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Research Article

EVALUATION OF OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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A R T I C L E I N F O

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A B S T R A C T

Introduction: Sleep disordered breathing (OSA) and chronic obstructive pulmonary disease are common pulmonary disorders with a great number of patients suffering from bothsimultaneously. The coexistence of both diseases has been termed as "Overlap syndrome".

Aims and Objectives: Aim of this study was to know the prevalence of OSA in COPD patients and to investigate the correlation of AHI with Body Mass Index and severity of COPD with severity of OSA.

Method and materials: We performed a cross sectional comparative study to evaluate OSA in diagnosed COPD patients. All patients included in this study underwent evaluation of overnight polysomnography (cut off value of AHI for OSA was >5), ESS, mMRC scale.

***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, AHI 26.03 ± 6.41, BPD 90.73±5.38 and nocturnal saturation 87.73 ± 1.95.

Conclusion: In our study population OSA was highly prevalent in COPD patients as compared to general population. The diagnosis of co-existing OSA in COPD patients has profound clinical significance as the management of patients with overlap syndrome is inherently different than either disease alone.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a major worldwide health problem that has an increasing prevalence, morbidity and mortality. COPD is a progressive disease that is characterized by long term poor airflow that makes it hard to breathe. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) and the World Health Organization (WHO) defines COPD as follows (www.goldcopd.org, 2017).

"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".

COPD is currently the fourth leading cause of death in the world but is projected to be the 3rd leading cause of death by 2020. COPD is a major cause of chronic morbidity and mortality throughout the world. Many people suffer from this disease for years, and die prematurely from it or its complications. 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

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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.

Aims and Objective

Aims of this study was

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

If not previously documented/tested, all such patients were documented for COPD with post bronchodilator pulmonary function test confirmation (FEV1 / FVC < 0.7) with irreversible airway obstruction and were screened for other causes of breathlessness like exacerbation of Bronchial Asthma, Interstitial lung diseases, worsening of Dyspnea due to heart failure etc., by channeling through detailed history, thorough physical examination and a battery of relevant investigations. Each patient's height and weight was recorded at the time of polysomnography and used to calculate the body mass index. In here obesity was defined by a BMI of ≥ 30 kg/m^2. The statistical analysis was done using statistical software SPSS for windows (Version 16). Chi-square 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 AHI ≥5 were taken as COPD with OSA also known as "OVERLAP SYNDROME" study group while those with 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 which were attend outdoor or indoor of our department. 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

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

Exclusion criteria

- Acute exacerbation of COPD.
- Patients with multiple organ failure.
- Haemodynamic instability.
- Those patients who are not giving consent.
- 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
- 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).
- Scoring the BODE Index

	0	1	2	3
FEV1% predicted	>65	50-64	36-49	<35
6MWD (m)	>350	250-349	150-249	<149
MMRC	0-1	2	3	4
BMI (kg.m-2)	>21	<21		

- Total BODE Index score = 0 to 10 units
- (FEV1% pred = predicted amount as a percentage of the forced expiratory lung volume in one second; 6MWD = six minute walking distance; MMRC = modified medical research council dyspnea scale; BMI = body mass index)

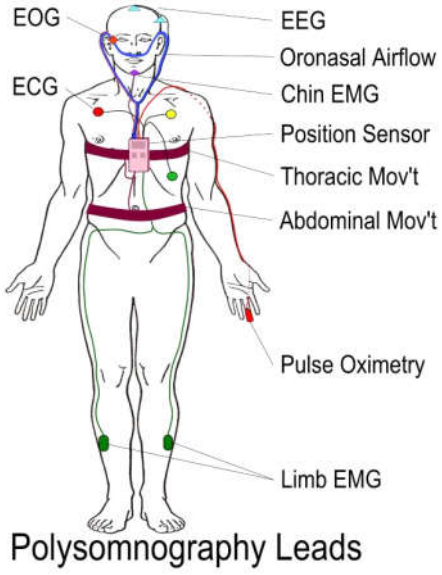
Epworth Sleepiness Scale

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.

