ORIGINAL ARTICLE

A Study to Evaluate Sleep-disordered Breathing in Patients with Chronic Respiratory Failure

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Abstract

Introduction: Sleep-disordered breathing (SDB) in patients with chronic respiratory failure (CRF) due to pulmonary disease remains an underrated and undiagnosed entity.

Materials and methods: A prospective descriptive study in patients with CRF with history suggestive of SDB was carried out using polysomnography (PSG) over a period of 12 months.

Results: Thirty patients with the Epworth sleepiness scale greater than 11 and CRF underwent PSG. Ninety percent patients had obstructive sleep apnea (OSA) syndrome using the respiratory disturbance index (RDI) of 5 as cut-off. Mean RDI was 13.4 and mean apnea-hypopnea Index (AHI) was 10.5. Besides, the patients had a poor sleep quality; sleep efficiency was 69.38 ± 14.44%, sleep onset time was 30.35 ± 24.31 minutes. Wake after sleep onset (WASO) was 107.25 ± 57.71 minutes. Rapid-eye-movement (REM) sleep latency was 126.08 ± 66.61 minutes. N1 was 23.75 ± 14.89, N2 was 45.22 ± 12.69, N3 was 20.02 ± 12.57, and REM sleep period was 11.33 ± 8 minutes. The body mass index (BMI) and Epworth sleepiness score (ESS) had a significant correlation with AHI with p value < 0.005.

Conclusion: Sleep-disordered breathing is an important comorbidity in patients with CRF leading to increased morbidity and mortality. A high of suspicion must be kept for the same especially in patients with higher BMI and high ESS. Such patients have a poor quality of sleep besides increased incidence of sleep apnea.

Keywords: Chronic respiratory failure, Comorbidity, Sleep-disordered breathing, Undiagnosed.

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Introduction

Sleep-disordered breathing (SDB) refers to a wide variety of breathing anomalies ranging from habitual snoring to upper airway resistance syndrome (UARS) to obstructive sleep apnea (OSA), central sleep apnea, and obesity hypoventilation syndrome (OHS), OSA being the most common subtype.

In the general population, prevalence of OSA estimates range from 5–22%. However, OSA has been reported with increased prevalence in patients with chronic respiratory failure (CRF) patients to as high as 80–90% in patients with diffuse parenchymal lung disease (DPLD) and 20–40% in chronic obstructive pulmonary disease (COPD) patients.[1] The major complications of OSA include hypertension, diabetes mellitus, pulmonary arterial hypertension, coronary artery disease, cerebrovascular accident, and exacerbated gastro esophageal reflux disease (GERD). Early diagnosis and effective intervention of this comorbidity in these patients may lead to a significant decrease in mortality.[2]

Respiratory failure can occur because of failure of gas exchange in tiny air sacs in the lungs, failure of the higher centers that control breathing, or failure of the respiratory muscles. Common causes include chronic obstructive lung disease, diffuse parenchymal lung disease, muscle disease, nerve disease, extreme obesity, and heart failure.

Restrictive pulmonary diseases have decreased lung volume, which can reduce upper airway stability—which in turn leads to upper airway collapse especially during rapid-eye-movement (REM) sleep when functional residual capacity (FRC) is further reduced due to intercostal muscle inactivity resulting in OSA. Similarly, obstructive airway disease patients are prone to develop SDB because of excessive negative intrathoracic pressures causing upper airway collapse, skeletal-muscle myopathy including steroid-induced local pharyngeal muscle myopathy, and involvement of the upper-airway dilator muscles or reflexes.[3]

Chronic respiratory failure patients with OSA are associated with more pronounced hypoxemia and hypercapnia and increased morbidity.[4] The coexistence of the two leads to increased cardiac dysrhythmias, severe pulmonary hypertension, and right heart failure.[5,6] These patients with history suggestive of OSA, such as snoring, choking or witnessed apneas, should be further evaluated by polysomnography (PSG).[7]

Continuous positive airway pressure (CPAP) therapy is the first-line treatment of OSA; it reduces work of breathing and provides rest to the respiratory muscles, which decreases hypoventilation and improves daytime oxygen in patients with CRF. Studies have shown CPAP also improves spirometry parameters, gas exchange parameters, and also reduces the number of hospital admissions and severe exacerbations besides correcting for the OSA.[8–10]

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Materials and Methods

It was a prospective descriptive study of SDB in patients with CRF conducted in Department of Pulmonary, Critical Care, and Sleep Medicine at a tertiary care center of North India. All the patients with CRF with history suggestive of SDB were included in the study over a 12 month study period. Patients with neurological diseases, severe psychiatric disease, taking drugs that affect sleep architecture, and age greater than 18 were excluded from the study. Institutional Ethical Committee (IEC) clearance was taken. An informed valid consent from the patient was taken.

