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Clinical and diagnostic profile of patients with COPD and evaluation by polysomnography for obstructive sleep apnea (overlap syndrome)

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Abstract

Background: COPD is among the most common lung diseases, becoming a major health issue worldwide. Sleep disorders are frequently present in COPD patients, particularly obstructive sleep apnoea syndrome (OSAS). Patients with OSAS have increased risk of mortality due to cardiovascular events. **Methodology:** The study was carried out in the Department of respiratory Medicine of a tertiary health care hospital. Duration of the study was from December 2017 to November 2019. 105 study subjects were included in the study. Careful history taking and detail clinical examination was done. Patients with COPD fulfilling inclusion criteria were included in the study, all the clinical data was collected and tabulated. All the patients were evaluated with spirometry and polysomnography for detection of obstructive sleep apnea. **Result:** Most of the study subjects i.e. 38.09% were from age group 51-60 followed by 28.58% in more than 61 years of age group. The prevalence of OSAS in COPD (i.e. overlap syndrome) amongst study group was 27.62%. 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. **Conclusion:** COPD patient's particularly overweight and obese individuals are at greater risk of having OSAS. Polysomnography in COPD patients can prove to be useful for early detection of OSAS and to prevent them from further complications.

Keywords: Spirometry, polysomnography, OSAS, COPD, sleep.

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Introduction

Chronic obstructive pulmonary disease (COPD) is characterised by a persistent and commonly progressive airflow limitation consequent to an abnormal inflammatory response of the airway and lung tissue due to noxious particles and gases.[1] COPD is ranked eighth among the conditions causing disability globally[2] and is the third leading cause of death

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among adults older than 40 years old. [3] A substantial number of patients suffering from COPD have major comorbidities, which is linked with increased mortality. [4] In this regard, sleep disorders are frequently present in COPD patients, particularly obstructive sleep apnea syndrome (OSAS). The coexistence of obstructive sleep apnea syndrome (OSAS) and chronic obstructive pulmonary disease (COPD) is termed as "overlap syndrome". Individually, both diseases are linked with a wide range of physiological disturbances, such as hypoxemia and inflammation.[5]

The coexistence of OSAS may 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. Patients with COPD often complain of poor quality of sleep with daytime fatigue. Sleep disorders are considered as the third most common factor affecting the quality of life in COPD patients, after dyspnea and tiredness. COPD patients have difficulty in initiating or maintaining sleep with frequent night time arousal. The coexistence of COPD and OSAS, the so-called overlap syndrome, leads to major social and healthcare-related consequences, mostly in the context of cardiovascular disease. [6]. 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 [9,10]. 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. [7] Patients with overlap syndrome have several mechanical disadvantages to breathing during sleep. Apart from upper and lower airway obstruction, a reduction in respiratory drive and functional residual capacity, [8] they also have respiratory muscles fatigue. 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 present study was planned to study clinical and diagnostic profile of patient with chronic Obstructive pulmonary disease and there evaluation with polysomnography for obstructive sleep apnea (overlap syndrome).

Materials And Methods

Study design- The present study was a hospital based longitudinal, prospective, descriptive cross-sectional study.

Study place- The study was carried out in tertiary health care hospital of a city in Maharashtra. The duration of the study was from December 2017 to November 2019.

Inclusion criteria- Suspected patients of chronic obstructive pulmonary disease coming for diagnosis & treatment in outpatient / Inpatient Pulmonary Medicine department, patients who were ready to give consent were included.

Exclusion criteria- Patients in acute exacerbation of COPD, with acute MI, and those who did not give consent for participation were excluded.

Sample size- According to the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2016 by India State-Level Disease Burden Initiative CRD Collaborators the prevalence of chronic obstructive pulmonary disease in India was 4.2% in 2016 [194]. Considering 95% confidence level and 5% allowable error, the sample size was calculated by following formula

$N = Z^2 \times p \times q / e^2$

In above equation, N = Sample sizeZ= 1.96
p = prevalence of COPDq = 100 – p,

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e = allowable error which was considered here as 5 %
$= (1.96)^2 \times 4.2 \times 95.8/ (5)^2$
= 61.82
10 % population added to 61.82 as non-response / incomplete answers.61.82 + 6.18 = 68
Sample size =68
Thus, 105 study subjects were included in the study.

Data analysis- The collected data was numerically coded and entered in Microsoft Excel 2007, and analysed by using SPSS (Statistical Package for Social Sciences) version 20.0 statistical software by maintaining anonymity and privacy of respondents. The analysed data was presented in the form of tables and text.

Ethical consideration- The study was approved by the Institutional Ethical Committee of a Government Medical College.

After careful history taking and detail clinical examination. patients with COPD fulfilling inclusion criteria were included in the study, all the clinical data collected and tabulated , 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 patient) for clinical presentation and severity of COPD and OSA , spirometry parameters and polysomnography parameters . After explaining the purpose of study, informed consent was taken from the patients. 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. Thorough clinical examination of each subject was carried out. The clinical examination included general physical examination and systemic examination.

Results

Table 1: Distribution of study subjects according to age

Age in Years	Total No.	(%)
13-40	16	15.24
41-50	19	18.09
51-60	40	38.09
≥61	30	28.58
Total	**105**	**100.00**

Table 1 shows age wise distribution of study subjects. The mean age of study subjects were 57 (±2.52 SD) years. Most of the study subjects i.e. 38.09% were from age group 51-60 followed by 28.58 % in more than 61 years of age group. Only 15.24% were in age group 13-40 years of age.

Table 2: 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

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

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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: Distribution of patients in two groups as COPD only & COPD with OSA (Overlap)

Sr. No.	Final diagnosis	No.	Percentage
1	COPD with OSA (overlap syndrome) i.e. AHI > 5	29	27.62
2	COPD without OSA i.e. AHI < 5	76	72.38
Total		105	100

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

Table 4: Prevalence of sleep related symptoms in study subjects.

