ORIGINAL ARTICLE

Pulmonary Functions in Obstructive Sleep Apnea Hypopnea Syndrome in a Cohort of Patients Attending the Sleep Center of a Tertiary Care Hospital

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Indian J Sleep Med 2007; 2.1, 21-27

Abstract

Eighty-nine patients (70 male and 19 female) of obstructive sleep apnea were retrospectively studied.

Material and Methods A detailed history was obtained and general physical, systemic and ENT examination performed. Their pulmonary function test reports, which included FVC, SVC, PEFR, PIFR, FEF_{25-75}, flow-volume loop analysis, were interpreted. An arterial blood gas analysis (at rest, with the patient breathing room air during daytime) was obtained. A whole night fully supervised, manually validated, level-I complete polysomnography was conducted on all patients. Various sleep-study parameters (which included apnea, hypopnea, flow-limitation, RDI, arousal index, minimum oxygen saturation during sleep and desaturation index) were obtained.

Results Among the 89 patients, 39 had mild obstructive sleep apnea (OSA) (RDI 5-19), 26 had moderate OSA (RDI 19-39), and 24 had severe OSA (RDI>40). The average BMI of the patient population was 29.54 +1.16. There was a mild restrictive ventilatory impairment in the study population. The mean value of PEFR / PIFR ratio was 1.47 and was found to be >1 in 92.6% patients, thus indicating significant upper airway obstructive pattern. The flow-volume loops showed flattening of the inspiratory limb in 62% of the patients and characteristic saw-tooth pattern / undulations in 35% of the patients. The mean PaO_2 was 73.85 mmHg indicating significant hypoxemia. There was a decreasing trend in the PaO_2 value with increase in severity of sleep-disordered breathing. No significant correlations were observed between pulmonary function test variables (SVC, FVC, FEF_{25-75}, PEFR and FEV_1/FVC) and the severity of OSA i.e. RDI, minimum O_2 saturation and desaturation index. However arousal index was found to correlate positively with the FVC (p=.0783) and SVC (p=.0545) (expressed as a percentage of the predicted value) respectively. There was also a significant negative correlation between daytime arterial PaO2 and RDI (p=0.0477), arousal index (p=0.0592), minimum O2 saturation (p=0.0458) and desaturation index (p=0.0316). A significant negative correlation was also seen between the PEFR / PIFR ratio and desaturation index (p=0.0515).

Conclusion On the basis of the present study it can be concluded that in a patient who presents with history suggestive of sleep disordered breathing, the presence of daytime hypoxemia, flattening of inspiratory limb of the flow volume loop with a PEFR/PIFR ratio>1 strengthen the suspicion of OSAS.

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Introduction

Abnormalities in pulmonary function tests have often been noticed among patients suffering from obstructive sleep apnea hypopnea syndrome (OSAHS). Clinical symptoms that may serve as predictors of sleep apnea syndrome (SAS) have long been examined. However specificity and sensitivity of symptoms were found to be low[1-6]. Some aspects of pulmonary functions like specific respiratory conductance (sGrs) and daytime arterial saturation (SaO_2) have been found to correlate with the severity of SAS.[7, 8] Components of the flow-volume loop, particularly extra-thoracic airway obstruction (FEF50/ FIF50 >1) and upper airway fluttering (saw-tooth aspect on the inspiratory curve) have been correlated with SAS.[9, 10] Spirometry data from various studies with respect to sleep apneic patients have yielded heterogenous results; some have opined that few parameters are helpful and others that there is no correlation between them and sleep apnea syndrome [11-14]. There is no study in the Indian population about pulmonary functions in sleep apnea patients.

This study aimed at observing retrospectively the pulmonary function data of 89 patients of diagnosed OSAHS who attended the sleep center of a tertiary care hospital in New Delhi over the last one year and looking into any correlation between them and the sleep parameters.

