

Research Article

Correlation between associating factors of obstructive airway disease with obstructive sleep apnoea

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ABSTRACT

Background: Several researchers reported that OSA may contribute to asthma symptoms and severity. But, the relation between associating factors of obstructive airway disease with obstructive sleep apnoea was not well documented. Therefore, the present study has been undertaken to investigate the relation between associating factors of OAD with obstructive sleep apnoea.

Methods: Pulmonary Function Test was done for assessing air flows and measuring absolute and predicted values of FEV1, FVC, FEV1/FVC and MMEF. PFT was interpreted as normal if FEV1/FVC >70 as per GOLD and >75 as per GINA, with normal FEV1 and normal FVC. Decreased FEV1, Decreased FVC, Decreased FEV1/ FVC, predicted (<70 as per GOLD and <75 as per GINA) was considered obstructive disorder. FEV1 used to follow severity in COPD. Decreased FEV1, Decreased FVC, FEV1/FVC normal or increased was considered restrictive disorder. The data were represented as percentages and mean + SD. Chi-square test and student 't' test was used to determine the statistical difference and a "p" value of less than 0.05 was considered the level of significance.

Results: The sleep efficiency, oxygen saturation, mean heart rate, arousal index and respiratory distress index in the OAD group and in the No OAD group was found to be statistically not significant (p>0.05). The Sleep Stages in the study group (OAD and No OAD group) was also statistically insignificant except for Stage III. The PFT-FEV1 was found to be statistically significant (p=0.043) when compared between OAD group and in the No OAD group.

Conclusions: Due to the consequences of the overlap syndrome, it is recommended to actively search for existence of OSA, and to treat it with continuous positive airway pressure (CPAP) concurrently with oxygen and optimal pharmacological treatment.

Keywords: Polysomnography, Obstructive sleep apnoea, MMRC Dyspnea scale, Obstructive airway diseases

INTRODUCTION

Sleep-disordered breathing is an extremely common medical disorder associated with important morbidity. It is present when there are repetitive episodes of cessation of respiration (apnea) or decrements in airflow (hypopnea) during sleep, associated with sleep fragmentation, arousals, and reductions in oxygen saturation. An apnea can be obstructive (absence of

airflow but continued respiratory effort), central (absence of airflow and respiratory effort), or mixed.¹

A mixed apnea starts as a central event and then becomes obstructive during the latter portion of the same episode. A majority of patients with obstructive sleep apnea (OSA) have both obstructive and mixed apneas. A hypopnea is defined as a decrement in airflow of 50 percent or more associated with a 4 percent fall in oxygen

saturation and/or electroencephalographic (EEG) arousal.² OAD are characterized by a limitation of airflow when measured by spirometry.

Chronic obstructive pulmonary disease (COPD) and Asthma are the two most common forms of obstructive lung diseases. COPD - is defined by the Global Initiative for Chronic Obstructive Lung disease (GOLD) as: "A preventable and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in airway and lung to noxious particles and gases".³

Repetitive upper airway collapse increases lower airway resistance leading airway obstruction.⁴ Patients with clinically significant OSA have EDS and/or fatigue, which may lead to higher smoking intensity versus those without OSA. Additionally, systemic inflammatory 'overspill' in OSA may have a significant effect on the redox equilibrium of the lower airways.⁵

Upper-lower airway interdependence has been proven by many investigators, and these interactions may explain how expiratory and inspiratory flow limitation is connected in the overlap syndromes.

Smoking is a shared risk factor for both conditions. Both smoking and COPD can lead to impaired sleep quality in direct correlation with the expiratory flow limitation severity, which can in fact lead to higher collapsibility of the upper airway and development of obesity.

Patients with frequent COPD (or OAD) exacerbations tend to receive more frequent corticosteroid courses, which may put them at risk to develop upper airway closure due to fat deposition in the neck, abdominal fat effect on the diaphragm and on functional residual capacity, or through a steroid induced myopathy.⁶ Elevated airway resistance leads to more negative intrapleural pressure which, with the added effect of reclined position, can lead to more collapsible upper airway.

OSA is more common in men than women with a ratio of 2:1. In a cross sectional study, it showed a four-fold higher prevalence of at least moderate OSA in postmenopausal women as compared with premenopausal women. And in postmenopausal women taking hormonal replacement therapy, the prevalence of OSA is similar to premenopausal women.⁷

Obesity is the major risk factor for the development of OSA, it is thought to be associated with anatomic alterations that predispose to upper airway obstruction during sleep, by increasing adiposity around the pharynx and body.

