EVALUATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA - OVERLAP SYNDROME

Vaddadi Sailendra[1], V. V. L. Srividya[2]

[1]Assistant Professor, Department of Pulmonary Medicine, Gayatri Vidya Parishad Institute of Healthcare and Medical Technology.
[2]Associate Professor, Department of Pathology, Gayatri Vidya Parishad Institute of Healthcare and Medical Technology.

ABSTRACT

BACKGROUND
The drop in oxygen saturation during sleep is more than during exercise and patients of COPD who spend more time in sleeping. Significant sleep desaturation and the sleep disturbances are greater in overlap syndrome than in OSA alone. The present study is conducted in Gayathri Vidya Parishad Institute of Healthcare and Medical Technology, Visakhapatnam, AP, India, to find the prevalence of obstructive sleep apnoea in the patients with COPD.

AIMS
The present study was a cross-sectional study prospectively carried out with an aim to evaluate the breathing disorders during sleep in patients with COPD and to correlate these disorders with the stage of the disease.

SETTINGS AND DESIGN
The study Cohort was constituted by patients of COPD registered into Chest OPD or admitted in Indoor units of Gayathri Vidya Parishad Institute of Healthcare and Medical Technology, Visakhapatnam, AP, India, from July 2014 to May 2016.

A total of thirty six consecutive COPD patients who consented to be enrolled into the study were classified into Mild, Moderate and Severe stages based on the Indian Guidelines for the management of COPD.

METHODS AND MATERIAL
Spirometric evaluation and bronchial reversibility testing was conducted in all the patients. Arterial Blood Gas Analysis was done using ABL3 arterial blood gas analyser (Radiometer, Copenhagen).

POLYSOMNOGRAPHY
Patients were hooked to Compumedics ProFusion Polysomnographic Machine (Compumedics Private Limited 2001, USA), by standard gold cups/electrodes. Thereafter, the patients were subjected to a full night sleep study (Overnight polysomnography). The electrode and sensor connection system utilises E-series EEG/PSG system in order to record the PSG study. The impedance of electrodes was checked and set to <10. A total of 20 leads were utilised for the study. The various parameters monitored included Electroencephalogram (EEG), Electro-oculogram (EOG), Electrocardiogram (ECG), chin and leg Electromyogram (EMG), nasal airflow, tracheal breath sounds, thoracic wall movements, abdominal movements, transcutaneous oxygen saturation and body position.

The sleep data recorded by the computer were manually scored for sleep stages, apnoeas and hypopnoeas. The sleep scoring was done according to R and K classification.

In the study of the 36 COPD patients, 6 patients had mild COPD, 22 had moderate COPD and 8 had severe COPD.

STATISTICAL ANALYSIS
A Significant Correlation (p value <0.05) between Neck Circumference and RDI is found to exist. There is a small, but insignificant positive correlation between BMI and RDI. No Correlation is found to exist between Sleep Efficiency and RDI.

A significant negative correlation (p value <0.05) is found to exist between PO_2 and RDI in patients with Severe COPD. None of the other parameters have any significant correlation with RDI.

RESULTS AND CONCLUSIONS
Our study which consisted of COPD in different stages of severity showed the occurrence of overlap syndrome is 13.88%. We found that neck circumference per se is responsible for the increased AHI in COPD patients ($r=0.381$, $p<0.05$).

3 patients from Mild COPD and 2 patients from Moderate COPD had OSA (overlap syndrome). None of the Severe COPD patients had OSA. Pulmonary functions did not predict the occurrence of obstructive sleep apnoea in COPD and only Neck circumference per se contributes to the raised AHI in COPD patients.

KEYWORDS
COPD, Overlap Syndrome, Polysomnography.

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Corresponding Author:
Dr. Vaddadi Sailendra,
#401A, East Court Apts, East Point Colony,
Visakhapatnam, Andhra Pradesh.
E-mail: vsailendra@yahoo.com
venu_doc2002@yahoo.co.in
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INTRODUCTION: All patients with COPD become more hypoxaemic during sleep than during restful wakefulness.[1-3] The drop in oxygen saturation during sleep is more than during exercise and because patients of COPD spend much more time in sleeping than exercising, sleep is a more significant cause of hypoxaemic load for these patients.[4] The dual occurrence of Obstructive Sleep Apnoea (OSA) in COPD is termed as 'Overlap syndrome' by Flenley,[5] which is recognised for causing lethal effects on the patient's haemodynamics. Different studies reflect conflicting prevalence of overlap syndrome ranging from 2%-28%.[6-9] Significant sleep desaturation and the sleep disturbances are greater in overlap syndrome than in OSA alone and these patients are particularly prone to complications of chronic hypoxaemia such as pulmonary hypertension, cor pulmonale and polycythaemia.[10,11]

In recognition of the importance, the present study is conducted in the well-equipped Sleep Laboratory of Gayatri Vidya Parishad Institute of Healthcare and Medical Technology, Visakhapatnam, AP, India, to find the prevalence of obstructive sleep apnoea in the patients with COPD.