Methods

Patient selection

Eighty-nine confirmed cases of OSAHS (70 males and 19 females) who attended the sleep clinic of the Department of Pulmonary, Critical Care & Sleep Medicine of Vardhman Mahavir Medical College & Safdarjang Hospital, New Delhi, were included in the study. All patients were overweight as defined by Body Mass Index (BMI) > 25 [taken as weight in kg/(height in meters)^2] [(15)] Exclusion criteria included history of tobacco smoking, cardiopulmonary disease, history of airway obstruction due to asthma or chronic obstructive pulmonary disease (COPD), alcohol abuse, regular use of hypnotic medication, history or clinical evidence of neuromuscular or chest-wall disease

History & physical examination

A detailed history was obtained from each patient and recorded. Special attention was taken to record history of snoring, excessive daytime somnolence, nocturia, witnessed apneas, choking, waking up un-refreshed in the morning and personality changes if any. Detailed physical findings including general physical examination, neck and waist circumference, height, weight and systemic examination as well as ENT examination were also recorded.

Spirometry and flow-volume curves

Spirometry and flow-volume curves were obtained in each patient using a spirometer (P.K.Morgan, UK). The highest value of three technically satisfactory forced and slow expiratory maneuvers was taken as representative data. The values were expressed as actual values as well as percentage of predicted normal values derived from normograms of Indian population. The criteria for interpretation of pulmonary function tests were taken as follows. FVC, SVC and FEV_1 / FVC greater than 80% of predicted normal meant normal. In general, a reduction in FEV and FEV_1 / FVC to 60-80% of predicted values indicated mild, 40-60% moderate and less than 40% severe restriction. PEFR / PIFR ratio of more than 1 was taken as evidence of upper airway obstruction.

Arterial blood gas analysis

Arterial blood sample was drawn after a relaxed rest period of 10 to 15 minutes in the sitting position while the patient was awake and breathing in room air. It was drawn from the radial artery. It was analyzed for pH, paO_2 and $paCO_2$ (Eischweiler System®).

Sleep studies

A whole night fully supervised, manually validated, level-I complete polysomnography was conducted on all patients. It included electro-encephalography, electro-oculography, chin electro-myography, oro-nasal airflow (by nasal thermistors and nasal pressure transducers), rib-cage and abdominal movements, arterial oxygen saturation monitored via a finger probe, electrocardiography and body position. An Alice 5 Healthdyne Polysomnography System (Respironics,USA) was used.

Sleep staging was performed using the criteria of Rechtshaffen & Kales [16]. A trained physician manually validated all the sleep studies. Apnea was defined as cessation of airflow lasting $\geq$10 seconds; hypopnea was defined as an event lasting at least 10 seconds characterized by 50% or greater reduction in a validated measure of breathing or a

50% or less reduction if associated with an oxygen desaturation of at least 3% or an arousal [17]. Flow limitation was defined as any series of two or more breaths, lasting >10 seconds, that have flattened or non-sinusoidal appearance on the inspiratory nasal cannula flow signal and end abruptly with a return to breaths with sinusoidal shape. Desaturation was defined as fall of >3% in saturation from the baseline following an obstructive event. The number of such episodes per hour was taken as desaturation index (DI). Respiratory distress index (RDI) was calculated as a sum of apnea, hypopnea and flow limitation. Arousal was defined as EEG alpha bursts exceeding 3 seconds during NREM sleep and bursts with accompanying chin muscle tone during REM. All non-respiratory arousals were eliminated. The number of arousals per hour was taken as the arousal index (AI). The minimum arterial blood oxygen saturation attained during sleep was also recorded. RDI values >5 per hour along with two or more of the following symptoms; choking or gasping during sleep, recurrent awakenings from sleep, unrefreshing sleep, daytime fatigue, and impaired concentration. Categorization of severity of OSA was done according to RDI values into three groups: mild (RDI =5-19), moderate (RDI= 20-39) and severe (RDI ≥40). All the above parameters were computed for each patient.

