ORIGINAL RESEARCH PAPER

Pulmonary Medicine

PREVALENCE OF OVERLAP SYNDROME AND ITS CORRELATION WITH VARIOUS COMORBIDITIES IN COPD PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL: A COHORT STUDY

KEY WORDS:
COPD,OSA,comorbidities

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ABSTRACT

Introduction: The overlap syndrome was first coined by David C. Flenley in 1985 to describe the coexistence of obstructive sleep apnoea (OSA) in patients with chronic obstructive pulmonary disease (COPD). Patients with Overlap Syndrome experience more profound nocturnal oxygen desaturation (NOD) than patients with OSA or COPD alone. Little is known about the possible predictors of the overlap syndrome and its association with comorbidities contributing to impaired outcome. **Objectives:** This study aimed to evaluate the prevalence and possible predictors of the overlap syndrome and its correlation with various comorbidities in a cohort of COPD patients. Materials & Methods: Individuals with COPD (GOLD, risk groups A–D) admitted in our hospital from March 2021 to December 2021. Information on age, gender, body mass index (BMI), waist-hip ratio, smoking status, Adjusted neck circumference Epworth sleepiness scale (ESS),STOP BANG, COPD assessment test score, comorbidities, was collected and a spirometry was performed. Participants underwent Level 1 sleep study in our hospital. An apnoea-hypopnea index (AHI) >5 per hour was considered to indicate OSA. Results: Around 50 patients were enrolled with a mean age of 60.7 of whom male is 52 % and female is 48%. During nocturnal polysomnography, 39.1% had evidence of OSA.AHI had statisticaly correlated with Diabetes,Hypertension (p value<0.005).Also in our study we found AHI had statisticaly correlated between ESS score and severity of COPD (GOLD Class B & C)(p value<0.005).Pulmonary Arterial Hypertension and Diabetes were more common in patients with overlap syndrome. **Conclusion:** The prevalence of COPD patients with OSA is 24%. BMI and smoking history seems to be a predictor of the overlap syndrome.These patients may be more affected by pulmonary arterial hypertension and diabetes.

INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is a common chronic lung disease that is both preventable and treatable that is affecting people worldwide. It includes emphysema and chronic bronchitis. It is the third leading cause of death worldwide,causing 3.23 million deaths in 2019. Nearly 90% of COPD deaths in those under 70 years of age occur in low- and middle-income countries (LMIC)(1).

The Overlap syndrome is defined as the coexistence of apneas or hypopneas during sleep secondary to obstruction of the upper airway in patients with COPD(2). During sleep, patients with COPD experience nocturnal hypoxemia and hypoventilation mainly during the rapid eye movement (REM) phase of the sleep due to relaxation of intercostal muscles and reduced chest wall mobility. On the other hand, patients with OSA experience episodes of apnoea and hypopnea mainly through upper airway collapse, reduced intrathoracic pressures, and activation of the sympathetic nervous system resulting in night time arousals and excessive daytime sleepiness(2). These episodes of nocturnal oxygen desaturation (NOD) with hypercapnia and hypoxemia are more profound in patients with Overlap syndrome in comparison to COPD or OSA alone.

AIMS & OBJECTIVES:

To evaluate the prevalence and possible predictors of the overlap syndrome and its correlation with various comorbidities in a cohort of COPD patients.

MATERIAL AND METHODS

Place of research: Rajarajeswari Medical college and hospital,Bangalore.

Study period: March 2021 to December 2021.

Sample size: 50

Inclusion criteria:Patients between 42 and 90 years of age with objectively confirmed COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines were consecutively included in this study .

Exclusion criteria: We excluded subjects with upper or lower respiratory tract infections and an exacerbation of COPD within the most recent 6 weeks. All patients signed informed consent and the study was approved by the Instituitional ethical committee RRMCH.

