Original Article

Prevalence of Obstructive Sleep Apnoea in Patients with Interstitial Lung Disease

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Abstract

Background. Interstitial lung disease (ILD) is a chronic respiratory illness with multiple co-morbidities including obstructive sleep apnoea (OSA). There are limited data available about the prevalence of OSA in ILD. The present study was designed to document the burden of OSA in patients with ILD.

Methods. In this cross-sectional, observational study, 27 stable ILD patients were enrolled over a period of one year. After baseline evaluation including spirometry and six-minute walk test, all the patients were subjected to overnight complete polysomnography. Patients diagnosed to have OSA were further classified into three severity grades of OSA.

Results. Twenty (74%) of the 27 patients studied had OSA with majority having mild (n=9) and moderate (n=9) severity. ILD patients with OSA were significantly older compared to those without OSA (P=0.031). There was no significant difference in the rest of the parameters in the group.

Conclusion. Obstructive sleep apnoea is an under recognised but a common entity associated with ILD. **[Indian J Chest Dis Allied Sci 2021;63:17-21]**

Key words: Obstructive sleep apnoea, Interstitial lung disease, Prevalence.

Introduction

Interstitial lung diseases (ILDs) are a group of heterogeneous disorders characterised by varying degrees of fibrosis and inflammation of lung parenchyma. Overall incidence and prevalence (per 100,000 population/year) of ILD has been observed to be 31.5, 80.9 in males and 26.1 and 67.2 in females, respectively[1]. ILDs are also common in India with regional variation.[2,3] Due to chronic nature of ILD, these patients often have associated co-morbidities that add to the symptom burden and affect the quality-of-life (QoL) of these patients. These include gastro-oesophageal reflux, pulmonary hypertension, *cor-pulmonale* and depression.[4] Recent evidence has shown that obstructive sleep apnoea (OSA) has also been associated with ILD.[4]

Obstructive sleep apnoea is a type of sleep disordered breathing characterised by repeated episodes of apnoea and hypopnoea during sleep due to narrowing or occlusion of the upper airway. A study conducted in Istanbul university showed a high prevalence of 68% OSA in ILD patients.[5] Other studies[6–8] conducted in the western world have also found the prevalence of OSA to be around 80% among patients with idiopathic pulmonary fibrosis (IPF).[6–8]

Obstructive sleep apnoea has been shown to affect the sleep structure, reduction in QoL and increased risk of mortality in patients with ILD. OSA is a treatable co-morbidity in ILD and its timely detection and treatment will likely improve the symptoms as well as the QoL of ILD patients. However, there is are lack of data on the prevalence of this association, particularly from India. Hence, the present study was conducted to find the burden of OSA in stable patients with stable ILD.

Material and Methods

This is a cross-sectional study done in the Department of Pulmonary Medicine, Government Medical College and Hospital (GMCH), Chandigarh over a period of two years duration from October 2016 to October 2018. Patients with stable ILD due to any underlying cause, diagnosed as per standard guidelines,[9-11] were enrolled. Patients with neurological disease, psychiatric disease, lower respiratory tract airway infection, acute exacerbation of IPF in the preceding one month, total sleep time less than 4 hours on polysomnography (PSG), associated chronic pulmonary disease, like

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asthma, chronic obstructive airway disease, lung cancer, anatomic upper airway obstructions, such as deviated nasal septum, nasal polyps, concha hypertrophy or tonsillar hypertrophy, thyroid disorder were excluded from the study. Informed consent was obtained from all the patients. The study was approved by the Institutional Ethics Committee of GMCH.