All patients presenting to the respiratory department with CRF in a stable state underwent a postbronchodilator spirometry (Medisoft Spiroair system) to confirm the diagnosis and were classified obstructive or restrictive disease. Each participant attempted up to six forced prebronchodilator maneuvers while sitting and wearing a nose clip. Each maneuver was carefully observed for maximal effort, with exhalation time 6 seconds or more. For analyzes, we chose participants with at least two forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC) measurements within 200 mL variability. The severity of lung function impairment was stratified based on the postbronchodilator FEV1 and FVC as mild, moderate, and severe.

History regarding excessive daytime sleepiness, snoring, early morning headache, lethargy, and fatigue was taken and Epworth sleepiness score (ESS) was calculated. Patients with scores ≥11 with sleepiness during work or driving were suspected to be having OSA. Arterial blood gas (ABG) analysis was done to differentiate between hypoxic and hypercapnic respiratory failure patients. Arterial blood was obtained by percutaneous needle puncture. The arterial blood sample was placed on ice during transport to the lab and then analyzed as quickly as possible. The analysis of arterial blood was performed by an automated blood gas analyzer to measure pH, partial pressure of carbon dioxide ($PaCO_2$), and partial pressure of oxygen (PaO_2).

The following information was collected from all study subjects: age, sex, occupation, past history of diabetes, hypertension, hyperlipidemia, hypothyroidism, exposure to biomass, and smoking. The body mass index (BMI) (weight in kilograms by the square of height in meters) was calculated for all subjects.

Polysomnography was performed in the night using Alice 6 LDX (Philips Respironics, USA). In PSG, body functions including brain (EEG), eye movements (EOG), muscle activity or skeletal muscle activation (EMG), and heart rhythm (ECG) during sleep were recorded. Nasal flow during breathing, chest, and abdominal movements was recorded to identify central and OSA. The PSG findings were scored in 30 second windows following the recommended criteria of the American Academy of Sleep Medicine (AASM) 2007 guideline. The sleep efficiency, sleep onset time, REM latency, wake after sleep onset (WASO), percentage of time in different sleep stages, apnea index (AI), hypopnea index (HI), apnea-hypopnea index (AHI), respiratory event-related arousal (RERA), and respiratory disturbance index (RDI) were calculated.

Then, AASM scoring manual definitions were used for scoring. The episode of apnea/hypopneas recorded more than five times and lasting for ≥10 seconds was regarded as significant. This was the AHI. When RERA was calculated and added to apnea-hypopnea it was called as RDI. The AHI/RDI was used to grade the degree of severity of SDB. The AHI of 5–14 was regarded as mild, 15–30 regarded as moderate, and greater than 30 as severe obstructive sleep apnea hypopnea syndrome (OSAHS). The BMI and ESS were correlated to RDI calculated in the PSG.

Statistical Analysis

Categorical variables were presented in number and percentage (%), and continuous variables were presented as mean ± SD. Normality of data was tested by the Kolmogorov–Smirnov test. If the normality was rejected, then nonparametric test was utilized.

Quantitative variables were compared using the Mann–Whitney test/independent *t* test. Qualitative variables were correlated using the Chi-square test. The Spearman rank correlation coefficient was used to assess the association of various parameters with each other. A *p* value of less than 0.05 was considered statistically significant. The data were entered in a MS Excel spreadsheet and the analysis was carried out using the Statistical Package for Social Sciences (SPSS) version 21.0.

Results

Thirty patients who presented to the pulmonary and critical care department were included in the study on the basis of their satisfying criteria of CRF.

The underlying sociodemographic profile of the patients was suggestive of a predominant male and middle-aged population. The mean ± SD age of the study population was 54.1 ± 12.31 years. Maximum patients (57%) belonged to the age group 40–60 years. Among 30 patients, 14 (46%) patients belonged to the interstitial lung disease (ILD) group and 16 (54%) patients belonged to the COPD group. Majority of the patients were in the age group of 40–60 years for both for ILD (57%) and COPD (57%). In the COPD group, 11(67%) were males whereas in the ILD group 6 (43%) were males. About 40% patients had hypertension and dyslipidemia, diabetes was present in 30% patients, whereas hypothyroidism and coronary artery disease were present in 14% cases (Tables 1 and 2). All the patients in the COPD group were smokers.