Statistical Analysis

Analysis of all data was performed using SPSS software. Data were expressed as Mean ± SD. Correlations between variables were evaluated using least-square linear regression techniques.

Subjects were classified based on their RDI. RDI values of ≥5 were considered abnormal. For all comparisons, p values <0.10 were considered significant.

Results

Of the eighty-nine patients included in the study, 70 were male and 19 female. Thirty-nine of them had mild OSAS (RDI 5-19), 26 had moderate OSAS (RDI 19-39), and 24 had severe OSAS (RDI≥40) (Table 1).

Table 1: Gender-wise distribution of patients

RDI Categories	Female (n)	Male (n)	Total
Mild (RDI = 5 to 19)	13	26	39
Moderate (RDI = 20 to 39)	3	23	26
Severe (RDI more than 40)	3	21	24

The average BMI of the patient population was 29.54, thus showing that it largely comprised of overweight subjects(Table 2). The mean values of FVC and SVC were 2.82 L and 2.92 L (73.36% and 75.87% of predicted normal) respectively (Table 2). On the basis of these values it can be inferred that there was a mild restrictive ventilatory impairment in the study population. The mean FEV_1 / FVC value was 86.03% of the predicted and that of FEF_{25-75} was 74.05% of predicted thus indicating no impairment in the expiratory flows. The mean PIFR value was 3.63 liters per second which was 40% of the predicted normal value indicating a severe reduction in the inspiratory flows. The mean PEFR value was 5.05 liters per second which again shows a mild reduction in the peak expiratory flows. The mean value of PEFR / PIFR ratio was 1.47 and was found to be >1 in 92.6% patients, thus indicating significant upper

Table 2: Average values of BMI, PFTs and ABG

BMI + SD	29.54 + 1.16	*FEF (25-75%)*	2.58
PO2 mmHg	73.85	*%FEF(25-75)*	74.05
PCO2 mmHg	31.84	*PEFR Liters / sec*	5.05
FVC Liters	2.82	*PIFR Liters / sec*	3.63
%FVC	73.36	*PIFR/PEFR*	1.47
SVC Liters	2.92	*FEV1/FVC*	86.03
%SVC	75.87		

Table 3: Body mass index and pulmonary function tests in various patients grouped according to severity of obstructive sleep apnea

Categories of severity of sleep disordered breathing	*BMI*	*FVC*		*SVC*		*%FEV1/FVC*		*FEF (25-75%)*	
		Patients value	*% Predicted*	*Patients value*	*% Predicted*	*Patients value*	*% Predicted*	*Patients value*	*% Predicted*
Mild (RDI – 5 to 19)	29.37 ± 1.82	2.56	69.67	2.68	72.21	86.08	107.50	2.26	68.89
Moderate (RDI – 20 to 39)	28.57± 1.97	2.94	74.86	3.02	77.24	87.91	109.38	2.78	79.86
Severe (RDI more than 40)	30.93+ 2.26	3.03	76.78	3.13	79.39	83.43	105.30	2.73	74.86

airway obstructive pattern. The flow-volume loops showed flattening of the inspiratory limb in 62% of the patients; and amongst those patients who showed flattening, 35% demonstrated characteristic saw-tooth pattern / undulations (Table 4). The flattening of the inspiratory loop was found in 50%, 55% & 75% in the mild, moderate and severe subgroups of OSAS respectively.

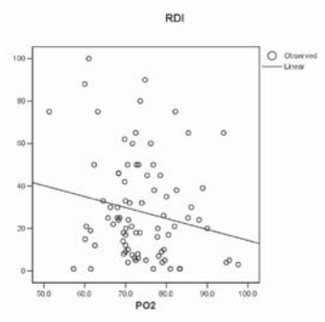
Table 4: Flow volume loop characteristics

Flow-volume inspiratory loop	Percentage of the total number of patients	Mild OSAS (as percentage of total number of patients in the subgroup)	Moderate OSAS (as percentage of total number of patients in the subgroup)	Severe OSAS (as percentage of the total number of patients in the subgroup)
Flattening	62%	50%	55%	75%
Saw tooth / undulations	38% of patients showing flattening	.	.	.

