseases being determined and appreciated.

At present, the prevalence of Overlap syndrome varies from 0.2%-28% globally. Data on overlap syndrome are sparse; perhaps because of failure to diagnose and report OSA on time.

Aims and Objective

1. To know the prevalence of obstructive sleep apnea in patients of chronic obstructive pulmonary disease.
2. To investigate correlation of AHI with Body Mass Index and severity of COPD with severity of OSA.

METHODS AND MATERIALS

We performed a cross sectional prospective comparative study to evaluate Obstructive Sleep Apnea in diagnosed COPD patients who attended OPD or Chest Ward of Department of T.B. & Respiratory Diseases, Sir Sunderlal Hospital, Institute of Medical Sciences, Banaras Hindu University, Varanasi U.P., after approval from ethical committee between June 2015 to July 2017.

Patient Selection

A diagnosis of COPD was established as per GOLD 2015 guidelines with post-bronchodilator FEV1/FVC ratio of < 0.70 . Each patient's height and weight was recorded and BMI was calculated before polysomnography. Obesity was defined by a BMI of $\geq 30 \text{ kg/m}^2$. The statistical analysis was done using statistical software SPSS for windows (Version 16). Chisquare test was used for non-parametric variables. Student's t test was used for comparing two groups and one-way ANOVA test was used for multiple group comparison.

Patients with $\text{AHI} \geq 5$ were taken as COPD with OSA also known as "OVERLAP SYNDROME" study group while those with $\text{AHI} < 5$ were taken as COPD without OSA as a control group or comparative group. A respiratory Disturbance Index (RDI) of greater than 15 events per hour indicates possible OSAHS.

Study Size

We did Polysomnography of 64 COPD patients who attended outdoor or indoor of our Department of SS-Hospital. The patients were then divided into two groups of those COPD without OSA and COPD with OSA on the basis of their AHI scores (cut off value for AHI was 5) and their various parameters (viz., GOLD groups, MMRC scale, CAT score, blood pressure, 6MWT, ESS) were recorded and compared between the two groups.

Inclusion criteria

1. Patients with stable COPD.
2. Age 40 to 80 year.
3. Patients as well as attendants willing to give informed consent.
4. Patients ready to undergo sleep study (PSG).

Exclusion criteria

1. Acute exacerbation of COPD.
2. Patients with multiple organ failure.
3. Haemodynamic instability.
4. Those patients who are not giving consent.
5. Women who are pregnant or currently lactating.

All selected patients underwent following investigations: Complete blood count, renal and liver function tests, random blood sugar, HbA1C, X-ray chest PA view, PFT, Arterial blood gas analysis, mMRC dyspnoea grading, BODE Index, Body Mass Index (BMI), HRCT thorax, (optional), ESS scoring, Polysomnography.

BODE Index

The BODE Index is a composite marker of disease taking into consideration the systemic nature of COPD (Celli et al., 2004).

Variable	Points on BODE Index			
	0	1	2	3
FEV ₁ (% of predicted)†	≥65	50–64	36–49	≤35
Distance walked in 6 min (m)	≥350	250–349	150–249	≤149
MMRC dyspnea scale‡	0–1	2	3	4
Body-mass index§	>21	≤21		

Epworth Sleepiness Scale

Validated tool for the systemic assessment of impaired daytime alertness is the ESS (Johns MW, 1991). ESS easy to use and is often applied routinely. From ESS one can measure the patient's ability to remain awake or the propensity to doze off in typical daily situations. Its main advantage is that the ability of it to represent average sleep propensity (Johns MW, 2000), and the test is frequently used in clinical practice (Sullivan SS et al, 2008).

