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Study the Clinical, Spirometric and Polysomnographic Profile Along with Sleep Related Symptoms in Patients with COPD

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ABSTRACT

Chronic obstructive pulmonary diseases (COPD) is the second leading cause of mortality and its prevalence continues to increase. While the debilitating effects of COPD on daytime functioning are well known, COPD's effects on sleep have been less fully investigated. Sleep problems affect as many as 50% of patients with COPD. The increased prevalence of obesity worldwide is associated with subsequent increase in the occurrence of sleep disordered breathing, especially obstructive sleep apnea (OSA). The study was carried out at the OPD and IPD Department of Respiratory Medicine at tertiary health care centre. The duration of the study period was from March 2018 to February 2019. Total 105 patients fulfilling the inclusion criteria were included in the study. Thorough clinical examination of each subject was carried out. Clinical and diagnostic profile of patient with chronic obstructive pulmonary disease was noted in predesigned pretested proforma. Patient evaluation was done with spirometry and polysomnography for detection of obstructive sleep apnea. About half of the study subjects were from overweight and obese BMI. Mean saturation was less in overlap syndrome as compared to COPD group and the difference was found to be statistically significant. Apnea hypopnea index was more in overlap group as compared to COPD group and the difference was statistically significant while difference in FEV1 and FEV1/FVC parameters between two groups was not statistically significant. Half of the study subjects (47.63%) were at stage IV followed by 38.09% in stage III. Only 3.81% were at stage I. COPD patient's particularly overweight and obese individuals are at greater risk of having OSA. So it is worthwhile to do polysomnography in COPD patients for early detection of OSA and to prevent them from further complications of OSA like uncontrolled hypertension, cerebrovascular accidents and coronary artery diseases.

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INTRODUCTION

Chronic obstructive pulmonary diseases (COPD) is the second leading cause of mortality and its prevalence continues to increase. While the debilitating effects of COPD on daytime functioning are well known, COPD's effects on sleep have been less fully investigated. Sleep problems affect as many as 50% of patients with COPD. The mild hypoventilation that is physiologically observed during sleep is heightened in this patient group and is often accompanied by ventilation/perfusion mismatch. Significant hypoxemia ensues that is often accompanied by hypercapnia. These gas exchange abnormalities (particularly nocturnal oxygen desaturation, NOD) place COPD patients at increased risk of pulmonary hypertension, arrhythmias and possibly cardiovascular death[1]. The increased prevalence of obesity worldwide is associated with subsequent increase in the occurrence of sleep disordered breathing, particularly obstructive sleep apnea (OSA)[2]. The coexistence of OSA and COPD, known as the overlap syndrome, has been estimated to occur in 1% of the general population. Overlap patients are a unique group of COPD patients who experience complex sleep disordered breathing, with nocturnal hypoxaemia and hypercapnia that is often disproportionately worse than their ventilatory impairments, pulmonary hypertension and significant cardiovascular comorbidity[3]. The lower baseline oxygenation and abnormal respiratory mechanics in patients with COPD become clinically important when combined with the normal physiologic alterations in ventilatory control and respiratory muscle tone that occur during sleep. In COPD patients, the more profound decrease in oxygen saturation during sleep is mainly attributed to the lower PaO2 during wakefulness. This PaO2 level is on a steeper section of the O2 dissociation curve; thus, a slight decline in oxygenation leads to a more profound reduction in oxygen saturation. Thus, nocturnal oxygen desaturation (NOD) is the most significant sleep abnormality associated with COPD[4,5].

The coexistence of OS may further increase the risk of cardiovascular events particularly pulmonary hypertension and atrial fibrillation, thereby resulting in poor outcome and increased risk of mortality than in patients with COPD or OSA alone. Nevertheless, COPD and OSAS do not share the same mechanisms leading to inadequate gas exchange. While COPD is characterized by a chronic baseline hypoxaemia due to a permanent airflow limitation, OSAS patients show recurrent desaturations that lead to a pattern of intermittent hypoxaemia during the night[6]. Therefore, the pattern of intermittent desaturation superposes to a pathological baseline hypoxaemia in patients showing both diseases. In this regard, heart rate variability (HRV) analysis, which is commonly used to assess autonomic imbalances linked with diseased states, has been found to provide relevant information on the effect of overlap syndrome on cardiac regulation[7,8]. Patients simultaneously showing both conditions have significant imbalances in cardiac autonomic modulation compared to those with COPD or OSA alone, such as higher sympathetic and lower parasympathetic activity[6]. Patients with OS have increased risk of pulmonary hypertension and right heart failure secondary to underlying NOD, daytime hypoxemia and hypercapnia as compared to patients with COPD and OSA alone.