Table 1 Prevalence of Overlap Syndrome

COPD without OSA (n=53)		**COPD with OSA (Overlap syndrome) (n=11)**		**Total**	
Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
53	82.81%	11	17.19%	64	100%

Table 2 Severity of Disease according to GOLD Grading

Gold grading	Copd without osa (n=53)		Copd with osa (overlap syndrome) (n=11)		Total	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Gold i	17	32.1%	2	18.2%	19	29.7%
Gold ii	23	43.4%	7	63.6%	30	46.9%
Gold iii	10	18.9%	2	18.2%	12	18.8%
Gold iv	3	5.7%	0	0.0%	3	4.7%
Total	53	100.0%	11	100.0%	64	100.0%

2 = 2.013, p=0.570

From the above table, 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 3 Body Mass Index (BMI)

Parameters	**COPD without OSA (n=53) MeanSD**	**COPD with OSA (Overlap syndrome) (n=11) MeanSD**	**Remarks**
BMI	22.813.29	27.573.54	t=-4.300 p=0.000 (HS)

Mean BMI in COPD without OSA was 22.813.29 whereas in COPD with OSA it was 27.573.54. Group comparison showed statistically highly significant statistical difference between the groups.

Table 4 Night time saturation (Night SpO_2)

Parameters	**COPD without OSA(n=53) MeanSD**	**COPD with OSA (Overlap syndrome) (n=11) MeanSD**	**Remarks**
Night SpO2	90.851.24	87.731.95	t=6.802 p=0.000 (HS)

Mean Night time SpO_2 in COPD without OSA was 90.851.24 whereas in COPD with OSA it was 87.731.95. Group comparison showed statistically highly significant statistical difference between the groups.

Correlation AHI vs BMI

Group 1 (COPD without OSA)
Group 2 (COPD with OSA)

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

Correlation AHI vs Night SpO_2

Group 1 (COPD without OSA)
Group 2 (COPD with OSA)

A significant negative correlation was found between AHI and Night SpO_2 in both the groups.

DISCUSSION

Chronic Obstructed Airways Disease (COPD) is fourth leading cause of death and it is estimated that it is going to be third by the year 2020. The World Health Organization (WHO) defines COPD as follows (www.goldcopd.org, 2017).

"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."

Obstructive Sleep Apnea (OSA) is a breathing disorder and it occurs during sleep. The condition is characterized by stoppage of breathing for ten seconds or longer and at least five times per hour during sleep. The combination of chronic obstructive pulmonary disease and sleep apnea-hypopnea syndrome has been denominated "overlap syndrome" by the late David Flenley. Sleep-disordered breathing (mainly obstructive sleep apnea) and COPD are among the most common pulmonary diseases, so a great number of patients have both disorders; 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.

The primary endpoint of this study was to show prevalence of Obstructive Sleep Apnea in Chronic Obstructive Pulmonary Disease, comparison of the various clinical parameters of COPD patients alone, which is consider as a control group with COPD-OSA Overlap syndrome, which is consider as a 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).

A total no. of 64 consecutive COPD patients enrolled into the study, between 40 to 80 years of age group which were chosen from the Department of TB & Respiratory Diseases of Sir Sunder Lal Hospital, BHU Varanasi. 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 see more male patients, there is relatively increased airway length 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 22.813.29 whereas in COPD with OSA was 27.573.54.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 1.301.33 whereas in COPD with OSA was 26.036.41. Group comparison showed statistically highly significant statistical difference between the groups ($p<0.001$ HS).

Night time SpO_2 in patient, COPD without OSA was 90.851.24 whereas in COPD with OSA was 87.731.95. 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.

Correlations

In our study we found a positive correlation between the AHI vs BMI, Night time SpO_2, ESS whereas negative correlation between BP (Systolic and Diastolic) and BODE index among COPD without OSA.