Central obesity has been associated with reduction in lung volume, which leads to a loss of caudal traction on

the upper airway, and hence, an increase in pharyngeal collapsibility.⁸ In a community-based cohort of middle-aged Caucasian subjects, a 1-SD increase in body mass index was associated with a four-fold rise in the prevalence of sleep apnoea, and 40 % of subjects from the community with OSA were moderately overweight but otherwise healthy.^{9,10} In subjects with severe obesity, BMI of >40, the prevalence of sleep apnoea was markedly increased to 40-90 %.¹¹

Several studies have investigated the association between OSA and obstructive airway disease (OAD), including both asthma and chronic obstructive airway disease (COPD). A high prevalence of OSA has been reported in asthma clinics, and asthma may also be common in OSA.¹²

Several researchers reported that OSA may contribute to asthma symptoms and severity. But, the relation between associating factors of obstructive airway disease with obstructive sleep apnoea was not well documented. Therefore, the present study has been undertaken to investigate the relation between associating factors of OAD with obstructive sleep apnoea.

METHODS

The present study was undertaken after the institutional ethical clearance and written and informed consent from all the patients. Patients with sleep complaints undergoing Polysomnography for diagnosis of OSA in department of Pulmonary Medicine were enrolled for the study. Patients with Congestive Cardiac Failure, Stroke, Hemoptysis and Acute Myocardial Infarction were excluded from the study.

After taking informed consent, patients are subjected to history of symptoms, personal and past history was taken. Grading of Breathlessness was done by MMRC (Modified Medical Research Council) Dyspnea scale. An in house sleep questionnaire with Epworth Sleepiness scale score of 0 to 3 was (0=would never doze, 1=slight chance of dozing, 2=moderate chance of dozing and 3=high chance of dozing).

The clinical examination included the measurement of Body mass index (BMI), Neck circumference and Mallampatti score. The presence or absence of obstructive sleep apnea was determined from polysomnographic analysis with manual scoring of sleep staging and respiratory events by an experienced sleep technologist.

Pulmonary function test (PFT) was done for assessing air flows and measuring absolute and predicted values of FEV₁, FVC, FEV₁/FVC and MMEF. PFT was interpreted as normal if FEV₁/FVC >70 as per GOLD and >75 as per GINA, with normal FEV₁ and normal FVC. Decreased FEV₁, Decreased FVC, Decreased FEV₁/FVC, predicted (<70 as per GOLD and <75 as per

GINA was considered obstructive disorder. FEV1 used to follow severity in COPD. Decreased FEV1, Decreased FVC, FEV1/FVC normal or increased was considered restrictive disorder.

In FEV1/FVC < 70, the grading of severity of obstruction was done according GOLD guidelines mild (FEV1 > 80%), moderate (FEV1 80-50%), severe (FEV1 50-30%), and very severe (FEV1 < 30%). The grading of severity of obstruction was done according GINA guidelines as mild (FEV1 > 80%), moderate (FEV1 80-60%), severe (FEV1 < 60%). Following the PFT, the subjects are divided into 2 groups based on FEV1/FVC – Obstruction (OAD) with FEV1/FVC < 75 and No Obstruction Group (No OAD) with FEV1/FVC > 75. Based on FEV1/FVC – Obstruction (OAD) with FEV1/FVC < 70 and No Obstruction Group (No OAD) FEV1/FVC > 70.

Statistical analysis

The discrete data for each parameter was represented as numbers and percentages and continuous data as mean +

standard deviation. Proportions were compared using Chi-square test of significance. The student ‘t’ test was used to determine whether there was a statistical difference between groups in the parameters measured. A ‘p’ value of less than 0.05 was accepted as indicating statistical significance. Data analysis was carried out using Statistical Package for Social Science (SPSS, V 10.5) package.

RESULTS

The Mallampatti Class among severe OSA patients were clustered around Class III and Class II. Among moderate OSA patients 7 patients each had Class II and Class III score. Among mild OSA patients, majority had Class III score which was found to be statistically insignificant (p=0.429, Table 1).

When the different degrees of Obstructive Sleep Apnea compared with Epworth Sleepiness scale in the recruited patients showed a significant difference (p=0.025, Table 2).

Table 1: Obstructive sleep apnoea and Mallampatti classification of upper airway obstruction in the recruited patients.

