PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN COPD PATIENTS

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ABSTRACT

Background: COPD is a major global epidemic and has recently become the 3rd leading cause of death in developed countries. The coexistence of COPD and OSA, known as Overlap Syndrome (OS) and is known to increase the risk of systemic diseases. Patients with COPD-OSA have a high risk of death as well as increased risk of exacerbations if OSA remains untreated.

Objectives: This work aimed to assess the prevalence of OSA in COPD patients.

Methods: This prospective observational study was conducted on 100 patients with stable COPD who were attended at chest department, outpatient clinic Benha university hospitals for follow up between June 2017 and June 2019. Overnight polysomnography (PSG) was made for all patients.

Results: Prevalence of OSA increased with increase COPD severity with total prevalence of 60% (P value <0.001). AHI was significantly higher in obese COPD patients (P value = 0.04). Significant positive correlations were found between AHI and oxygen desaturation index, neck circumference and BMI in obese COPD patients.

Conclusion: High prevalence of sleep disordered breathing in patients with moderate to severe COPD, Obese COPD more susceptible to develop OSA and AHI increased with increase COPD severity leading to more complication and exposed COPD patient to nocturnal hypoxaemia which decrease quality of life.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is the 3rd leading cause of death in developed countries (1). It is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases (2). Obstructive Sleep Apnea (OSA) which is a sleep-related breathing disorder characterized by repetitive episodes of complete or partial upper airway obstruction occurring during sleep resulting in nocturnal hypoxemia and arousals from sleep (3).

The coexistence of COPD and OSA, known as Overlap Syndrome (OS) was first described by David Flenley almost 30 years ago , he pointed out that a sleep study should be considered in obese COPD patients , in those who snore or those who complain of headache following nocturnal oxygen therapy to determine the presence of associated OSA (4). Patients with COPD-OSA have a high risk of death as well as increased risk of exacerbations if OSA remains untreated (5). In patients with OSA, the presence of COPD increases the risk of death 7 fold. Therefore, evaluating the presence of OSA in patients with advanced COPD seems logical as concurrence of these diseases may potentially explain the high cardiovascular morbidity and mortality in these patients (6).

2. Aim of the work

The aim of this study is to assess the prevalence of OSA in COPD patients.

3. Patients and methods

3.1. Study selection:

This prospective observational study was conducted on 100 patients with stable COPD who were attended at chest department, outpatient clinic Benha university hospitals for follow up in the period between June 2017 and June 2019. COPD patients were divided according to their BMI into two groups: (7)

Group A: 75 obese COPD patients (BMI ≥30 kg/m2).

Group B: 25 non obese COPD patients (BMI ≤ 30 kg/m2).

3.2. Exclusion criteria

- Patients with acute exacerbation of COPD
- Patients with decompensated heart failure, thyroid dysfunction & ENT causes of OSA.

3.3. Study description

Patients with technically compromised polysomnograms (including those where percentage failure of flow signal was 20% or greater) and patients who spent less than 4 h in bed.

All patients included in this work were subjected to the following:

1. Intensive history taking including smoking index (number of cigarette smoked per day × years of tobacco use) and clinical examination. Severity of dyspnea was surveyed by modified medical research council (mMRC) dyspnea scale (8). The mMRC dyspnea scale was translated into Arabic language according to Alyami et al.(9).
2. Questionnaires to assess sleep quality: the Epworth sleepiness scale (ESS) (10) which was translated into Arabic language according to

   Anwar et al., (11) and STOP-Bang questionnaire (12).
3. Pulmonary function tests (PFTs) were done using JAEGER carefusion Germany 234 GmbH Lelbnizstr .7, 97204 Hoechberg, Germany. PFTs were done during stability of the disease. Patients

were characterized by their postbronchodilator forced expiratory volume in first second (FEV1) into mild (FEV1 ≥ 80% anticipated), moderate (50%≤FEV1 < 80% anticipated), severe (30%≤FEV1 < 50% anticipated).

4. Echo cardiography.
5. Overnight Polysomnography (SOMNO Screen Plus; SOMNO Medics GmbH, Randersacker, Germany). The polysomnograghy consists of pulse oximetry, electroencephalogram, electrooculogram, ECG, electromyogram, thoracic and abdominal belts, body position sensor, assesement of respiraratory flow and pressure by nasal thermistor and nasal cannula and bipolar channel limb movements (tibialis anterior). Electrodes and sensors were directly attached to patients by sleep physiologist. Data acquisition was obtained immediately after signal detection by preprocessed computer (DOMINO Software, ver. 2.6.0; SOMNO Medics GmbH).

3.4. Statistical analysis (13)

The collected data were computerized and statistically analyzed using SPSS program (Statistical Package for Social Science) version **24**.