Polysomnography

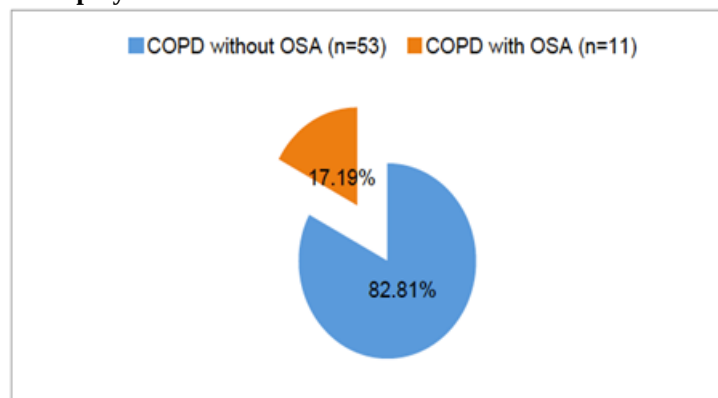
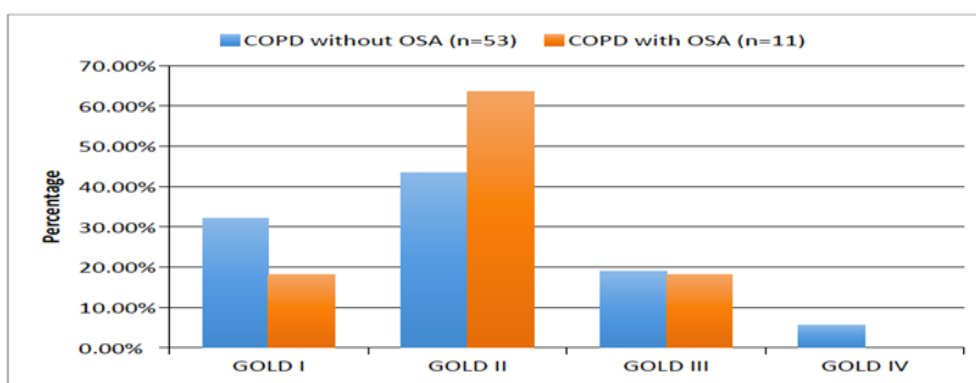
A sleep study or a polysomnogram is the standard diagnostic test for OSA. The test involves simultaneous recordings of multiple physiologic signals, including the right and left electro-oculograms, the submental electromyogram, and the electroencephalogram. Collectively, these surface recordings are used to distinguish wakefulness from sleep and determine the distribution of different sleep stages over the course of the night. A typical 8-hour nocturnal laboratory PSG involves measurement of multiple channels of physiologic parameters, including electroencephalogram, electrooculography, chin movements, leg movement via electromyography, ECG, heart rate, respiratory effort, chest wall movement, abdominal wall movement, airflow, and oxygen saturations.

The primary measure of sleep-disordered breathing is the AHI, which is the number of apneas and hypopneas per hour of sleep. An apnea is defined as an interruption of airflow lasting at least 10 seconds in adults or the equivalent of two breaths in children. A hypopnea is a specified reduction in airflow and an associated oxygen desaturation or arousal, lasting at least 10 seconds in adults or the equivalent of two breaths in children. The AHI is the primary measure used to determine the

severity of OSA and effectiveness of treatment. OSA is classified as mild (AHI 5–15), moderate (AHI 15–30) and severe (AHI >30) [American academy of sleep medicine task force.

OBSERVATIONS AND RESULTS

A total number of 64 COPD patients between 40 to 80 years of age group were evaluate. The patients were divided into two groups of those COPD without OSA and COPD with OSA on the basis of their AHI scores (cut off value for AHI was 5) and their various parameters (viz., GOLD groups, MMRC scale, CAT score, blood pressure, ESS) were recorded and compared between the two groups.

Figure 1: Prevalence of Overlap Syndrome**Figure 1: Showed that the prevalence of OSA among COPD patients is 17.19%.****Figure 2: Severity of Disease according to GOLD Grading.**

From the above Figure 2, it is evident that maximum patients (46.9%) belonged to GOLD II standard of severity of disease followed by GOLD I standard of

severity of disease (29.7%) followed by GOLD III standard of severity of disease (18.8%) and GOLD IV standard of severity of disease 4.7%.

Table 1: Body Mass Index (BMI).