All stable ILD patients reporting to Pulmonary Medicine Out-patient clinic in the first year of the study were enrolled. Each patient was subjected to detailed history and physical examination. Blood investigations including haemoglobin and arterial blood gas analysis were done. Routine spirometry was performed as per standard American Thoracic Society guidelines[12] using a spirometer (*Spiro Analyzer*, RMS HELIOS-40). Six-minute walk test (6MWT) was performed[13] to assess the exercise capacity. The test measures the distance what a patient can walk in six minutes duration at their own pace on a flat hard surface. After explaining the procedure, each patient was subjected to the test. The test was performed on a hospital hall-way measuring 100 feet in length.

All the patients underwent overnight complete polysomnography using Somnoscreen TN plus, SomnomedicGmbh, Germany performed at sleep laboratory in the Department of Pulmonary Medicine. Various parameters including electroencephalogram (EEG), electrooculogram (EOG), chin and leg electromyogram (EMG), electrocardiogram (ECG), body positioning, thoracic and abdominal inductive respiratory plethysmography, pulse oximetry, airflow monitoring and snoring recording were included. Sleep was scored in 30s epochs while analysis and interpretation were performed according to standard criteria.[14] Diagnosis of OSA was based on (AHI)>5 on PSG as per guidelines of the American Academy of Sleep Medicine.[15] Diagnosed OSA patients were categorised into mild (AHI ≥5 to ≤15), moderate (AHI ≥15 to ≤30) and severe (AHI ≥30).[15]

Statistical Analysis

The continuous variables were summarised as mean±standard deviation or median (range) as per their distribution. The categorical variables and the burden of OSA in ILD was summarised as percentages. The comparison of continuous and categorical variables between ILD patients with and without OSA was done using Mann-Whitney U test and Chi-square test, respectively. Correlation between body mass index (BMI) and AHI was done using Spearman correlation. Continuous variables among the severity of OSA was assessed with the Kruskal–Wallis test. A P-value <0.05 was taken as significant. All analysis was conducted using Statistical Package for the Social Sciences (SPSS) for windows (IBM SPSS Statistics 21.0; Armonk, NY, USA).

Results

Twenty-seven ILD patients were enrolled. Most of them (n=18) were females. IPF constituted the majority of the patients (n=10) followed by connective tissue disease (n=7) (Table 1). Out of 27 patients, 20 (74 %) were diagnosed to have OSA by overnight PSG. Majority had mild (33%, n=9) to moderate (33%, n=9) severity of OSA.

On comparing, ILD patients with OSA were significantly older as compared to those without OSA (P=0.031). There was no significant difference in the rest of the parameters in the group (Table 2). No difference in BMI, baseline forced vital capacity (FVC) and partial pressure of oxygen (PaO_2) was seen in between the patients of ILD with or without OSA. However, BMI showed a positive correlation with AHI in the study group (r=0.567; P=0.002) (Figure).

On comparing parameters, among the different grades of OSA, statistically significant difference seen in gender (P=0.03) and PaO_2 (P=0.01).

Table 1. Baseline characteristics of the study population

Variable	Value
Age (years)*	58.9±10.3
Gender (No.)	
Male	8
Female	19
BMI (kg/m^2)*	23.9±5.07
Obese patients [No. (%)]	10 (37)
Subtypes of ILD [No. (%)]	
IPF	10 (37)
CTD-ILD	7 (26)
HSP	4
NSIP	3
Sarcoidosis	2
Occupational	1
Breathlessness [No. (%)]	26 (96.3)
Cough [No. (%)]	19 (70.4)
Haemoglobin (g/dL)*	12.6±3.16
PaO_2 (mmHg)*	67±13.9
FVC (%)*	69.6±27.7
6-minute walk distance (metres)*	304.2±101.4

* Data are presented as mean ±standard deviation

Definition of abbreviations: BMI=Body mass index, ILD=Interstitial lung disease, IPF=Idiopathic pulmonary fibrosis, CTD-ILD=Connective tissue disease associated interstitial lung disease, HSP=Hypersensitivity pneumonitis, NSIP=Non-specific interstitial pneumonia, FVC=Forced vital capacity.