Considering this fact, the above study was conducted to study clinical and diagnostic profile of patient with chronic Obstructive pulmonary disease and their evaluation with polysomnography for obstructive sleep apnea (overlap syndrome).

MATERIALS AND METHODS

Study place: The study was carried out at the OPD and IPD Department of Respiratory Medicine at tertiary health care centre from March 2018 to February 2019.

Study design: Longitudinal, prospective, descriptive cross-sectional study.

Inclusion criteria: Patients who are confirmed case of chronic obstructive pulmonary disease and those willing to participate in the study.

Exclusion criteria: Patients with myocardial infarction, in acute exacerbation of copd and those who were unwilling to participate in the study.

Sample size: 105 patients were included for the study.

Data analysis: Face to face interview was carried out. The collected data was entered in Microsoft Excel 2007.Furthere analysis was done by using SPSS (Statistical Package for Social Sciences) version 20.0 statistical software.

Ethical considerations: All the necessary ethical permissions were taken from the Institutional Ethics Committee.

Face to face interview was carried out in local language (Marathi/Hindi). At the time of interview, the study subjects were informed about the study and its purpose. Data was collected using predesigned, pre-tested, semi-structured questionnaire. For testing proforma and feasibility of the study, a pilot study was carried out on 20 subjects and required modifications were incorporated in the proforma and information on these modifications were again collected from the subjects included in the pilot study. After explaining

the purpose of study, informed consent was taken from the patients. Information regarding demographic factors such as name, age, gender, educational status, residence, religion, occupation, habits like alcohol consumption, smoking, chewing of tobacco and gutakha etc. was obtained from the study population as per the predesigned proforma. All the patients were evaluated with spirometry and polysomnography for detection of obstructive sleep apnea. The patients found to have OSA on Polysomnography were grouped together (overlap syndrome) and compared them with patients without OSA (COPD only pt) for clinical presentation and severity of COPD and OSA, spirometry parameters and polysomnography parameters. The spirometry was performed as per the American thoracic society guidelines using spirometry machine. The patients were diagnosed and classified into mild, moderate, severe and very severe as per the GOLD guidelines[9,10].

RESULTS

Table 1 shows sex wise distribution of study subjects. Most of the study subjects were male (75.24%) and remaining 24.76 % were female.

Most (78) of the study subjects were habitual of smoking, followed by Gutakha chewing by 38 study participants followed by tobacco chewing (24). Only 3 study subjects were there who didn't have any habit (Table 2).

Most of study participants have symptom of shortness of breath especially during physical activity, followed by 92 study participants were having wheezing, 88 were having chest tightness. 75 study participants were having chronic cough with expectoration, 65 complains of frequent respiratory infections and 71 were say that they feel lack of energy, while only 18 study subjects complain about swelling over ankle, feet or leg (Table 3).

Majority i.e., 71.43% of study subjects were having symptoms since more than 3 years followed by 18.09% were having symptoms since 2-3 years. Only 10.48 % study subjects were there who were having symptoms since less than two years (Table 4).

Out of total 105 study subjects it was found that 27.62% study subjects were having COPD with OSA (overlap syndrome) (Table 5).

In the Table 6, sleep related symptoms were more prevalent in overlap group of patients as compare to patients without overlap and the difference is statistically significant between two groups for every symptom.

Table 7 shows the distribution of study subjects according to BMI among two groups, it was found that most of the study subjects were from overweight and obese BMI. The association between two groups and BMI was found to be statistically significant.

Table 1: Distribution of study subjects according to sex

Gender	Total no.	Percentage
Male	79	75.24
Female	26	24.76
Total	105	100.00

Table 2: Personal habits of study subject

Personal habits	No. of subject	Percentage
Alcohol	18	17.14
Tobacco	24	22.85
Betel nut	15	14.28
Gutakha	38	36.19
Smoking	78	74.28
No any habit	03	2.85

*Multiple responses

Table 3: Presenting symptoms of study subject

Symptoms	No. of subject*	Percentage
Shortness of breath	100	95.23
Wheezing	92	87.61
Chest tightness	88	83.80
Chronic cough with expectoration	75	71.42
Frequent respiratory infections	65	61.90
Lack of energy	71	67.61
Swelling in ankles, feet or legs	18	17.14

*Multiple responses

Table 4: Distribution of the study subjects according to the duration of illness in years

Duration in years	Total no.	Percentage
<2	11	10.48
2-3	19	18.09
>3	75	71.43
Total	105	100.00

Table 5: Distribution of patients in two groups as COPD only and COPD with OSA (Overlap)

Final diagnosis	No.	Percentage
COPD with OSA (overlap syndrome) i.e., AHI >5	29	27.62
COPD without OSA i.e., AHI <5	76	72.38
Total	105	100.00

Out of total study subjects we found 29 study subjects were having overlap syndrome, above table shows the severity of obstruction between only COPD patients and among patients having overlap syndrome. It was found that study subjects having overlap have more severity of obstruction (Table 8).