MATERIALS AND METHODS: The present study was a cross-sectional study prospectively carried out in the well-equipped sleep laboratory of Gayatri Vidya Parishad Institute of Healthcare and Medical Technology, Visakhapatnam, AP, India, with an aim to evaluate the breathing disorders during sleep in patients with COPD and to correlate these disorders with the stage of the disease.

Study Period: The study Cohort was constituted by patients of COPD registered into Chest OPD or admitted in Indoor Units of Gayatri Vidya Parishad Institute of Healthcare and Medical Technology, Visakhapatnam, AP, India, from July 2014 to May 2016.

Sample Size: A total of thirty six consecutive COPD patients who consented to be enrolled into the study were classified into mild, moderate and severe stages based on the Indian guidelines for the management of COPD, i.e. Mild COPD: FEV_1/FVC <70%, FEV_1 >80% predicted; Moderate COPD: FEV_1/FVC <70%, FEV_1 30-80% predicted; Severe COPD: FEV_1/FVC <70%, FEV_1 <30% predicted.

The inclusion criteria followed for enrolling the patients in the study were age >40 years; clinical history consistent with COPD; Irreversible Airflow Obstruction, i.e. Forced Expiratory Volume in one second (FEV_1)/Forced Vital Capacity (FVC) <70% and post-bronchodilator change in FEV_1 <15% (or) if FEV_1 <1.5 L, change in FEV_1 <200 mL.

Patients with active tuberculosis, congestive heart failure, chronic renal failure, morbid obesity (BMI >40), pregnant women, age <40 years and >80 years were excluded from the study.

METHOD: Detailed history, complete general and systemic physical examination and all relevant laboratory investigations were conducted as per the protocol.

Anthropometry: Weight and height were measured to the nearest 500 g and one cm, respectively, and the Body Mass Index (BMI) was calculated based on the formula [BMI = weight (kg)/height^2(m^2)]. Neck circumference (cm) was measured at the level of cricothyroid membrane.

Pulmonary Functions: Spirometric evaluation and bronchial-reversibility testing was conducted in all the patients. The patients were instructed to withhold the morning dose of inhaled bronchodilators on the day of pulmonary function testing. Arterial Blood Gas Analysis was done using ABL3 arterial blood gas analyser (Radiometer, Copenhagen).

Based on the spirometric evaluation, patients were further classified into mild, moderate and severe COPD groups in accordance to the Indian Guidelines for COPD. An informed consent was taken from each patient.

Polysomnography: Patients reported to the Sleep Laboratory at 8:00 p.m. on the day of their appointment. They were hooked to Compumedics ProFusion Polysomnographic Machine (Compumedics Private Limited 2001, USA), by standard gold cups/electrodes after cleansing the area of attachment by spirit and savlon. Thereafter, the patients were subjected to a full night sleep study (Overnight polysomnography). The electrode and sensor connection system utilises E-series EEG/PSG system in order to record the PSG study. The impedance of electrodes was checked and set to <10. A total of 20 leads were utilised for the study. The various parameters monitored included Electroencephalogram (EEG), Electro-oculogram (EOG), Electrocardiogram (ECG), chin and leg Electromyogram (EMG), nasal airflow, tracheal breath sounds, thoracic wall movements, abdominal movements, transcutaneous oxygen saturation and body position.

The polysomnographic study was started at a time, which coincides with the normal sleeping habits of the patient. The sleep data recorded by the computer were manually scored for sleep stages, apnoeas and hypopneas. The sleep scoring was done according to R and K classification.

Obstructive Sleep Apnoea-Hypopnea Syndrome (OSAHS) is defined as characterised by recurrent episodes of partial or complete upper airway obstruction during sleep. This manifests as a reduction in (hypopnea) or complete cessation (apnoea) of airflow despite ongoing inspiratory efforts. Mild: 5 to 15 events (RDI) per hour, Moderate: 15 to 30 events (RDI) per hour, Severe: greater than 30 events (RDI) per hour.

RESULTS: The mean age was 53.31 years (range 40 to 77 years, 35 males, 1 female). The mean BMI was 18.424 (range 13.7 to 28.7), mean neck circumference was 374.903 (range 14 to 28). Most of the patients enrolled into the study were heavy smokers with the mean pack years of 30.69, (range 15 to 60).

Of these, 6 patients had mild COPD, 22 had moderate COPD and 8 had severe COPD. Mean age of mild, moderate and severe COPD patients are 58.17, 53.5 and 49.38, respectively.