Study Design: In this cross-sectional, subjects performed a spirometry and were accordingly categorized in COPD GOLD stages I–IV. In a clinical examination, height, weight, body mass index (BMI) and blood pressure were measured. Smoking history and exacerbation rate in the most recent 12 months, comorbidities and medications were recorded during a structured physician-led interview. Participants completed the Epworth sleepiness scale (ESS) and the COPD assessment test (CAT). Patients were asked to perform a Level iii sleep study at with the Apnea Link TM (ResMed, MAP Medicine Technology, Martinsried, Germany) device during one night. Examinations took place between september 2020 and December 2021. Alice night one device were used .

Materials Spirometry:

The degree of airflow limitation was assessed by performing both spirometry and COPD staging according to guidelines(3).

Exacerbation Frequency: An exacerbation was defined as a sustained worsening of the patient's condition from the stable state and beyond normal day to-day variations that was acute at onset and might have warranted additional treatment, such

as antibiotics and/or steroids. Subjects were asked about the number of exacerbations in the most recent 12 months (4).
Epworth Sleepiness Scale:

The ESS is a self-administered item to assess sleep propensity during normal daily activities. The German version of the questionnaire was used in this study(5). Clinically relevant daytime sleepiness was assumed if individuals had a score of greater than [5].

COPD Assessment Test: The CAT is a self-assessed questionnaire in which patients have to rate eight COPD-related symptoms, on a scale from 0 (impact low) to 5 (impact very high). It is used to assess the impact of COPD on an individual's quality of life and has been proven to be reliable, repeatable and sensitive for variations in disease severity(6) . Level iii sleep studies were performed using the Alice night one device. The device records the patient's nasal respiratory pressure signal and finger oximetry during sleep, and has been validated as an accurate instrument with which to detect snoring, apnoea-hypopnea and oxygen desaturations(7) . The results of the sleep study were scored automatically with dedicated software and manual review to ensure the accuracy of the data. Apnoea is defined as a cessation of airflow lasting more than 10 s and hypopneas as a reduction in airflow of at least 30% lasting more than 10 s, associated with a drop in oxygen saturation of >4% . An apnoea-hypopnea index (AHI) of >5 events per hour was considered to indicate the presence of OSA.

Analysis:
Data were analyzed using SPSS version 19 and STATA 12 (StataCorp, College Station, Tex., USA). Data are presented as median (quartiles) and mean (standard deviation, SD), unless otherwise stated. Descriptive data analysis was performed and value distribution was analyzed with the Shapiro-Wilk normality test. Normally distributed data were analyzed with the t test. If data were not distributed normally, the Wilcoxon rank-sum test was used, and for categorical variables the 2 test was applied. Univariate regression was used to investigate relationships between AHI (dependent variable) and possible determinants. Further multivariate analysis involved regression of variables that showed a univariate p value.

RESULTS:
We recruited 50 patients with diagnosed COPD and history of excessive day time sleepiness. The patient characteristics are presented in detail in table 1

Table No 1: Characteristics of study participants

Characteristics	Mean	Standard Deviation
Age	60.74	10.25
Height	166.40	8.93
Weight	92.96	1049
BMI	33.68	3.92
SPO2	92.76	2.19
Pack in years	14.26(0.0)	17.11()
Waist Hip Ratio	0.87	0.06
ESS	11.56	1.96
Stop Bang Score	6.88	1.11
APNEIC	39.01	19.30
CAT Score	27.98	5.87
FEV1/FVC	69.02	13.28
FEV1	61.26	15.18
ANC	46.54	2.74
P HTN2dEcho	48.64	9.57
EF 2D Echo	47.50	8.13

Calculated ESS score which inferred a mean of 11.56 and according to Berlin distribution of study 22% were having low risk,78% were having high risk. The participatory population were 52% males and 48% females with a mean age of 60.7 ,with a mean BMI of 33.68.

Patients were classified according to GOLD based on history, CAT score, spirometry into Group A (mean 6),Group B(mean 8),Group C(mean 12) and Group D (mean 24).STOP BANG questionnaire was used as a screening test in the OPD to assess the COPD patients with OSA.AHI was classified as less than 10 and more than 10.The correlation of apnoeic index was statistically significant with waist-hip ratio,Fev1 and 2D echo. Patients were assessed day time sleepiness through ESS . Metabolic syndrome which include in this study, Diabetes mellitus(p value=0.046) and hyperlipidemia (P value 0.017),hypothyroidism(P value0.056) are statistically significant in correlation with apnoea-hypopnoea index score.