Obstructive sleep apnea	Mallampatti score				Total	‘p’ value
	Class I	Class II	Class III	Class IV		
Mild	0	2	5	0	7	0.429
	0%	28.6%	71.4%	0%	100.0%	
Moderate	0	7	7	0	14	
	0%	50.0%	50.0%	0%	100.0%	
Severe	3	24	42	12	81	
	3.7%	29.6%	51.9%	14.8%	100.0%	

Table 2: Obstructive sleep apnoea and Epworth sleepiness scale in the recruited patients.

OSA	N	Epworth sleepiness scale		‘p’ value
		Mean	SD	
Mild	7	10.86	6.962	0.025
Moderate	14	8.14	6.848	
Severe	81	12.59	5.303	

The sleep efficiency, oxygen saturation, mean heart rate, arousal index and respiratory distress index in the OAD group and in the No OAD group was found to be statistically not significant (p>0.05, Table 3).

Whereas, the Sleep Stages in the study group (OAD and No OAD group) was not statistically significant except for Stage III. The PFT-FEV1 was found to be statistically significant (p=0.043) when compared between OAD group and in the No OAD group (Table 3).

Among 7 patients with an obstruction (FEV1/FVC < 70), majority (71.4%) patients had severe OSA. There is no statistically significant difference between patients with obstruction or no obstruction in the upper airway (P=0.717, Table 4).

Among 13 patients with an obstruction (FEV1/FVC < 75), majority of the patients had severe OSA. There is no statistically significant difference between obstruction or no obstruction patients (P = 0.794, Table 5).

Table 3: Distribution of PFT and PSG parameters in patients with obstruction (FEV1/FVC<75) in the recruited patients.

PSG	FEV1/FVC	N	Mean	SD	'p' value
Sleep Efficiency	<75	13	87.40	13.00	0.884(NS)
	≥75	89	88.01	14.09	
Stage I	<75	13	25.69	27.93	0.603(NS)
	≥75	89	29.67	25.39	
Stage II	<75	13	41.35	20.31	0.291(NS)
	≥75	89	48.06	21.44	
Stage III	<75	13	26.23	22.29	0.032
	≥75	89	15.51	15.64	
REM	<75	13	6.71	12.08	0.989(NS)
	≥75	89	6.67	8.305	
Sleep Latency(Mins)	<75	13	22.84	28.96	0.499(NS)
	≥75	89	17.57	25.74	
Lowest Spo2	<75	13	72.15	17.21	0.765(NS)
	≥75	89	73.53	15.33	
Mean HR	<75	13	91.61	7.22	0.943(NS)
	≥75	89	91.79	8.32	
Arousal Index	<75	13	23.16	15.43	0.309(NS)
	≥75	89	29.64	22.01	
RDI(/HR)	<75	13	54.86	28.04	0.440(NS)
	≥75	89	62.28	32.71	
PFT-FEV1	<75	13	1.67	0.47	0.043
	≥75	89	2.12	0.76	

Table 4: Pulmonary function test and obstructive sleep apnea in patients with FEV1/FVC<70.

OSA	FEV1/FVC		Total	'p' value
	<70	≥70		
Mild	1	6	7	0.717(NS)
	14.3%	6.3%	6.9%	
Moderate	1	13	14	
	14.3%	13.7%	13.7%	
Severe	5	76	81	
	71.4%	80.0%	79.4%	

Table 5: Pulmonary function test and obstructive sleep apnea in patients with FEV1/FVC<75.

OSA	PFT-FEV1/FVC		Total	'p' value
	<75	≥75		
Mild	1	6	7	0.794(NS)
	7.7%	6.7%	6.9%	
Moderate	1	13	14	
	7.7%	14.6%	13.7%	
Severe	11	70	81	
	84.6%	78.7%	79.4%	

DISCUSSION

Out of 102 patients, 13 patients were found to have obstructive airway disease (FEV1/FVC<75), 53 patients had restriction in PFT and 36 patients had normal PFT.

According to GINA in 13 patients with FEV1/FVC<75, 7 (53.84%) of them had moderate and 6 (46.15%) patients had severe obstruction. According to GOLD in 7 patients with FEV1/FVC<70, 5 (71.4%) patients had severe and 2 (28.6%) patients had moderate obstruction.

Majority of the patients with obstruction were in age group 60-69 years and were males and belong to obesity group and had class III Mallampatti score.