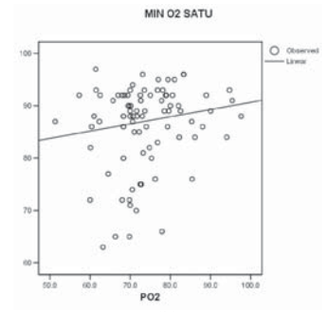
The mean PaO_2 was 73.85 mmHg indicating significant hypoxemia. The mean $PaCO_2$ was 31.84 mmHg showing significant hypocapnia. The mean pH was 7.45 indicating mild alkalemia (Table-5). The arterial blood gas values in the three groups of disease severity are depicted in Table 5. There was a decreasing trend in the PaO_2 value with increase in severity of sleep-disordered breathing. The arterial $paCO_2$ and pH values were similar in all the three groups.

The pulmonary function data and BMI of patients sub-grouped according to severity of sleep-disordered breathing is outlined in Table 3. All the patients were overweight, and the body mass index (BMI) did not vary among the above three groups. A mild decrease in value of the vital capacity (expressed as a percentage of the predicted normal) was observed in all the three groups. The mean FVC was 69.67%, 74.86% and 76.78% of predicted in the mild, moderate and severe groups respectively. The mean SVC was 72.21%, 77.24% and 79.39% of predicted in the mild, moderate and severe groups respectively (Table 3). There was an increasing trend observed in the vital capacity with increase in the RDI.

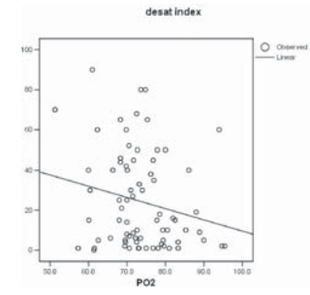
No significant correlations were observed between pulmonary function test variables (SVC, FVC, FEF_{25-75}, PEFR and FEV_1/FVC) and the severity of OSA i.e. RDI, minimum O_2 saturation and desaturation index. However arousal index was found to correlate positively with the FVC (p=.0783) and SVC (p=.0545) (expressed as a percentage of the predicted value) respectively. There was also a significant negative correlation between daytime arterial PaO_2 and RDI (p=0.0477), arousal index (p=0.0592), minimum O_2 saturation (p=0.0458) and desaturation index (p=0.0316) (Table 6). A significant negative correlation was observed between the PEFR / PIFR ratio and desaturation index (p=0.0515), which is also a marker of severity of OSAS.The scatter plots of PaO_2 with RDI, minimum O_2 saturation and desaturation index respectively are depicted in Figure 1.



(a)



(b)



(c)

Fig 1: Scatter Plots showing correlations between **a.** RDI & paO_2 **b.** Min Sat O_2 & **c.** paO_2, Desat index & paO_2

Discussion

Awareness and knowledge about sleep disordered breathing have constantly been on the rise[28,29]. The prevalence of sleep-related breathing disorders has been demonstrated to be significantly high. The sheet anchor in the diagnosis of obstructive sleep apnea syndrome (OSAS) is