Table 2. Comparison of various parameters in ILD patients with and without OSA

Parameters	ILD with OSA (n=20)	ILD without OSA (n=7)	P-value
Age (years)*	61.5±9.9	51.7±8.4	0.031
Gender (No.) Female	13	6	0.63
Male	7	1	
BMI (kg/m^2)*	24.5±5.3	22.2±4.05	0.28
Haemoglobin (g/dL)*	12.9±1.5	11.7±2.8	0.31
FEV_1*	75.3±23.8	80.3±45.4	0.71
FVC*	67.6±18.3	73.2±40.8	0.83
FEV_1/FVC*	88.3±6.5	85.1±16.7	0.96
PaO_2 (mmHg)*	69.8±12.1	60.7±17.3	0.16
6-min walk distance (metres)*	287.6±108.9	339.5±78.4	0.33

* Data are presented as mean± standard deviation

Definition of abbreviations: BMI=Body mass index, FEV_1=Forced expiratory volume in one second, FVC=Forced vital capacity, PaO_2=Partial pressure of oxygen.

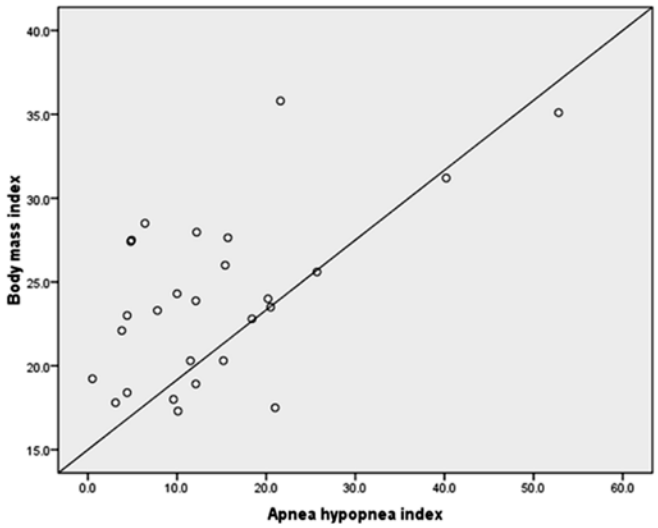

Figure. Correlation between BMI and AHI.

Definition of abbreviations: BMI=Body mass index, AHI=Apnoea-hypopnea index.

Discussion

Our study revealed a high prevalence of OSA in individuals with ILD (74%). Initially a higher association of OSA with IPF was observed. In our study, IPF was the most common subtype with a prevalence of 37%. In a study[7] on patients with IPF (n=50) for the presence of OSA, similar to our observations, the authors[7] found 88% (n=44) prevalence of apnoea-hypopnoea episodes. Out of 44 patients, 34 had moderate to severe OSA. In our study also 80% (n=8) of patients with IPF had AHI ≥5. But none of them had AHI more than 30 (severe OSA). IPF is one of the ILD that has a rapid clinical course with severe parenchymal destruction. In patients of severe lung parenchymal involvement, like IPF, the chances of airway collapsibility also increase, that may predispose to the development of OSA.

Few hypotheses have been proposed in previous studies,[16,17] explaining the development of OSA in ILD. The first one was the increased upper airway collapsibility. In ILD patients, the low lung volume reduces the caudal traction force on trachea resulting in increased pharyngeal collapsibility. This mechanism can be augmented during rapid eye movement (REM) sleep because of the reduced activity of the intercostal muscles resulting in reduced functional lung capacity.[16,17]

Another hypothesis for the development of OSA in ILD is the ventilatory control system instability that results in over-sensitive/over-responsiveness of the chemoreceptor circuits involving medulla leading to hypocapnia.[18] The low partial pressure of carbon dioxide ($PaCO_2$) level results in apnoea and this cycle repeats as the centre attempts for homeostasis. Intermittent hypoxaemia in ILD may be an explanation for over-stimulation of chemo responsiveness and ventilatory control instability.[19] Apart from the development of OSA in ILD patients, a recent study[20] has also proposed OSA to be a risk factor for ILD. Cyclic-hypoxia reoxygenation with intermittent breathing and cyclic alveolar deformation in OSA are the proposed mechanisms for the development of ILD.[21–23]