The Patients with Obstructive airway disease also had frequent Oxygen de-saturations and had high Respiratory Distress Index. The Patients with Obstructive airway disease had severe OSA. In the present study, mean ESS score was 11.86 ± 5.797 . In other studies by Marin JM et al and Min Kwang et al mean ESS was 12 ± 4 and 10.38 ± 4.8 respectively which was similar to present study.^{13,14}

The mean lowest saturation noted during polysomnography was $73.36 \pm 15.5\%$ which was lower than other studies by Chauot et al, Marin JM et al and Alharbi et al where the mean lowest saturation noted was $85 \pm 6\%$, $90 \pm 4\%$ and $81.7 \pm 11.6\%$ respectively. In the present study, among overlap patients with obstruction FEV1/FVC < 75 the mean lowest saturation noted was $72.154 \pm 17.21\%$ which was lower compared to other studies by Chauot et al 85 and Alharbi et al with overlap, the mean lowest saturation was $84 \pm 7\%$ and $79.6 \pm 13.4\%$.^{12,13,15}

In a study by Alharbi et al the mean arousal index noted was 52.7 ± 33.9 and with overlap was 55.7 ± 33.1 /hour which was higher compared to the present study with the mean arousal index of 28.82 ± 21.33 /hour, probably related to higher RDI and severe OSA.¹² In the present study, the mean RDI noted was 61.34 ± 32.12 /hour and with overlap was 54.86 ± 28.04 /hour.

In other studies by Chauot et al, Weitzenblum et al the mean RDI was 77 ± 33 /hour, 78 ± 33 /hour, which was higher compared to our study. Kristina et al, Marin et al with overlap, the mean RDI noted was 41.8 ± 24.9 /hour and 34 ± 12 /hour respectively which was lower compared our study. In study by Alharbi et al the mean RDI was 53.9 ± 37.8 /hour which was similar to present study. In patients with Overlap RDI is higher.^{12,15,16}

In the study by Chauot et al the mean FEV1 (absolute value) was 1.580 ± 0.560 which was lower compared to our study in which the mean FEV1 was 2.064 ± 0.741 .¹⁵ In our study the mean FEV1 % predicted noted was $75.38 \pm 19.04\%$. In other studies by Marin JM et al, Kristina et al and Weitzenblum et al the mean FEV1 % predicted noted was $57 \pm 16\%$, $75.8 \pm 20\%$ (severe obstruction in 12.1%) and $84.21 \pm 21\%$ respectively.^{13,16}

In study by Marin et al Severity of COPD was mild (FEV1 80% predicted) was 14 %, moderate (FEV1 50–79% predicted) was 46%, severe (FEV1 30–49% predicted) was 31 % and severe (FEV1 $< 30\%$ predicted) was 9%.¹⁷ In present study, out of 7 patients, 5 (71.4%) patients had moderate and 2 (28.6%) had severe obstruction. The difference noted may be due to variation of sample size.

In the study by Chauot et al, the mean FVC % was $82 \pm 21\%$. In our study the mean FVC % was $71.42 \pm 18.20\%$. In our study the mean FEV1/FVC predicted noted was 81.41 ± 7.56 .¹⁵ In other studies by Chauot et al, Kristina et al and Weitzenblum et al, the mean FEV1 /FVC noted was 50 ± 6 , 64.1 ± 7.4 and 73 ± 10 respectively which was lower compared to present study.¹⁵⁻¹⁷

The prevalence of OAD in patients with OSA in studies by Chauot et al was 11%, Weitzenblum et al was 18%, Alharbi et al was 35.1%.^{12,13,15,16} In a study by Greenberg et al, prevalence of asthma with OSA was 10.4% and COPD with OSA was 7.6%.¹⁸ Resta and colleagues found 16% had overlap syndrome.¹⁹ Zamarron and colleagues found 15.4% overlap.²⁰ O'Brien and Whitman found overlap in 11.9%.²¹ In a study by Rizzi et al, observed an associated COPD in 19% of OSA patients.²² The prevalence of OAD in patients with OSA in present study was 12.7% (FEV1/FVC < 75) which was similar to other studies.

CONCLUSION

Obstructive airway diseases and sleep disorders are both common conditions with a complex intertwined relationship. The overlap syndrome is associated with worst pulmonary implications, systemic consequences, morbidity and mortality than those of either COPD or OSA alone. Due to these consequences of the overlap syndrome, it is recommended to actively search for its existence, and to treat it with continuous positive airway pressure (CPAP) concurrently with oxygen and optimal pharmacological treatment.

Further studies with a larger study population may be needed to know the exact prevalence of overlap syndrome. The results found in our study may not be extrapolated to general population as it is a study done on a small population. Follow up prospective studies involving overlap syndrome patients may be needed to know the prognosis, morbidity, mortality and treatment in comparison to standard OSA patients.

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