Sleep efficiency was 69.38 ± 14.44%, sleep onset time was 30.35 ± 24.31 minutes. Wake after sleep onset was 107.25 ± 57.71 minutes. The REM sleep latency was 126.08 ± 66. 61 minutes. N1 was 23.75 ± 14.89, N2 was 45.22 ± 12.69, N3 was 20.02 ± 12.57, and the REM sleep period was 11.33 ± 8 minutes (Table 3).

Events were predominantly hypopneas, HI was 7.25 (5.1–17.7). The CA index was 0 (0–0.2), the OA index was 0.35 (0–4.4), and the RERA index was 1.55 (0.5–4), amounting to a total AHI of 10.5 (5.7–25.5) and RDI 13.4 (9.4–26) (Tables 3 and 4).

Mean ± SD of BMI was 25.21 ± 2.28 for COPD patients and 22.82 ± 2.65 for ILD patients, *p* value 0.013. Mean ± SD of FEV1 was 55.62 ± 8.55 for COPD patients and 77.79 ± 5.91 for ILD patients, *p* value < 0.001. Mean ± SD of FVC was 71.69 ± 6.28 for COPD patients and 55.5 ± 8.57 for ILD patients, *p* value < 0.001. Patients in the COPD group were in type-2 respiratory failure, so PCO_2 mean ± SD 52.75 ± 1.84 and that for ILD was 35.71 ± 2.76. The BMI and ESS had a significant correlation with AHI with *p* value < 0.005 (Table 5).

Discussion

Among the 30 patients of CRF included in this study, 25 (83%) patients had SDB (5 normal, 15 mild, 4 moderate, 6 severe) when AHI was used for severity classification. This figure changes to 27 (90%) having SDB (3 normal, 7 mild, 13 moderate, 10 severe) when RDI was used for severity classification. Thus, 90% of the patients in the study with CRF with high ESS score/symptoms suggestive of SDB actually had OSA confirmed in PSG.

Table 1: Sociodemographic and baseline characteristics of study population

Sociodemographic characters	*Frequency*	*Percentage*
Age		
30–39	4	13.33
40–49	8	26.67
50–59	9	30.00
60–69	4	13.33
70–79	5	16.67
Sex		
Male	17	56.67
Female	13	43.33
Comorbidities		
Diabetes	9	30.00
Hypertension	12	40.00
Hypothyroid	4	13.33
CAD	4	13.33
Dyslipidemia	12	40.00
Interstitial lung disease		
Mild	5	35.71
Moderate	7	50.00
Severe	2	14.29
COPD		
Mild	6	37.5
Moderate	6	37.5
Severe	4	25

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease

Table 2: Baseline functional status of patients

Variable (mean ± SD)	*COPD*	*ILD*
BMI	25.21 ± 2.28	22.82 ± 2.65
PH	7.39 ± 0.01	7.44 ± 0.02
PCO_2	52.75 ± 1.84	35.71 ± 2.76
PO_2	57.06 ± 1.39	56.57 ± 1.09
HCO_3	28.25 ± 1.18	22.36 ± 1.22
FEV1/FVC	63.12 ± 4.67	84.14 ± 2.93
FEV1	55.62 ± 8.55	77.79 ± 5.91
FVC	71.69 ± 6.28	55.5 ± 8.57

PCO_2, partial pressure of carbon dioxide; PO_2, partial pressure of oxygen; HCO_3, serum bicarbonate; BMI, body mass index; FEV1, forced expiratory volume; FVC, forced vital capacity; ILD, interstitial lung disease; COPD, chronic obstructive pulmonary disease

Table 3: Sleep architecture and respiratory events of patients

	PSG	*Accepted normal value*
Sleep parameters (mean and SD)		
Sleep efficiency (%)	69.38 ± 14.44	>80%
Sleep onset (minutes)	30.35 ± 24.31	<30
REM Latency (minutes)	126.08 ± 66.61	60–120
WASO	107.25 ± 57.71	
MIN SPO_2	73.87 ± 7.47	
N1	23.75 ± 14.89	5–10
N2	45.22 ± 12.69	50
N3	20.02 ± 12.57	20
REM	11.33 ± 8.26	20–25
Respiratory events (median and IQR)		
CA index	0 (0–0.2)	<5
OA index	0.35 (0–4.4)	
A index	0.5 (0–6.3)	
H index	7.25 (5.1–17.7)	
AH index	10.5 (5.7–25.5)	<5
RERA index	1.55 (0.5–4)	
RD index	13.4 (9.4–26)	<5