polysomnography. This laboratory diagnostic procedure, however, demands trained technical and medical manpower and financial resources. Moreover it is not widely accessible to the large number of patients who may require the facility, particularly in a developing country like India. So there is a need to develop simple tools to screen patients from the general population with suspected sleep disordered breathing, who can be later subjected to detailed polysomnography for confirmation the diagnosis. Various instruments on the basis of questionnaires, physical examination and cephalometry with varying degrees of specificity and sensitivity have been developed[30,31]. Pulmonary function tests have traditionally had little role in the diagnosis of OSAS. Spirometry data from various studies with respect to this group of disorders have demonstrated varied results. Components of the flow volume loop, particularly extra-thoracic airway obstruction (FEF 50/ FIF 50 >1) and a saw-tooth pattern on the inspiratory loop have been correlated with OSAS [9,10]. Other studies have revealed no correlation between them and sleep-apnea syndrome [11-14]. Data on pulmonary function tests in OSAS in the Indian population is virtually non-existent. In the backdrop of these facts, the present study retrospectively reviewed the arterial blood gas and spirometry data in a group of overweight Indian patients with OSAS. It also attempted to observe correlations, if any, between such data and polysomnography parameters in this group of patients.

The patients in this study were overweight; the mean $\pm$ SD of BMI being 29.54 $\pm$ 1.16. The value of BMI $\pm$ SD of patients in the three subgroups was not significantly different (Table-3), thus having a similar confounding effect of BMI on the PFT parameters in the three groups of disease severity. The mean vital capacity of the whole group as well as the subgroup of patients was suggestive of mild restrictive lung disease. There was an increasing trend in the mean vital capacity with increasing RDI although there was no significant correlation between them. However, the arousal index, which is also a parameter of severity of sleep disordered breathing, had a positive correlation with the vital capacity [FVC (p=0.0783) and SVC (p=0.0545)], i.e. those with lesser restriction had a higher RDI and higher AI, than those with higher restriction who had a lower RDI and AI. These findings have not been reported in other studies.

There was no impairment in the mean values of expiratory flows (FEV_1/FVC and FEF_{25-75}) seen in the present study. In one of the earlier studies FEV_1/FVC has been found to be slightly but significantly lower in subjects with apneic snorers with desaturation [22]. An obstructive ventilatory defect (FEV_1 / FVC <60%) was also found in 30 of 264 consecutive OSAS patients with similar BMIs in another study [23,24]. Another study found FEV_1/FVC to decrease significantly as AHI increased[8]. A significant and considerably larger decrease in expiratory flow rates at 50% and 75% of vital capacity (FEV_{50} and FEV_{25}) and FEF_{25-75} with increasing AHI was also seen in the same study[8]. However, no such observations were made in our study .

The present study failed to demonstrate any correlations between SVC, FVC, FEF_{25-75}, PEFR or FEV_1/FVC with severity of OSA (i.e. RDI, minimum O_2 saturation & desaturation index). Similar observations, where no correlation could be obtained between PFT variables and severity of sleep apnea, were made in other studies as well[22,27].

The mean PIFR value observed in this study was 3.63 liters per second (40% of predicted normal); the mean PEFR /PIFR ratio was 1.47 thus indicating significant upper airway obstructive pattern. A flattening of the inspiratory limb was seen in 62% patients. The flattening of the inspiratory limb was seen in a significantly higher percentage (75%) of patients with severe sleep apnea than those with mild (50%) and moderate (55%) disease. In another study,[26] forty percent patients with sleep-disordered breathing had abnormal flow-volume curves consistent with variable extrathoracic airway obstruction as compared to 8% among those with no breathing disorder.

Signs of upper airway fluttering (the saw-tooth sign) was present in 61% of patients with OSAS and in 46% of patients with central sleep apnea or no sleep apnea in another study earlier [9]. However in our study, a characteristic saw-tooth / undulating pattern of the inspiratory limb was seen in 35% amongst those patients with flattening. Another study observed that the presence of the saw tooth sign was found to have a high specificity (92%) with a greater fall in oxygen saturation in OSAS patients who had saw-toothing than in those without sawtoothing[25]. In our study the distribution of saw-tooth pattern of the inspiratory limb was similar in all three groups of disease severity. Flow-volume curve alterations have been reported in OSAS, in several other studies[11,12]. Other studies found the flow-volume loop to be unhelpful[13,14]. The presence of PEFR/PIFR>1 in 92% of the OSAS patients in this study can be taken as a strong predictor of the diseases. There was no correlation between PEFR/PIFR ratio and the RDI, apnea index and minimum saturation seen in this study. However, there was a significant correlation observed between the PEFR / PIFR ratio and desaturation index (p=0.0515) which is also a marker of