Sleep related symptoms	Only COPD (n=76)		Overlap (n=29)		P value	Statistical significance
	N	%	N	%		
Disruptive Snoring	53	69.73	27	93.10	0.01195	Significant
Excessive day time somnolence	42	55.26	22	5.86	0.02653	Significant
Sleep Fragmentation	50	65.78	25	86.20	0.01920	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
Un-refreshing sleep	25	32.89	20	68.96	0.0008395	Significant
Personality changes	14	18.42	10	34.48	0.03985	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

Above tables shows the sleep related symptoms in study subjects. 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 5: Distribution of study subjects according to their Body Mass Index

Body Mass Index	Only COPD (n=76)	Overlap (n=29)
Mean BMI $\pm$ SD	20.68 $\pm$ 9.98	31.74 $\pm$ 5.42
Mean waist circumference $\pm$ SD	58.12 $\pm$ 19.98	96.58 $\pm$ 17.85

Above table shows the distribution of study subjects according to BMI among two groups, it

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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 6: 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%)

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

Parameter	Only COPD	Overlap	P value
	Mean ± SD	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

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 8: 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; P value= 0.04814

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Above table 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- Value <0.05)

Table 9. 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	32.4 ± 16.3	<0.05
AHI_{REM}	4.5 ± 2.5	30.2 ± 15.9	<0.05
$AHI_{SUP-NONSUP}$	4.3 ± 1.9	28.4 ± 11.2	< 0.05
LNS_{MEAN}	92.83 + 3.68	81.78 + 7.25	<0.001

Calculated using students't' test

Above table shows the polysomnographic profile of study subjects, 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.

Discussion

In present study Most of the study subjects i.e. 38.09% were from age group 51-60 followed by 28.58 % in more than 61 years of age group. Similarly **Stepnowsky CJ, Ancoli- Israel S.**[9] In their study of Sleep and its disorders in seniors and **Anto JM, Vermeire P, Vestbo J, Sunyer J.**[10] In their study of epidemiology of chronic obstructive pulmonary disease found that OSAS and COPD are more common in the elderly and **Chaouat and coauthors** [11] reported that overlap patients in their sleep clinic cohort were older than patients with OSAS alone. In present study 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.

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.[12] The nature of these complaints is quite variable and can be nonspecific but includes symptoms like insomnia, non-restorative sleep, daytime fatigue, and nocturnal cough. In addition, other sleep disorders are common in COPD patients. 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.[13] 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.

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In this 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.

Similarly, **Daniel Álvarez et al**[14] al in their study of Influence of Chronic Obstructive Pulmonary Disease and Moderate-To-Severe Sleep Apnoea in Overnight Cardiac Autonomic Modulation: Time, Frequency and Non-Linear Analyses found that COPD + OSAS patients showed significantly lower minimum saturation than patients with COPD or OSAS alone, which agrees with the deeper desaturations typical of overlap patients during the night. On the other hand, patients in the OSAS group had significantly higher baseline saturation than patients with COPD or overlap syndrome. Similarly, patients with OSAS alone had lower minimum saturation than COPD patients. Finally, patients with COPD + OSAS showed significantly lower overnight average saturation than patients with COPD or OSAS alone. Regarding the pulmonary function, no significant differences between COPD patients with and without OSAS were found in terms of forced expiratory volume in 1 s (FEV1) improvement, forced vital capacity (FVC) improvement, and the ratio FEV1/FVC after post bronchodilator spirometry. In the COPD group, five patients (22.7%) showed an AHI < 5 events/h and 17 patients (77.3%) showed 5 $\leq$ AHI < 15 events/h from PSG, which excluded moderate-to-severe OSAS. A total of five patients (22.7%) reported witnessed apneas and 13 (59.1%) loud snoring. The average Epworth score was 10.4 points. In the moderate-to-severe OSAS group, 50 patients (23.5%) had 15 < AHI < 30 events/h and 163 (76.5%) AHI > 30 events/h. Within this group, 150 patients (70.4%) reported witnessed apneas and 208 (97.7%) loud snoring while sleeping. The average Epworth score was 10.8 points. Finally, 16 patients (25.8%) had 15 < AHI < 30 events/h and 46 (74.2%) AHI > 30 events/h in the overlap group.

In present study out of 105 study subjects 76 were having only COPD and 29 were having overlap. In the **Wisconsin Sleep Cohort Study** [15] of 602 middle-aged working adults (36), 4% of males and 2% of females had an apnea–hypopnea frequency (AHI) of at least 5/hour together with daytime sleepiness, which are the minimal criteria for the clinical syndrome (37). However, an AHI of at least 5/hour alone without daytime symptoms occurred in 24% of males and 9% of females. The widely accepted definition of OSAS by an international task force (37) requires obstructed breathing events and compatible daytime symptoms for diagnosis. Thus, the lower prevalence in the Wisconsin Sleep Cohort Study refers to OSAS. However, pathophysiological interactions between COPD and OSAS relate more to sleep-disordered breathing than daytime symptoms; thus, the higher prevalence figures previously cited for OAH alone may be more relevant in this context. Thus, a prevalence for subclinical forms of the overlap of 4% in males could be speculated from a simple calculation based on the prevalence of 16.8% for GOLD stage I in the NHANES Study and 24% among males for an AHI of at least 5/hour in the Wisconsin Sleep Cohort Study. Although the clinical relevance of an isolated AHI of at least 5/hour is uncertain, this finding has been independently associated with hypertension in the Wisconsin Sleep Cohort Study.[15]

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

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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

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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