In our study we found a positive correlation between the AHI vs BMI, BP (Diastolic), Night time SpO_2, 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

- 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 our study.
- Out of 64 subjects, 11 (17.19%) had overlap syndrome.
- Mean BMI in patient, COPD without OSA was 22.813.29 whereas in COPD with OSA was 27.573.54.
- Mean AHI in patient, COPD without OSA was 1.301.33 whereas in COPD with OSA was 26.036.41.

References

1. 1. Agusti AG. Global Strategy for the Diagnosis, Management and Prevention of COPD. *Gold* 2017. http://goldcopd.org.
2. American Academy of Sleep Medicine Task Force Report. Sleep related breathing disorders in adults: recommendations for syndrome, definition and measurement techniques in clinical research. *Sleep* 1999;22:667-689.
3. American Academy of Sleep Medicine. International Classification of Sleep Disorders: Diagnostic and Coding Manual. 2nd Edn. Westchester, American Academy of Sleep Medicine, 2005.
4. Barvaux VA, Aubert G, Rodenstein DO. Weight loss as a treatment for obstructive sleep apnoea. *Sleep Med Rev* 2000;4:435-452.
5. Bednarek M, Plywaczewski R, Jonczak L, *et al*. There is no relationship between chronic obstructive pulmonary disease and obstructive sleep apnea syndrome: a population study. *Respiration* 2005;72(2):142-9.
6. Collop N. Sleep and Sleep Disorders in Chronic Obstructive Pulmonary Disease. *Respiration* 2010; 80:78-86.
7. Diaz-Guzman E, Mannino DM. Epidemiology and Prevalence of Chronic Obstructive Pulmonary Disease. *Clinics in Chest Medicine* 2014;35:7-16
8. Greenberg-Dotan S, Reuveni H, Tal A, *et al*. Increased prevalence of obstructive lung disease in patients with obstructive sleep apnea. *Sleep and Breathing* 2014; 18:69-75.
9. Johns MW. Sensitivity and specificity of the multiple sleep latency test (MSLT), the maintenance of wakefulness test and the Epworth Sleepiness Scale: failure of the MSLT as a gold standard. *J Sleep Res* 2000; 9: 5-11.
10. Kim J, In K, Kim J, *et al*. Prevalence of sleep-disordered breathing in middle-aged Korean men and women. *Am J Respir Crit Care Med* 2004; 170: 1108-1113.
11. McNicholas WT. Chronic Obstructive Pulmonary Disease and Obstructive Sleep Apnea: Overlaps in Pathophysiology, Systemic Inflammation, and Cardiovascular Disease. *American Journal of Respiratory and Critical Care Medicine* 2009; 180:692-700.
12. McNicholas WT. Screening for sleep-disordered breathing: the continuing search for a reliable predictive questionnaire. *The Lancet Respiratory Medicine* 2016; 4:683-685.
13. Punjabi NM, Caffo BS, Goodwin JL, *et al*. Sleep-Disordered Breathing and Mortality: A Prospective Cohort Study. PLoS Medicine 2009; 6:e1000132.
14. Sharma SK, Kumpawat S, Banga A, *et al*. Prevalence and risk factors of obstructive sleep apnea syndrome in apopulation of Delhi, India. *Chest* 2006; 130: 149–156.
15. Sharma, S.K., T.S. Reddy, A. Mohan, K.K. Handa, S. Mukhopadhyay and J.N. Pandeal, 2002. Sleep disordered Breathing in Chronic Obstructive Pulmonary Disease. *Indian J. Chest Dis Allied Sci*., 44: 99-105.
16. Soler X, Gaio E, Powell FL, *et al*. High Prevalence of Obstructive Sleep Apnea in Patients with Moderate to Severe Chronic Obstructive Pulmonary Disease. *Annals of the American Thoracic Society* 2015; 12:1219-1225.

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