Pulmonary Functions: The mean value of FEV_1/FVC ratio was 52.03 (range 26 to 79), mean FEV_1 % pred. was 50 (range 19 to 83).

The daytime Arterial Blood Gas (ABG) analysis showed that the Mean PH was 7.41 (range 7.34 to 7.49), the mean PCO_2 was 42.18 (range 32.3 to 68.3). Out of the 36 patients, 6 patients had daytime hypercapnia (PCO_2>45 mmHg). The mean PO_2 was 79.156 (range 49 to 107.2). Two patients had daytime hypoxia (PO_2<60 mmHg.). The mean arterial oxygen saturation was 95.033% (range 82 to 98.2) with one patient having a SpO_2 <90%.

Apnoea-Hypopnoea Index/Respiratory Disturbance Index:

RDI	
Mean	1.92±1.933
Range	6.4 (0 - 6.4)
NREM RDI	
Mean	1.889±1.93
Range	6.7 (0 - 6.7)
REM RDI	
Mean	2.311±4.78
Range	21.2 (0 - 21.2)

Table 1: Respiratory Disturbance Index

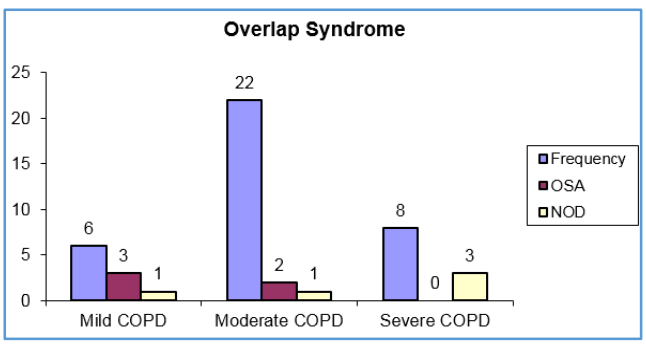
Table 1 shows Respiratory Disturbance Index (Total Number of Apnoeas and Hypopnoeas/Total Sleep Time (TST)) estimates the occurrence of Sleep Apnoea Syndrome. Most of the respiratory events (Apnoeas as well as Hypopnoeas) observed were obstructive with very occasional central apnoeas noticed. An RDI of ≥5 is required for the diagnosis of Obstructive Sleep Apnoea syndrome (OSA). A mean RDI of 1.92 was observed with a range between 0 to 6.4.

"Overlap Syndrome" [Obstructive Sleep Apnoea (OSA) and COPD].

A total of five COPD patients had concomitant OSA with an RDI ≥5 constituting 13.88% of the total study cohort. Subgroup analysis showed that 3 of mild COPD patients and 2 of Moderate COPD patients had Overlap Syndrome. None of the severe COPD group had OSA.

COPD	OSA
Mild	3 (50%)
Moderate	2 (9.09%)
Severe	0
Total	5 (13.88%)

Table 2



CORRELATIONS:

Parameter	r value	p value
BMI and RDI	0.281	>0.05
Neck Circumference and RDI	0.381	<0.05
Sleep Efficiency and RDI	-0.026	>0.05

Table 3: COPD (n=36)

A Significant Correlation (p value <0.05) between Neck Circumference and RDI is found to exist. There is a small, but insignificant positive correlation between BMI and RDI. No correlation is found to exist between Sleep Efficiency and RDI.

SUBGROUP ANALYSIS:

Parameter	r value	p value
Spirometry		
FEV_1% and RDI	0.412	>0.05
FEV_1% and Supine RDI	0.262	>0.05
FEV_1% and REM RDI	-0.022	>0.05
ABG		
$PaCO_2$ and RDI	0.644	>0.05
PaO_2 and RDI	-0.075	>0.05

Table 4: Mild COPD (n=6)

Parameter	r value	p value
Spirometry		
FEV_1% and RDI	0.343	>0.05
FEV_1% and REM RDI	0.029	>0.05
FEV_1% and Supine RDI	0.366	>0.05

ABG		
$PaCO_2$ and RDI	-0.082	>0.05
PaO_2 and RDI	0.012	>0.05

Table 5: Moderate COPD (n=22)

Parameter	r value	p value
Spirometry		
FEV_1% and RDI	-0.584	>0.05
FEV_1% and REM RDI	0.406	>0.05
FEV_1% and Supine RDI	-0.260	>0.05
ABG		
$PaCO_2$ and RDI	0.3	>0.05
PaO_2 and RDI	-0.752	<0.05

Table 6: Severe COPD (n=8)

Above tables describes a significant negative correlation (p value <0.05) is found to exist between PO_2 and RDI in patients with Severe COPD. None of the other parameters have any significant correlation with RDI.