Data were tested for normal distribution using the Shapiro Walk test. Qualitative data were represented as frequencies and relative percentages. Chi square test ($\chi 2$) and Fisher exact was used to calculate difference between qualitative variables as indicated. Quantitative data were expressed as median and range for being non-parametric data (not normally distributed). Mann Whitney test were used to calculate difference between quantitative variables in two groups for non-parametric variables. Spearman's correlation tests were used for correlating non-parametric

variables. The (+) sign was considered as indication for direct correlation i.e. increase frequency of independent lead to increase frequency of dependent & (-) sign as indication for inverse correlation i.e. increase frequency of independent lead to decrease frequency of dependent, also we consider values near to 1 as strong correlation & values near 0 as weak correlation. All statistical comparisons were two tailed with significance Levelof P-value≤ 0.05 indicates significant, p <0.001 indicates highly significant difference while, P> 0.05 indicates Non-significant difference. Enter multiple linear regression analysis was performed in order to model the relationship of AHI with other variables.

4. Results

In the current study, COPD patients were divided into two groups (obese and non obese), both group were matched regarding age and sex distribution, BMI and neck circumference were significantly higher in obese COPD (Table 1).

Stop Bang, ESS, mMRC, AHI, RDI and ODI were significantly higher in obese COPD (Table 2), OSA severity (presented by AHI) increased with increase COPD severity with statistically significant difference (Table 3).

60% of COPD patients were found to have OSA and the higher prevalence was found in severe COPD (Table 4).

OSA severity (represented by AHI) was significantly correlated BMI, FEV1, smoking index, sleep questionnaire and polysomnographic parameter (Table 5).

Multivariate logistic regression analysis revealed that BMI, Post FEV1, smoking index and baseline oxygen were independent predictors of OSA in COPD patients (Table 6).

Table (1): Comparison between the studied groups regarding clinico-demographic data:

Group / parameter		Non-obese N=25	Obese N=75	MW test*	P
		Median (Range)	Median (Range)		
Age(years)		66 (41-87)	66 (50-79)	-0.8	0.409
Smoking Index(pack/year)		30 (10-140)	60 (10-150)	-4.2	<0.001
BMI(kg/m2)		26.7 (20.4-28.5)	43 (31-64)	-7.5	<0.001
Neck Circumference(cm)		32 (30-36)	34 (30-37)	-2.6	0.01
		N (%)	N (%)	X^2	P
Sex	Male	20 (19.5%)	58 (58.5%)	0.08	0.78
	Female	5 (5.5%)	17 (16.5%)		

(MW) Mann Whitney test* Chi-square X^2 test

BMI: body mass index

Table (2): Comparison of polysomnographic parameters between both OSA groups:

	Non obese Median (Range)	Obese Median (Range)	test	P
Stop Bang	3(2-5)	4(3-7)	-2.8	0.005
ESS	20(11-24)	22(11-24)	-2.7	0.007
mMRC	2(2-3)	3(2-4)	-2.5	0.01
Sleep efficiency	69.4(27-79.5)	67.2(14.2-79)	-0.63	0.52
AHI	18.2(6-72)	30.9(7.6-106.8)	2.01	0.04
RDI	18.2(6-72)	33.2(10-106.8)	2.2	0.03
ODI	15.8(1.6-84.9)	48.5(11-116.1)	2.7	0.007

ESS: Epworth sleepiness scale

mMRC: modified medical research council

AHI: apnea hypopnea index

RDI: respiratory disturbance index

ODI: oxygen desaturation index

Table (3): Comparison of AHI in different degrees of COPD severity:

COPD severity / *AHI index*	*Mild*	*Moderate*	*Severe*	*KWT*	*P*
	6 (0.7-16.7)	16.2 (0.5-85.2)	59.6 (25-106.8)	16.7	**<0.001**

KWT Kruskal-Wallis Test

COPD: chronic obstructive pulmonary disease

AHI: apnea hypopnea index

Table (4): prevalence of OSA in COPD :

COPD severity / *OSA*	Mild(N=15)		Moderate(N=51)		Severe(N=34)		*Total(N=100)*		X^2	*P*
	N	%	N	%	N	%	N	%		
	5	33.3%	25	49.02%	30	88.2%	60	60%	20.5	**<0.001**

COPD: chronic obstructive pulmonary disease

OSA: obstructive sleep apnea

Table (5): Correlations between AHI index and certain studied parameters within each group