WASO, wake after sleep onset; CA, central apnea; OA, obstructive apnea; A, apnea; H, hypopnea; AHI, apnea hypopnea index; RERA, respiratory effort-related arousal; RD, respiratory disturbance; RDI, respiratory disturbance index; REM, rapid eye movement; PSG, polysomnography

Table 4: AHI and RDI severity of patients

Severity	*On basis of AHI (no. and %)*	*On basis of RDI (no. and %)*
Normal	5 (16.67)	3 (10.00)
Mild	15 (50.00)	14 (46.67)
Moderate	4 (13.33)	7 (23.33)
Severe	6 (20.00)	6 (20)

AHI, apnea hypopnea index; RDI, respiratory disturbance index

Table 5: Correlation of ESS and BMI with disease severity

		Severity RDI
BMI	Correlation coefficient	0.644
	p value	0.0001
	n	30
ESS	Correlation coefficient	0.834
	p value	<0.001
	n	30

BMI, body mass index; ESS, Epworth sleepiness score; RDI, respiratory disturbance index

It was observed that patients with higher BMI had higher AHI, correlation coefficient 0.644, with *p* value of 0.0001. Fat accumulation in the tissues surrounding the upper airway can result in a compromised lumen and collapsibility of the upper airway, leading to apnea. Studies have shown that patients with mild OSA who gain 10% of their baseline weight are at a six times higher risk of progression of OSA, and a similar weight loss can result in over 20% improvement in severity of OSA.[11]

Patients with higher ESS had a higher AHI, correlation coefficient was 0.834 with a *p* value of <0.001. Besides, all the patients had decreased sleep efficiency, increased sleep onset time, worsened REM latency time, increased WASO time, and decreased REM sleep time. Combined hypoxia and hypercapnia have a multiplicative effect at the carotid body, resulting in a potent stimulus for arousal.[12] Frequent arousals prevent the patients from entering into REM sleep and increase WASO, thus resulting in a nonrefreshing, nonrestorative sleep that has multiple impact on the health status of an individual. This finding illustrates that a simple questionnaire like ESS can easily be employed for clinically screening CRF for underlying OSA. The patients with higher ESS can be further subject

to PSG to confirm OSA, and titrated accordingly. As CPAP can provide effective symptom control in OSA, it is prudent to search for this correctable comorbidity in all CRF patients.

Most COPD patients had significant daytime hypoxemia with hypercapnia. This can be explained by the fact that nocturnal hypoventilation leads to daytime sleepiness, which leads to increased sleep and further hypoventilation in daytime, which triggers a vicious cycle. A recurring increase in $PaCO_2$ during sleep can possibly lead to bicarbonate retention and blunting of the ventilatory drive, which in turn worsens diurnal hypercapnia. Obesity causes increased upper airway resistance and overloading of respiratory muscles, and is associated with blunted chemosensitivity.[13] Thus, by correcting nocturnal hypoventilation, we can break this cycle and prevent daytime hypercapnia and its effects. It is one of the reasons why PAP therapy is indicated in COPD patients who have documented nocturnal hypoventilation even without OSA. Sleep-related hypoventilation results from a worsened increase in $PaCO_2$ in sleep owing to mechanisms detailed above, including decreased ventilatory drive, increased upper airway resistance, and mechanical compromise imposed by hyperinflation.

The strengths of this study include calculation of AHI, AI, and RDI. It has been postulated that a patient with severe COPD may have the same AHI labeled as severe OSA (based on a large number of hypopneas) as another patient with a highly collapsible upper airway without lung disease (who has apneas). In addition, a 10 minute-long desaturation due to hypoventilation may be scored as a single event since event duration has no effect on the criteria used. The apnea index, or scoring based on cessation of airflow alone, might be useful in establishing a confident diagnosis.[14] Most of the patients in our study had predominantly hypopneas and RERA, which may be amenable to oxygen therapy as oxygen may shift the oxygen dissociation curve to the less steep portion, thereby preventing such desaturations. This brings out the limitation of our study. Transcutaneous CO_2 monitoring was not done in the PSG, which is the standard to diagnose hypoventilation, as these hypopneas may be simply prolonged hypoventilation. The sample size was small to make any direct conclusions. An echocardiography to screen for pulmonary hypertension was not done in all the patients.