Parameter	r value	p value
NC and RDI	0.759	>0.05
BMI and RDI	0.717	>0.05
FEV_1 and RDI	0.419	>0.05
$PaCO_2$ and RDI	0.607	>0.05
PaO_2 and RDI	0.430	>0.05
SpO_2 and RDI	0.359	>0.05

Table 7: Correlations: Overlap Syndrome (n=5)

Table 7 shows none of the daytime parameters could show any significant correlation with the occurrence of OSA in COPD (Overlap syndrome) patients.

DISCUSSION: The influence of sleep on the ventilatory parameters of COPD patients has received much importance in the past few decades. For a long time, the mechanisms responsible for the profound nocturnal hypoxaemia in these patients remained elusive. With the advancement in the technology and the ever-broadening frontiers of Sleep Medicine answers to the many persistent questions were found and are being confirmed by sleep researchers in different parts of the world.

The present study was conducted in the sleep lab of Gayatri Vidya Parishad Institute of Healthcare and Medical Technology with an aim to evaluate the breathing disorders during sleep in the patients with COPD and to correlate these disorders with the stage of the disease.

The mean BMI and neck circumference of the study cohort are 18.42 and 34.9, respectively. This suggests the poor nutritional status of the patients, which might be due to the chronicity of the disease. Earlier studies enrolled subjects who were obese, which itself is an important confounding factor for obstructive sleep apnoea.[12,13] Radwan et al studied sleep disordered, breathing in obese patients with and without COPD.[14] They did not find any statistically significant difference in AHI, mean nocturnal saturation and BMI between the two groups. Our observations suggest that it is the neck circumference per se that contributes to increased AHI in patients with COPD.

In the present study, COPD patients are grouped into 3 categories in accordance with the Indian guidelines into mild, moderate and severe COPD and the nocturnal breathing disturbances are studied in each of these groups. Earlier study by S.K. Sharma et al classified COPD patients into those having Chronic Respiratory Failure (CRF) and those who were not in CRF.[15] The study done by Thomas V.D. et al grouped the patients of COPD from a south Indian population into nocturnal desaturators and non-desaturators.[16]

S. A. Little et al studied the factors predicting NOD in COPD patients and enrolled patients of moderate and severe COPD groups as per the ATS guidelines. They have excluded patients who had respiratory failure from their study.[17] Careful scrutiny on the internet could not reveal any other study of this kind, which might place the present study the one of its kind.

Various authors studied the occurrence of OSA in COPD patients. Earlier studies by Resta O et al and de Miguel J et al have documented OSA in 16% and 28.5% of COPD patients, respectively.[8,9] These studies had a selection bias as they included patients from sleep clinics into the study. Those patients had excessive daytime somnolence as one of the chief complaints and moreover these patients were obese. Our patients were enrolled from the chest clinics with primarily respiratory symptoms and their BMI was not high. The study conducted by S. K. Sharma et al has quoted a 6% occurrence of OSA in COPD patients with most of the patients having significantly severe disease at the time of enrollment. They proposed that BMI per se is responsible for AHI with neck circumference having a small contribution.[15]

Our study, which consisted of COPD in different stages of severity showed the occurrence of overlap syndrome of 13.88%. Of the 5 patients with overlap syndrome, 1 (20%) patient had significant nocturnal oxygen desaturation. This patient had mild COPD and the daytime ABG was also normal, but had profound nocturnal hypoxaemia in REM sleep with a REM stage RDI of 16.1 compared NREM RDI of 3.5. The lowest O_2 saturation achieved by the patient was 55%. 2 of the patients with OSA had daytime hypercapnia, but no daytime hypoxaemia or significant nocturnal desaturation. We found that neck circumference per se is responsible for the increased AHI in COPD patients ($r=0.381$, $p<0.05$). In patients with overlap syndrome, no significant correlation is found to exist between any of the awake pulmonary functions viz., FEV_1, FEV_1/FVC, PaO_2, SpO_2, $PaCO_2$ or the anthropometric variables viz., NC, BMI and AHI.

It can be finally concluded that the pulmonary functions do not predict the occurrence of obstructive sleep apnoea in COPD and only neck circumference per se contributes to the raised AHI in COPD patients. Nocturnal oxygen desaturators have raised daytime $PaCO_2$. Awake SpO_2 is found to be the single most useful parameter that can predict independently NOD in COPD.

CONCLUSION: The prevalence of obstructive sleep apnoea syndrome in COPD in this study is found to be 13.88%. 3 patients from mild COPD and 2 patients from moderate COPD had OSA (overlap syndrome). None of the severe COPD patients had OSA. No significant central sleep apnoea syndrome or sleep hypoventilation syndromes were noticed.

Pulmonary functions do not predict the occurrence of obstructive sleep apnoea in COPD and only neck circumference per se contributes to the raised AHI in COPD patients.

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