While comparing the saturation at the time of admission between two groups and also the overnight average saturation between two groups, it was found that mean saturation was less in overlap syndrome as compared to COPD group. And the difference was found to be statistically significant. Apnea hypopnea index was more in overlap group as compared to COPD group and the difference was statistically significant while difference in FEV1 and FEV1/FVC parameters between two groups was not statistically significant (Table 9).

Above Table 10 denotes the distribution of cases in two groups according to GOLD COPD stage, it was found that about half of the study subjects (47.63%) were at stage IV followed by 38.09 % in stage III. Only 3.81% were at stage I. While comparing between patients suffering only from COPD and patients with overlap syndrome it was found that, at stage IV more number of people were from overlap group (68.97%) as compared to only COPD patients. The association between the two groups with stage of COPD were found to be significant ($p<0.05$).

Table 6: Prevalence of sleep related symptoms in study subjects

	Only COPD (n = 76)		Overlap (n = 29)			
Sleep related symptoms	No.	Percentage	No.	Percentage	p-value	Statistical significance
Disruptive snoring	53	69.73	27	93.10	0.01195	Significant
Excessive day time somnolence	42	55.26	22	75.86	02653	Significant
Chocking and gasping	32	42.10	19	65.51	0.03186	Significant
Morning headache	29	38.15	17	58.62	0.02941	Significant
Nocturia	35	46.05	19	65.51	0.02535	Significant
Day time fatigue	32	42.10	18	62.06	0.03353	Significant
Depression	7	9.21	9	31.03	0.005400	Significant
Insomnia	18	23.68	12	41.37	0.03636	Significant

*Multiple responses calculated using students 't' test

Table 7: Distribution of study subjects according to their body mass index

	Only COPD (n = 76)		Overlap (n = 29)	
Body mass index	No.	Percentage	No.	Percentage
Underweight (<18.5)	8	10.52	0	0
Normal (18.5-24.9)	18	23.68	0	0
Overweight (25.0-29.9)	35	46.05	11	37.93
Obese (>30)	15	19.73	18	62.07
Mean BMI±SD	20.68±9.98		31.74±5.42	
Mean waist circumference±SD	58.12±19.98		96.58±17.85	

χ^2: 23.05 and p<0.0001

Table 8: Comparison between two groups with respect to severity of obstruction on spirometry

Severity of obstruction	Only COPD (n = 76)	Overlap (n = 29)	Total
Mild (FEV1≥80%)	5 (6.57%)	0 (0%)	5 (4.76%)
Moderate (FEV1 = 50-79%)	8 (10.53%)	4 (13.79%)	12 (11.43%)
Severe (FEV1 = 30-49%)	28 (36.84%)	11 (37.94%)	39 (37.14%)
Very severe (FEV1≤29%)	35 (46.06%)	14 (48.27%)	49 (46.67%)
Total	76 (100%)	29 (100%)	105 (100%)

Table 9: Distribution of cases in two groups according to polysomnography and spirometry

	Only COPD	Overlap	p-value
Parameters	Mean±SD		
Saturation on admission	92.03±6.52	82.98±6.41	0.001
AHI*	4.22±3.49	32.02±15.98	<0.001
Overnight average saturation	95.83±3.68	85.78±7.25	<0.001
FEV1	39.12±13.25	38.98±9.98	0.889
FEV1/FVC	55.10±4.98	55.98±9.10	0.412

*AHI: Apnea hypopnea Index

Table 10: Distribution of cases in two groups according to GOLD COPD stage

COPD Stage	Only COPD (n = 76)	Overlap (n = 29)	Total
I	4 (5.26%)	0 (0%)	4 (3.81%)
II	9 (11.85%)	2 (6.89%)	11 (10.47%)
III	33 (43.42%)	7 (24.14%)	40 (38.09%)
IV	30 (39.47%)	20 (68.97%)	50 (47.63%)
Total	76 (100%)	29 (100%)	105 (100%)