Parameters	COPD without OSA (n=53) Mean±SD	COPD with OSA (Overlap syndrome) (n=11) Mean±SD	Remarks
BMI	22.81±3.29	27.57±3.54	t=-4.300 p=0.000 (HS)

Mean BMI in COPD without OSA was 22.81 ± 3.29 whereas in COPD with OSA it was 27.57 ± 3.54 . Group

comparison showed statistically highly significant statistical difference between the groups.

Table 2: Night time saturation (Night SpO₂).

Parameters	COPD without OSA (n=53) Mean±SD	COPD with OSA (Overlap syndrome) (n=11) Mean±SD	Remarks
Night SpO ₂	90.85±1.24	87.73±1.95	t=6.802 p=0.000 (HS)

Mean Night time SpO₂ in COPD without OSA was 90.85 ± 1.24 whereas in COPD with OSA it was 87.73 ± 1.95 . Group comparison showed statistically

highly significant statistical difference between the groups.

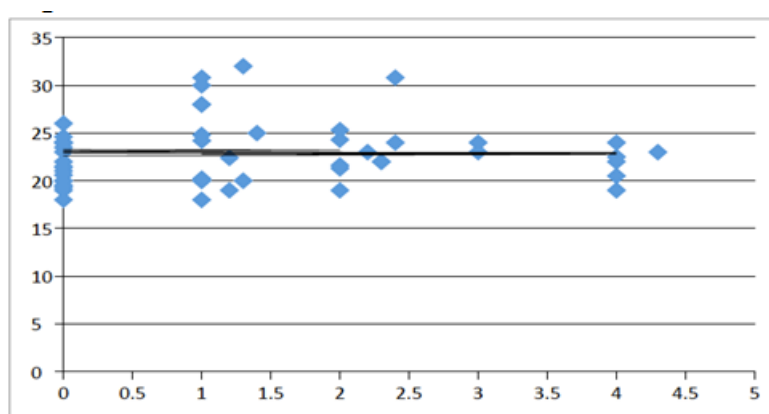


Figure 3: Correlation AHI vs BMI.

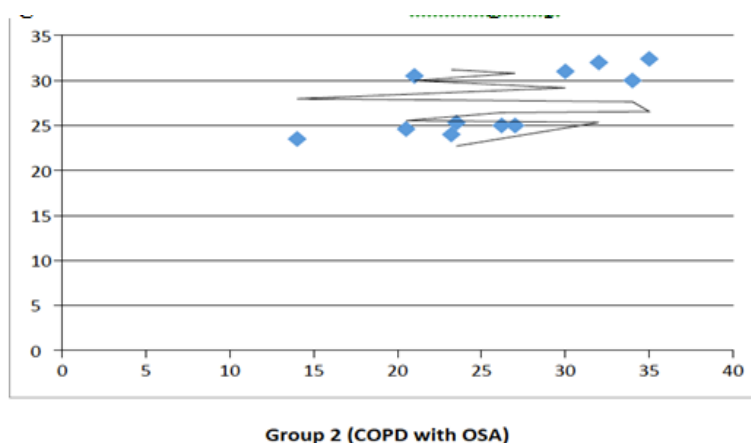


Figure 4: Correlation of AHI vs BMI group 2.

A significant positive correlation was found between AHI and BMI in Group 2.

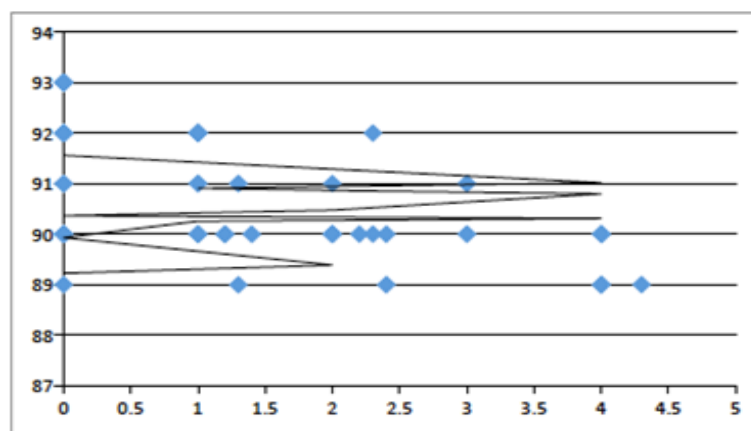


Figure 5: Correlation AHI vs Night SpO₂.