During nocturnal polysomnography, 39.1% had evidence of OSA.AHI had statistically correlated with Diabetes, Hypertension (p value<0.005). Also in our study we found AHI had statistically correlated between ESS score and severity of COPD (GOLD Class B & C)(p value<0.005. Comparing characteristics between the group with an AHI ≤ 10 events per hour and the group with an AHI >10 events per hour, individuals with evidence for the overlap syndrome presented with higher BMI, higher FEV 1 and less frequent exacerbations(Table 2).Significantly higher rates of pulmonary arterial hypertension and diabetes mellitus were found in the group of COPD patients with evidence for OSA.

Table No 2: Comparison of different parameters by APNEIC

Parameters	APNEIC (mean)		
	<=10	>10	
Age	61.44±11.92	60.59±10.01	0.823
Male	33.3	61.0	0.0013
Female	66.7	39	0.0018
Height	165.67±12.36	166.56±8.18	0.789
Weight	95.89±6.21	92.32±11.17	0.360
BMI	35.57±5.85	33.26±3.31	0.109
SPO2	93.33±1.73	92.63±2.28	0.391
Pack Years	8.11±13.68	15.61±17.63	0.180
Waist HIP Ratio	0.84±0.06	0.88±0.05	0.057
EPWORTH SS	10.89±1.62	11.71±2.02	0.261
Stop Bang score	6.78±1.39	6.90±1.07	0.765
Cat SCORE	28.00±5.00	27.98±6.10	0.024
FEV1/FVC	63.44±10.64	70.24±13.59	0.167
FEV1	55.00±9.67	70.44±16.12	0.0420
ANC	46.12±2.85	46.63±2.74	0.618
DM	14.2	11	0.001
P HTN 2D Echo	23.29±9.75	45.67±8.62	0.0308
EF 2DECHo	46.27±8.09	53.11±5.86	0.010
Mallampati	2.67±1.23	2.49±0.87	0.179

DISCUSSION:
In our study the prevalence of 24% of the overlap syndrome was found suggesting that COPD and OSA have a common pathophysiological background. In patients with overlap syndrome, the mortality due to cardiovascular events has been shown to be higher in comparison to one single disease alone [8] .

Some preliminary evidence that both diseases may lead to systemic inflammation [9] , and accelerate atherosclerosis [10] and vascular dysfunction , and thus might increase comorbidities such as arterial hypertension , have been presented before. This is in line with our findings that those with the overlap syndrome had a higher rate of Pulmonary arterial hypertension and diabetes.

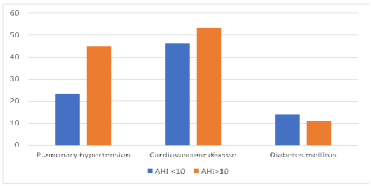

Fig.1 Comorbidities in COPD with and without evidence for OSA. AHI thresholds represent events per hour. p < 0.05

In OSA patients, a high prevalence of COPD ranging from 11 up to 41% has been reported.Both obese and non-obese COPD patients showed significant positive correlations between AHI and pack years, SBQ, ESS, and adjusted neck circumference (ANC).. In COPD on the other hand, while some studies found a higher prevalence of OSA in patients with COPD compared to subjects without COPD.

CONCLUSION:

This study showed a prevalence of OSA almost 24% in COPD patients. Increased BMI (waist-hip ratio) and pack years (mean=0.180) with STOP BANG criteria were used to recruit the patients. Comorbidities such as pulmonary hypertension and diabetes mellitus were found more often in patients with overlap syndrome compared to patients with COPD alone. Careful assessment of comorbidities should become standard clinical practice for OSA patients.

ABBREVIATIONS:

COPD(Chronic obstructive pulmonary diseases),OSA(Obstructive sleep apnoea), ESS(Epworth sleepiness score),SBQ(Stop Bang Questionnaire)

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