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PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN IDIOPATHIC PULMONARY FIBROSIS.

Pulmonary Medicine

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ABSTRACT

Patients with Idiopathic Pulmonary fibrosis exhibit abnormal sleep architecture and increased sleep fragmentation . Studies have shown that sleep disordered breathing is prevalent in patients suffering from IPF. Our study aims to find out the prevalence of sleep disordered breathing , especially obstructive sleep apnea in IPF patients.30 willing and stable IPF patients underwent overnight attended polysomnography. Their demographic and clinical data were collected.OSA was found in 56.6% of the cases. 6 patients (20%) had mild OSA (AHI- 5-15 events/hr),7 patients (23.3%) had moderate OSA (AHI- 15-30 events/hr) and 4 patients (13.3%) had severe OSA (AHI- > 30 events /hr).Patients with OSA had disturbed sleep with poorer sleep efficiency and more arousals.Hypopneas were more frequently found. Considering the high prevalence of OSA in IPF patients in our study, it is imperative that all patients with IPF, having symptoms of sleep disturbance should be screened and evaluated by polysomnography for OSA.

KEYWORDS

IPF (Idiopathic Pulmonary Fibrosis), OSA (Obstructive Sleep Apnea), AHI (Apnea-Hypopnea Index)

Introduction:

IPF is defined as a specific form of chronic, progressive fibrosing interstitial pneumonia of unknown cause, limited to the lungs, occurring primarily in older adults with presentation typically occurring in the sixth and seventh decades. A study from the United States estimated the incidence of IPF to be between 6.8 and 16.3 per 100,000 and in developing countries like India IPF constitutes about 13.7% of all Intestitial lung diseases. Sleep-related breathing disorders, particularly obstructive sleep apnoea syndrome (OSAS) are highly prevalent and represent an increasing part of clinical respiratory practice with a global prevalence of about 0.3 % to 5.1% in general population and 4.4% to 13.7% in Indian Population[1,2].The incidence of obstructive sleep apnea syndromes is on the rise as it occurs concomitantly with many systemic diseases, IPF being one such disease. The proposed theory of connection between IPF and OSA is based on traction of the trachea. Restrictive pulmonary diseases like IPF which exclusively affects the lung are characterized by decreased lung volumes that can reduce upper airway stability and increase resistance because of decreased traction on the upper airway. These changes facilitate upper airway collapse leading to apneas especially during REM sleep, when the reduced activity of the intercostal muscles[3-6] further reduces the functional residual capacity of the lung. This gives rise to significant oxyhemoglobin desaturations during sleep leading to sleep fragmentations and microarousals. Our study aims to find out the prevalence of OSA and characteristics of sleep abnormalities in patients suffering from IPF.

Material and methods:

The study was conducted over a period of one year from August 2016 to August 2017 in the Department of Pulmonary And Sleep Medicine , Kamla Nehru Chest Hospital, Dr S.N. Medical College, Jodhpur. This was a cross-sectional, prospective type of study with a sample size of 30 patients, who were diagnosed with Idiopathic Pulmonary Fibrosis based on the 2013 ATS/ERS/ALAT Classification of Idiopathic Interstitial pneumonia[7].Detailed clinical and demographic parameters were evaluated. Other chronic respiratory diseases, cardiac diseases and metabolic diseases like diabetes mellitus, hypothyroidism were ruled out. A thorough otorhinolaryngological evaluation was done to rule out anatomic defects and after taking proper written consent all patients were subjected to overnight level 1 Polysomnography. The result was analysed manually using standard American Academy of Sleep medicine criteria (Version 2.1)[8].The study was cleared by the Institute's ethics Committee.

Data was entered using Microsoft Excel 2007 and analyzed using Software SPSS 24th Version. Statistical analysis was done by using Chi square test, student t-test, Anova with p Value <0 .05 as significant.

Instrument: RMS Quest 32 Polysomnography machine

Results:

Out of the 30 patients,17 patients (56.67%) had Obstructive sleep Apnea (AHI > 5 events /hr) of which 6 patients (20%) had mild OSA,7 patients (23.3%) had moderate OSA and 4 patients (13.34%) had severe grade OSA(Fig.1). Males had higher prevalence of OSA (62 %) compared to females (52%). The mean AHI was 13.73.The demographic characteristics of the patients are depicted in Table 1.Most of the patients having OSA had a Mallampatti class > 2.Smoking did not contribute significantly to OSA in these patients. The BMI increased with an increase in AHI. The BMI only weakly correlated (BMI: r=0.26; p=0.1). Tiredness (46.6%) was the most common symptom among the patients followed by disturbed sleep and snoring. The mean minimum oxygen saturation was 77% and the mean baseline awake oxygen saturation was 94% at the start of PSG.

Patients having OSA had significantly reduced forced vital capacity (mean 62.35± 9.82){p<0.05} and decreased 6 min-walk distance (mean 254.47±56.33){p<0.05}compared to patients without OSA. Patients with OSA had increased wakefulness, increased stage 1 sleep (mean 7.85±2.19) and a decreased REM sleep (mean 17.18±3.9).Sleep efficiency was decreased and sleep onset and REM onset latency was increased with mean values of 28.22±4.66 and 112.08 ±12.76 minutes respectively (Table 2.). Hypopnea was a more common event.AHI was affected more in REM sleep compared to non-REM sleep with an increasing trend towards more severe grade of OSA. Events during REM sleep and non-REM sleep were more balanced in patients with moderate OSA. Total body movements{p < 0.001} and snoring events were higher in the group having OSA.