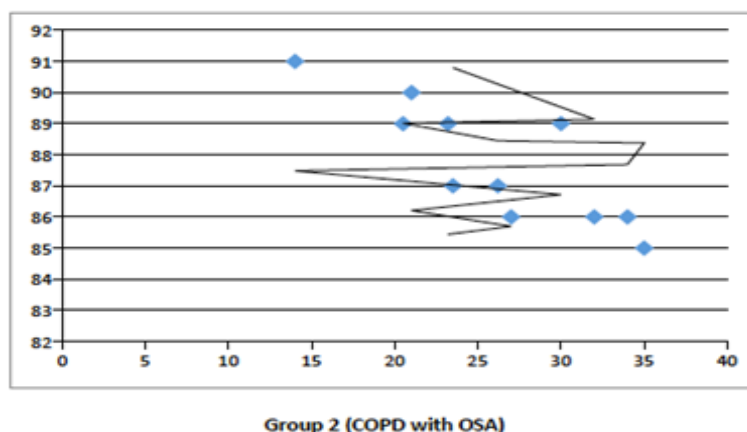


Figure 6: Correlation AHI vs Night SpO2.

A significant negative correlation was found between AHI and Night SpO2 in both the groups.

DISCUSSION

The primary endpoint of this study was to know the prevalence of Obstructive Sleep Apnea in Chronic Obstructive Pulmonary Disease in Indian Population. The comparison of the various clinical parameters of COPD patients (control group) with COPD-OSA Overlap syndrome (study group). The various features studied were the age, sex, blood pressure, severity of disease according to GOLD group, body mass index, neck circumference, day time and night time saturation, BODE index and ESS score of the patients and the degree of OSA (positive/negative).

Majority of the cases of our study lies between 50 to 70 years of age group (31 out of 64) whereas 10 cases were in the age group of 40 to 50 years and 12 cases were in 71 to 80 years of age group. There were 49 male (76.56%) and 15 female (23.43%) in this study group suggesting high prevalence of COPD amongst male population which was supporting to existing study and fact that COPD is more prevalent in male population due to habit of smoking.

Obstructive sleep apnea is known to be more prevalent among male population than female population and so was the observation in our study out of 11 patients, 9 (81.18%) were male and 2(18.18%) were female. Here, we saw more male patients, there is relatively increased airway length(neck) in males compared to females, male predisposition of OSA can be explained (Malhotra et al., 2002).

In our study, out of 64 subjects, 11 (17.19%) had overlap syndrome. Earlier studies by Resta O et al. (2002) and de Miguel J et al. (2002) have documented OSA in 16% and 28.5% of COPD patients respectively. Another study showed that Overlap syndrome has a prevalence of 14% among patients with mild COPD. The study conducted by SK Sharma et al in an Indian scenario has quoted a 6% occurrence of OSA in COPD patients with most of the patients having significantly severe disease at the time of enrolment. Another study conducted by Harish et al. (2014) in Indian scenario have documented OSA in 5.55% of COPD patients. The prevalence of overlap syndrome in Kouismi et al. (2013) was 13.6%.

Prevalence of Overlap Syndrome

Author	Study Details	Findings
Sanders et al. (2003)	Prospective community sample of 5,964 adults >40 yr undergoing spirometry and polysomnography; sample enriched for cardiovascular risk factors including smoking	19% had FEV1/FVC ratio, 70%; 3.8% had FEV1/FVC ratio 60%. This group had lower AHI, largely as a consequence of lower BMI
Bednarek et al. (2005)	Prospective community sample of 356 adult males and 320 females aged 41–72 yr	11.3% had AHI >5 with sleepiness; 31.8% had AHI >5 alone; 10.7% had FEV1/FVC ratio, 70%. Overlap syndrome in 1% but FEV1/FVC, 70% and AHI >5 alone in 3%