Untreated OSA can lead to increased metabolic complications (hypertension, dyslipidemia), cardiovascular complications (angina, arrhythmia), motor vehicle accidents, neurodegeneration, decreased libido, psychiatric diseases (depression, anxiety), stroke, and pulmonary hypertension.[15] Most of these can be prevented and halted by appropriate PAP therapy.

Conclusion

Sleep-disordered breathing is an important comorbidity in patients with CRF leading to increased morbidity and mortality. A high of suspicion must be kept for the same especially in patients with higher BMI and high ESS. Such patients have a poor quality of sleep besides increased incidence of sleep apnea. In view of having treatment modalities like PAP for OSA, one must actively search for this hidden yet correctable comorbidity in all patients with CRF.

References

1. Romem A, Iacono A, McIlmoyle E, et al. Obstructive sleep apnea in patients with end-stage lung disease. J Clin Sleep Med 2013;9(7):687–693. DOI: 10.5664/jcsm.2840.
2. Lancaster LH, Mason WR, Parnell JA, et al. Obstructive sleep apnea is common in idiopathic pulmonary fibrosis. Chest 2009;136(3):772–778. DOI: 10.1378/chest.08-2776.
3. Mermigkis C, Bouloukaki I, Schiza SE. Obstructive sleep apnea in patients with interstitial lung diseases: past and future. Sleep Breath 2013;17(4):1127–1128. DOI: 10.1007/s11325-013-0836-1.
4. Shteinberg M, Weiler-Ravel D, Adir Y. The overlap syndrome: obstructive sleep apnea and chronic obstructive pulmonary disease. Harefuah 2009;148(5):333–336. , 348.
5. Shepard JW, Garrison MW, Grither DA, et al. Relationship of ventricular ectopy to nocturnal oxygen desaturation in patients with chronic obstructive pulmonary disease. Am J Med 1985;78(1):28–34. DOI: 10.1016/0002-9343(85)90457-7.
6. Chaouat A, Weitzenblum E, Krieger J, et al. Association of chronic obstructive pulmonary disease and sleep apnea syndrome. Am J Respir Crit Care Med 1995;151(1):82–86. DOI: 10.1164/ajrccm.151.1.7812577.
7. Chaouat A, Weitzenblum E, Krieger J, et al. Pulmonary hemodynamics in the obstructive sleep apnea syndrome. Results in 220 consecutive patients. Chest 1996;109(2):380–386. DOI: 10.1378/chest.109.2.380.
8. Mansfield D, Naughton MT. Effects of continuous positive airway pressure on lung function in patients with chronic obstructive pulmonary disease and sleep disordered breathing. Respirology 1999;4(4):365–370. DOI: 10.1046/j.1440-1843.1999.00206.x.
9. de Miguel J, Cabello J, Sánchez-Alarcos JM, et al. Long-term effects of treatment with nasal continuous positive airway pressure on lung function in patients with overlap syndrome. Sleep Breath 2002;6(1):3–10. DOI: 10.1007/s11325-002-0003-6.
10. Peker Y, Hedner J, Johansson A, et al. Reduced hospitalization with cardiovascular and pulmonary disease in obstructive sleep apnea patients on nasal CPAP treatment. Sleep 1997;20(8):645–653. DOI: 10.1093/sleep/20.8.645.
11. Peppard PE, Young T, Barnet JH, et al. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013;177(9):1006–1014. DOI: 10.1093/aje/kws342.
12. Hornbein TF, Griffo ZJ, Roos A. Quantitation of chemoreceptor activity: interrelation of hypoxia and hypercapnia. JNeurophysiol 1961;24:561–568. DOI: 10.1152/jn.1961.24.6.561.
13. Agusti A, Hedner J, Marin JM, et al. Night-time symptoms: a forgotten dimension of COPD. Eur Respir Rev 2011;20(121):183–194. DOI: 10.1183/09059180.00004311.
14. Chakrabarti S, Ish P, Rathi V. Obstructive sleep apnea and chronic obstructive pulmonary disease overlap syndrome - double trouble. J Adv Res Med 2018;5(4):25–30. DOI: 10.24321/2349.7181.201821.
15. André S, Andreozzi F, Van Overstraeten C, et al. Cardiometabolic comorbidities in obstructive sleep apnea patients are related to disease severity, nocturnal hypoxemia, and decreased sleep quality. Respir Res 2020;21(1):35. DOI: 10.1186/s12931-020-1284-7.