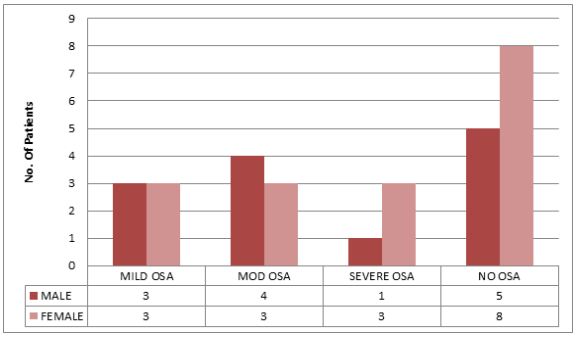

Fig 1. Prevalence of OSA

TABLE 1 – *Demographics : Personal Characteristics*

PARAMETERS		IPF WITHOUT OSA (*n=13*)	IPF WITH OSA (*n=17*)	*P* Value
AGE	<40 41-60 >60	3 7 3	4 8 5	*CHI-Square Test* 0.9
SEX	MALE FEMALE	5 8	8 9	*CHI-Square Test* 0.9
BMI	<18.5 18.5-24.9 25-29.9 ≥30	2 6 2 3	3 2 6 6	*CHI-Square Test* 0.1
NECK CIRCUMFERENCE		34 ± 9.72	38.9 ± 9.06	*t-Test* 0.008
TOTAL DURATION OF ILLNESS		20.23 ± 17.84	29.4 ± 14.54	*t-Test* 0.004

Values are given as the mean ± 2SD

TABLE 2. *Sleep Architecture*

SLEEP PARAMETERS	ILD WITHOUT OSA (n=13)	ILD WITH OSA (n=17)	P-Value
AWAKE	5.05 ± 3.78	8.47 ± 9.92	0.02
STAGE 1	5.30± 3.58	7.85 ± 4.38	0.002
STAGE 2	50.44± 7.36	47.05 ± 13.62	0.116
STAGE 3	18.75 ± 8.48	19.50 ± 12.28	0.70
NREM	74.58 ± 4.76	72.46 ± 32.1	0.64
REM	21.2 ± 6.18	17.18 ± 7.8	0.004
Sleep Efficiency	75.33 ± 19.3	66.34 ± 25.68	0.04
Sleep Onset Latency	18 ± 9.88	28.22 ± 9.32	<0.0001
REM Onset Latency	98.3 ± 28.36	112.08 ± 25.52	0.009
Snoring Events	0.462 ± 1.92	9.05 ± 17.04	0.0012
Mean Heart Rate	87.30 ± 15.74	87.11 ± 28.14	0.978
TBM/hr	3.92 ± 2.9	8.44 ± 7.1	0.0002

Values are given as the mean ± 2SD
Comparison among all groups in t-test

Discussion:

Our study found significant association of sleep disordered breathing in patients with IPF with more than half of our subjects having various grades of Obstructive sleep apnea. These patients presented with independent risk factors like daytime tiredness, disturbed sleep, snoring and observed apneas. Patients with high neck circumference stands greater chances of developing OSA. So, excessive steroid use in IPF can be detrimental. The body mass index weakly correlated with apneic events suggesting that OSA also develops in IPF patients with normal BMI. Krishnan V. in his study found that poor sleep quality was not associated with body mass index.

GERD was found in 53.33% of the study group and 64.7% of those patients having OSA complained of GERD. Some authors have hypothesized that microaspiration could be a cause of both IPF and acute exacerbation of IPF.

Prolonged periods of illness has been associated with increased chances of developing OSA. Increased resistive load during sleeping such as with reduced functional vital capacity in severe IPF can lead to alveolar injury causing further progression of fibrosis. This can reduce the exercise capacity of such patients as was evident from the 6-minute walk distance covered by patients having OSA.

OSA is characterized by intermittent hypoxia (IH) that results in overproduction of reactive oxygen species, reactive nitrogen species and oxidative stress. As our study showed that patients having OSA had a mean minimum saturation of 77% although the average oxygen saturation at the beginning of the test was 94%.Overproduction of free radicals can affect many cellular mechanisms by damaging lipids, proteins and DNA.[9,10]. Studies [56-59] have showed that hypoxia mediates epithelial proliferation and fibrosis in pulmonary fibrosis through hypoxia-inducible factor1a, deoxycytidine kinase expression thereby suggesting that OSA may have a role in pulmonary fibrosis pathogenesis or disease progression.

IPF causes disruption of sleep architecture. Decreased REM sleep, increased stage 1 sleep and increased wakefulness occurs leading to poor quality of sleep. Sleep efficiency is decreased and latency of sleep onset is increased in IPF patients leading to unrefreshing sleep and daytime tiredness and drowsiness. Frequent arousals during sleep further contribute to poor sleep quality. Mermigkis C et al showed similar results in their study.

Conclusion:

A high index of suspicion is warranted for the overlap of OSA and IPF, particularly in the presence of GERD, longer duration of IPF, severe airway restriction, frequent exacerbations and in patients with severe disease. Thus the presence of sleep disorders is acknowledged as a co-morbidity in IPF patients, and it is very important to understand the relationship between IPF and OSA and how important it is that OSA be considered, identified, and treated in patients with IPF. IPF ,being a fatal disease with poor response to medication demands an overall approach for management of associated co-morbidities like OSA to improve the quality of life of the patient.

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