Definition of abbreviations: AHI = apnea–hypopnea index; BMI = body mass index; OSAS = obstructive sleep apnea syndrome

Mean BMI in patient, COPD without OSA was 22.81 ± 3.29 whereas in COPD with OSA was 27.57 ± 3.54 . Group comparison showed statically highly significant statistical difference between the groups with a p value=0.000. Our findings are in line with previous studies which found a positive association between AHI and BMI (Bixler *et al.* 1998, 2001). In a study by Sanders *et al.* (2003) patients with COPD have elevated BMI, thus predisposing to OSA, and the finding of a higher RDI in overweight patients with airflow obstruction supports this possibility.

Radwan *et al.* Studied sleep disordered breathing in obese patients with or without COPD. They did not find any significant difference in AHI, mean nocturnal saturation and BMI between the two groups. This study is not in conformity with the result of our study. Obesity remains one of the main risk factors for Obstructive Sleep Apnea. Previous studies have shown that incidence of OSA in obese populations ranges from 40% (Vgontzas *et al.*, 1994) to 93% (Daltro *et al.*, 2007).

Mean AHI in patient, COPD without OSA was 1.30 ± 1.33 whereas in COPD with OSA was 26.03 ± 6.41 . Group comparison showed statistically highly significant statistical difference between the groups ($p < 0.001$ HS).

Night time SpO₂ in patient, COPD without OSA was 90.85 ± 1.24 whereas in COPD with OSA was 87.73 ± 1.95 . Group comparison showed statistically highly significant statistical difference between the groups ($p < 0.001$ HS). Patients with overlap syndrome experience more significant nocturnal desaturation than patients with COPD and OSA alone (Tsai and Lee-Chiong, 2009). Sharma *et al.* (2002) also found that BMI per se contributes to the AHI and nocturnal desaturation in patients with COPD.

CORRELATION

In our study we found a positive correlation between the AHI vs BMI, Night time SpO₂ & ESS whereas negative correlation between BP (Systolic and Diastolic) and BODE index among COPD without OSA.

We also found a positive correlation between the AHI vs BMI, BP (Diastolic), Night time SpO₂, BODE index, ESS whereas negative correlation between BP (Systolic) among COPD with OSA.

Despite the high prevalence of the overlap syndrome, few data are available on its pathophysiological and clinical consequences. Long-term follow-up studies are lacking on the pathophysiological and clinical consequences of overlap syndrome, although some clinical outcome studies in this area have commenced.

SUMMARY AND CONCLUSION

There is considerable evidence of important interactions between both disorders that influence epidemiology, clinical manifestations, co-morbidities, and management.

The recognition of co-existing OSA in COPD patients has important clinical relevance as the management of patients with overlap syndrome is different from COPD alone. The possibility that COPD may predispose to OSA and OSA to COPD has been explored in many studies over the past two decades. It is notable that increasing body mass index (BMI) and smoking history positively correlate with the likelihood of OSA in COPD patients. Both COPD and OSA are associated with a range of overlapping physiological and biological disturbances that include hypoxia and inflammation, which likely contribute to cardiovascular and other co-morbidities.

Thus, the probability is high that the overlap syndrome will be associated with a greater risk of co-morbidity than with either disease alone.

Different studies reflect conflicting prevalence of overlap syndrome, ranging from study 0.2% - 28%. Significant sleep desaturation and the sleep disturbances are greater in overlap syndrome than OSA and COPD alone.

The major findings arising out of this study are presented as follows:

1. Majority of the cases of our study lies between 50 to 70 years of age group (31 out of 64) whereas 10 cases were in the age group of 40 to 50 years and 12 cases were in 71 to 80 years of age group.
2. There were 49 males (76.56%) and 15 females (23.43%) in our study.
3. Out of 64 subjects, 11 (17.19%) had overlap syndrome.
4. Mean BMI in patient, COPD without OSA was 22.81 ± 3.29 whereas in COPD with OSA was 27.57 ± 3.54 .
5. Mean AHI in patient, COPD without OSA was 1.30 ± 1.33 whereas in COPD with OSA was 26.03 ± 6.41 .

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