severity of OSAS. All the parameters of disease severity namely RDI, apnea index, minimum saturation and desaturation index, in turn, strongly correlated with each other. The presence of flattening of the inspiratory limb in 75% of patients with severe OSAS further strengthens the suspicion of sleep apnea.

The differences between the result of our study and the previous study could be due to the different parameters chosen to measure the disease severity. In most of older studies the parameter of severity of OSAS was AHI. In the present study, the parameter is RDI which includes flow limitation in addition to apneas and hypopneas.

Most of the patients in the studied population showed hypoxemia with a significant decreasing trend in the PaO_2 value with increasing severity of sleep-disordered breathing (p=0.0477). A strong correlation was also observed between PaO_2 and other sleep parameters of disease severity, namely, arousal index, minimum O_2 saturation and desaturation index (Table-6 & Figure-1). Thus daytime hypoxemia may be taken as an important pointer towards the presence & severity of sleep disordered breathing in patients with symptoms suggestive of OSAS in whom other causes of hypoxemia have been ruled out. The $paCO_2$ & pH values were similar in all three groups of severity of disease. A similar decreasing trend in PaO_2 with increasing severity has been observed in another study earlier [8].

Table 5: Arterial blood gas parameters in patients grouped according to severity of obstructive sleep apnea

ABG parameters (expressed as mean)	Mild (RDI = 5 to 19)	Moderate (RDI = 20 to 39)	Severe (RDI more than 40)
paO_2	76.05	74.66	71.80
$paCO_2$	31.80	31.57	32.52
pH	7.44	7.45	7.46
HCO_3	23.59	35.00	24.50

Conclusion

On the basis of the present study it can be concluded that in a patient who presents with history suggestive of sleep disordered breathing, the presence of daytime hypoxemia, flattening of inspiratory limb of the flow volume loop with a PEFR/PIFR ratio > 1 strengthen the suspicion of OSAS.

Acknowledgement

The authors wish to thank Dr Padm Singh, formerly Additional Director General, Indian Council of Medical Research and Director, Institute for Research in Medical Statistics, for his kind help in the statistical analysis of this data

Table 6: Correlations between various pulmonary functions, arterial blood gas parameters and sleep study variables

Correlations Table

		RDI	Arousal index	MIN O2 SATU	Desat index
PO2	Pearson Correlation	-0.1831	-0.1738	0.1852	-0.2157
	Sig. (1-tailed)	0.0477	0.0592	0.0458	0.0316
PH	Pearson Correlation	0.1311	0.1542	-0.0113	0.0746
	Sig. (1-tailed)	0.1173	0.0833	0.4592	0.2625
HCO3	Pearson Correlation	-0.0386	-0.1056	-0.3559	0.1223
	Sig. (1-tailed)	0.3637	0.1726	0.0004	0.1480
%FVC	Pearson Correlation	0.0475	0.1569	-0.0984	0.1009
	Sig. (1-tailed)	0.3330	0.0783	0.1852	0.1929
%SVC	Pearson Correlation	0.0654	0.1772	-0.0728	0.1329
	Sig. (1-tailed)	0.2759	0.0545	0.2539	0.1263
%FEV1/FVC	Pearson Correlation	-0.0768	-0.1252	-0.0051	-0.0261
	Sig. (1-tailed)	0.2437	0.1312	0.4817	0.4119
PIFR/PEFR	Pearson Correlation	-0.0906	-0.1279	0.0492	-0.1937
	Sig. (1-tailed)	0.2106	0.1307	0.3313	0.0515

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