X^2: 7.899, df: 3 and p = 0.04814

Table 11: Polysomnographic profile of study subjects

Polysomnographic variables	Only COPD (n = 76)	Overlap (n = 29)	p-value
AHI	4.22±3.49	32.02±15.98	<0.001
AHI NREM	4.9±3.1	32.40±16.3	<0.05
AHI REM	4.5±2.5	30.20±15.9	<0.05
AHI SUP-NONSUP	4.3±1.9	28.40±11.2	<0.05
LNS mean	92.83±3.68	81.78±7.25	<0.001

Calculated using students 't' test

AHI in overlap syndrome is higher than COPD group and the difference was statistically significant. Also the positional difference (AHI SUP-NONSUP), AHI in REM and NREM sleep is greater in overlap group and the difference is statistically significant between two groups. Mean lowest oxygen saturation during night in COPD patients was greater than overlap patients and the difference was statistically significant (Table 11).

DISCUSSIONS

In the above study, most of the study subjects were male (75.24%) and remaining 24.76% were female. Esther Helen Steveling *et al*.[11] in their study on Predictors of the Overlap Syndrome and Its Association with Co morbidities in Patients with Chronic Obstructive Pulmonary Disease found that, in multiple regression analysis, including age, gender, BMI, pack years, ESS, daytime SpO2 exacerbation

frequency, mean nocturnal SpO 2 and diabetes mellitus as independent variables and with AHI as the dependent variable, only BMI and pack years were found to be significantly associated with AHI. Similarly, Gothi *et al*.[12] in her study of Impact of overlap syndrome on severity of acute exacerbation of chronic obstructive pulmonary disease found that There were 34/38 and 11/13 men in only COPD and overlap group respectively. Male: Female ratio between only COPD and overlap was statistically insignificant (p = 0.220).

Most of study subjects were habitual of smoking 74.28% followed by gutakha chewing 36.19 followed by tobacco chewing 22.85%. 71.43% of study subjects having symptoms more than 3 year followed by 18.09% having symptoms 2-3 years. 10.48% study subjects were there having symptoms less than 2 years. Sleeping disorders and snoring campaign and management facilities should be considered to raise the awareness about the issue and manage their risk factor.

In present study it was found that most of the study subjects were from overweight and obese BMI. The association between two groups and BMI was found to be statistically significant (p<0.0001). Several confounding factors may influence relationships between COPD and OSAS, particularly BMI and smoking. Obesity is a key factor in OSAS, yet low BMI is common in COPD, especially in patients with advanced disease[13,14]. This feature may protect against OAH and is supported by the finding of a lower RDI in subjects with airflow obstruction, relating to lower BMI[15]. On the other hand, many other patients with COPD have elevated BMI, thus predisposing to OAH and the finding of a higher RDI in overweight patients with airflow obstruction supports this possibility[16]. Smoking is a risk factor for COPD and OSAS and several reports found a higher AHI in smokers than non-smokers[17]. A report based on the Wisconsin Sleep Cohort including 811 adults found that an AHI of at least 5/hour was three times more likely in current smokers than in never-smokers[18]. Heavy smokers (>40 cigarettes/day) had an odds ratio of 6.74 for AHI of at least 5/hr. Gothi *et al.*[12] in her study of Impact of overlap syndrome on severity of acute exacerbation of chronic obstructive pulmonary disease found that Majority of subjects in only COPD were underweight or normal weight whereas majority of subjects in overlap were obese. Mean BMI in only COPD was 20.70±8.03 kg m^{-2} and that in overlap was 31.82±5.80 kg m^{-2}. The mean waist circumference in only COPD was 58.21±20.07 cm and in overlap was 96.62±17.61 cm. Both mean BMI and waist circumference in overlap were significantly higher as compared to only COPD (p<0.001).

In present study, most of the study participants have symptom of shortness of breath especially during physical activity, followed by 92 study participants were having wheezing, 88 were having chest tightness. 75 study participants were having chronic cough with expectoration, 65 complains of frequent respiratory infections and 71 were say that they feel lack of energy, while only 18 study subjects complain about swelling over ankle, feet or leg.