In the present study, patients with ILD-OSA were significantly older than the patients without OSA (P=0.031). But the age was not significantly different among the different grades of OSA (P=0.51). The higher age in OSA group could be due to increase prevalence of OSA in the elderly as also documented in a survey of sleep-disordered breathing in elderly population.[24] The reason for OSA in elderly may be due to increased anatomical upper airway collapsibility in these age group as compared to the younger population.

Various population and hospital-based studies[25,26] in India suggest that OSA in India has high male prevalence. But there are no Indian studies that link the gender association with OSA in ILD. The present study also did not have any association of OSA-ILD with any particular gender (P=0.63).

According to the Asian-Pacific cut-off of BMI[27], the present study had 37% (n=10) of obese patients with BMI of ≥25 km/m^2 and ≤30 km/m^2. It has been known that obesity reduces the lung volume in lying posture and predisposes to upper airway

collapsibility. With low lung volume already in ILD, obesity in these patients should logically increase the airway collapsibility and produce higher AHI. In a study[28] assessing the sleep structure, oxygenation and breathing pattern in ILD patients, it was observed that 64% of the study population had OSA. No significant difference was observed in BMI between patients with and without OSA. In the present study also, there was no statistically significance between patients with and without OSA groups (P=0.28), though the OSA group had a slightly higher BMI. On comparing the 3 grades of OSA, severe OSA patients had the maximum BMI even though the difference cannot be validated due to small number of patients in each group. However, there was a positive correlation between BMI and AHI (r=0.567) (P=0.002) supports the role of BMI in the causation of OSA.

Spirometry is an important lung function tool as it directly reflects the parenchymal involvement and reduced lung volume of the patient. So, as per the hypothesis, severe OSA with accompanying severe restriction (decreased FVC) will likely cause more apnoeic events. But in contrast, there was no significant difference in the flow rates among different severity grades of OSA (P=0.74). However, the results should be interpreted in lieu of low sample size in each group of OSA. Previous studies[5,7] have also shown similar results regarding lung functions and AHI. Possible explanation could be that sleep study and spirometry are done in different positions, hence may not have significant correlation. Spirometry in the supine position is difficult but may accurately correlate with sleep lung volumes.

Six-minute walk test is used to assess the functional capacity of the lung in chronic respiratory disease. In the present study, the ILD with OSA group has walked (287.6±108.9 metres) less than the ILD without OSA group (339.5±78.4 metres). But the difference was not statistically significant (P=0.33).

The strength of the present study was that we evaluated all major subtypes of ILD for the presence of OSA and found evidence for higher burden of OSA in ILD patients. Hence, it is suggested that all ILD patients should be screened for OSA and managed comprehensibly.

The main limitation of our study was a low sample size that might have affected the results. Most of the evidence on the association between ILD and OSA has been generated in low sample size studies done outside India. Clinical assessment for OSA and its association with AHI values was not done in the study as all consecutive patients of ILD were enrolled for PSG test. Correlation of AHI values with the symptom score might be useful to decide the ideal treatment protocol in such patients, especially those with high AHI but no OSA symptoms.

Conclusions

Obstructive sleep apnoea is a highly prevalent co-morbidity in interstitial lung disease patients that may contribute to morbidity and mortality. The results of the present study show that all patients with ILD should be screened for OSA at the time of initial evaluation. Management of OSA along with ILD treatment might help in better and comprehensive management of the illness. Future studies are required to evaluate the follow up and response to continuous positive airway pressure therapy among ILD patients with OSA, especially those who do not have overt symptoms OSA.

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