Research indicates that more than 60% of patients with COPD experience sleep symptoms and/or bothersome dyspnea/cough at night, although these complaints are often underreported by patients and are not part of routine clinical management[19]. The nature of these complaints is quite variable and can be nonspecific but includes symptoms like insomnia, nonrestorative sleep, daytime fatigue and nocturnal cough. In addition, other sleep disorders are common in COPD patients. For example, one-third of COPD patients are estimated to have restless leg syndrome, which can further negatively affect sleep quality[20]. Although patients with mild COPD have relatively preserved sleep quality, severe disease is associated with objectively measured worse sleep quality, including decreased total sleep time, decreased sleep efficiency and increased sleep fragmentation. Poor sleep quality in COPD predicts subjective health-related quality of life (HRQoL) and poor sleep has been associated with adverse outcomes including exacerbation and hospitalization[21]. Therefore, nocturnal and sleep symptoms should be part of the routine clinical evaluation for COPD patients and this often forgotten aspect of COPD care warrants further clinical investigation.

In the above study, while comparing the saturation at the time of admission between two groups and also the overnight average saturation between two groups, it was found that mean saturation was less in overlap syndrome as compared to COPD group. And the difference was found to be statistically significant. Apnea hypopnea index was more in overlap group as compared to COPD group and the difference was statistically significant while difference in FEV1 and FEV1/FVC parameters between two groups was not statistically significant. Out of total study subjects we found 29 study subjects were having overlap syndrome, above table shows the severity of obstruction between only COPD patients and among patients having overlap syndrome. It was found that study subjects having overlap have more severity of obstruction. Gothi *et al*.[12] in her study of Impact of overlap syndrome on severity of acute exacerbation of chronic obstructive pulmonary disease found that The mean forced expiratory volume in one second (FEV1)% predicted was 39.24±13.06% in only COPD and 39.62±10.04% in overlap. FEV1/forced vital capacity (FVC) in only COPD was 54.68±5.08% and in overlap was 56.32±9.24%. The difference between the two groups was statistically insignificant. The majority of the patients in both the groups were in stage III and IV.

Overall there was more number of patients in only COPD group. Hence, the number of patients with COPD stage I and II was higher in only COPD (21.1%) as compared to overlap (7.7%) but the difference was not found to be significant statistically (p = 0.473). Thus, there was no difference between the two groups in spirometry. Similarly, Steveling *et al.*[11] in their study on Predictors of the Overlap Syndrome and Its Association with Comorbidities in Patients with Chronic Obstructive Pulmonary Disease found that Sixty-one subjects (35%) had an AHI of >5 events per hour and 33 patients (19%) had an AHI of >10, 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.

In above study, out of 105 study subjects 76 were having only COPD and 29 were having overlap. Dipti Gothi *et al*.[12] in her study of Impact of overlap syndrome on severity of acute exacerbation of chronic obstructive pulmonary disease found that Out of a total of 51 patients, 38 (74.5%) did not have OSAS i.e., they had only COPD, while 13 (25.5%) had COPD with OSAS i.e., overlap syndrome. The majority of only COPD cases had mild and moderate exacerbations whereas majority of cases in overlap had severe, very severe and life threatening exacerbations. Statistically, the difference between two groups was significant (p = 0.021). Also, with the increasing severity of exacerbation, the mean apnea hypopnea index (AHI) increased.

In present study 46.06 of total 76 COPD patients have very severe obstruction and 48.27% of 29 total overlap patients have very sever obstruction. Obesity and chronic COPD seems to synergize with each other, with decreasing FEV1 associated with both conditions leading to worsening airflow obstruction and hypoxia. In overlap syndrome of COPD with OSA there is greater risk for respiratory failure and corpulmonale as compared to COPD only.

CONCLUSION

Sleep related symptoms were more prevalent in overlap group of patients as compared to patients without overlap and the difference is statistically significant between two groups for every symptom. About half of the study subjects were from overweight and obese BMI. The association between two groups and BMI was found to be statistically significant. Mean saturation was less in overlap syndrome as compared to COPD group. And the difference was found to be statistically significant. Apnea hypopnea index was more in overlap group as compared to COPD group and the difference was statistically significant while difference in FEV1 and FEV1/FVC parameters between two groups was not statistically significant. The association between the two groups with stage of COPD were found to be significant. AHI in overlap syndrome is higher than COPD group and the difference was statistically significant. Also the positional difference (AHI SUP-NONSUP), AHI in REM and NREM sleep is greater in overlap group and the difference is statistically significant between two groups. Mean lowest oxygen saturation during night in COPD patients was greater than overlap patients and the difference was statistically significant.

Hence, it can be concluded from present study that, COPD patient's particularly overweight and obese individuals are at greater risk of having OSA. So it is worthwhile to do polysomnography in COPD patients for early detection of OSA and to prevent them from further complications of OSA like uncontrolled hypertension, cerebrovascular accidents and coronary artery diseases.

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