Parameters	*AHI index*			
	Non-obese		Obese	
	r	P	R	P
Age	0.158	0.45	-0.066	0.574
BMI	0.188	0.368	0.504	**<0.001**
PRE FEV1	-0.68	**<0.001**	-0.702	**<0.001**
PRE FVC	-0.007	0.974	-0.653	**<0.001**
FEV1\FVC	-0.505	0.01	-0.456	**<0.001**
POST FEV1	-0.708	**<0.001**	-0.732	**<0.001**
Smoking Index	0.662	**<0.001**	0.746	**<0.001**
Stop Bang	0.435	0.03	0.505	**<0.001**
Ep worth	0.747	**<0.001**	0.734	**<0.001**
mMRC	0.497	0.011	0.571	**<0.001**
Average O2 Saturation	-0.866	**<0.001**	-0.861	**<0.001**
O2 Desaturation Index	0.689	**<0.001**	0.864	**<0.001**
Base Line O2 %	-0.751	**<0.001**	-0.631	**<0.001**
Neck Circumference	0.536	0.006	0.337	0.003

r = Correlation Coefficient

mMRC: modified medical research council

BMI: body mass index

Pre FEV1: previous bronchodilator forced expiratory volume in one second

Pre FVC: previous bronchodilator forced vital capacity

FEV1/FVC: forced expiratory volume in one second on forced vital capacity ratio

Post FEV1: post bronchodilator forced expiratory volume in one second

Table (6): Multiple regression analysis of age BMI, post FEV1, smoking index, base Line O2 % and neck circumference as an independent variable for AHI:

	Unstandardized Coefficients		*Standardized Coefficients*	*T*	*Sig.*	*95.0% Confidence Interval for β*	
	B	SE	β			Lower Bound	Upper Bound
Age	-0.058	0.218	-0.016	-0.268	0.789	-0.491	0.374
BMI	-0.44	0.185	-0.154	-2.376	**0.02**	-0.808	-0.072
POST FEV1	-0.55	0.221	-0.325	-2.482	**0.015**	-0.989	-0.11
Smoking Index	0.198	0.093	0.263	2.132	**0.036**	0.014	0.383
Base Line O2 %	-2.343	0.469	-0.362	-4.992	**<0.001**	-3.276	-1.411
Neck Circumference	1.746	0.923	0.124	1.892	0.062	-0.087	3.579
Pulmonary hypertention(PHT)	0.158	0.203	0.049	0.777	0.439	-0.246	0.562
(Constant)	224.749						

β: regression coefficient; SE: standard error $p < 0.05$ is significant.

Dependent Variable: AHI index

BMI: body mass index

Post FEV1: post bronchodilator forced expiratory volume in one second

5. Discussion

The presence of both COPD and OSA co-existing was termed by Flenley as the "Overlap" Syndrome (4). Poor sleep quality has further identified based on both ESS scale, STOP Bang questionnaire and low sleep efficiency in full polysomonography in these patients. These findings may be important causative risk factors among COPD patients (e.g. increased cardiovascular events, reduced quality of life) in affected individuals (14). In the current study, there was significant difference regarding smoking

index, BMI, neck circumference in obese and non obese groups as they were higher in obese groups. Soler et al., had found that from the 44 COPD patients enrolled in their study diagnosed by pulmonary function tests, an overnight polysomnograpy (PSG) and questionnaires (PSQI, HRQL) were done. They demonstrated that their participants were generally elderly (age 66.8 ± 12.1 years), 56% were male. Also they had found that subjects with COPD-OSA had increased BMI ($p<0.01$), neck circumference ($p=0.04$), and borderline significant greater smoking history ($p=0.06$). One out of four subjects with a BMI <25 were found to have OSA (14). Also, Gunduz et al**.,** had done a study on 183 COPD patients from Ege University Hospital outpatient clinic, dyspnea was assessed by COPD assessment test (CAT), all patients underwent electrocardiography and transthoracic echocardiography, daytime sleepiness was assessed by the Epworth Sleepiness Scale and all patients underwent sleep test with a portable device. They showed that BMI was significantly higher in OS group who were obese compared to COPD group who were non obese (29.6 ± 6.6 vs 25.6 ± 4.9, respectively, $P = 0.03$) (15). Turcani et al**.,** enrolled seventy-nine COPD patients in a study and in 35 of these subjects polygraphy was performed. They found statistically significant relationship between (oxygen desaturation index) ODI and weight ($P=0.007$), BMI ($P=0.020$), neck circumference ($P=0.001$). Patients with ODI over 15/h, compared with those with ODI under 15/h, had a greater weight, BMI and neck circumference. They also found that with increase patients' weight, AHI increased reflecting the effect of weight on AHI (16). In the study done by Marin et al**.,** on 4241 COPD patients who were assessed by Epworth Sleepiness Scale and underwent an attended overnight polysomnography. They had found that ODI, RDI and AHI were

higher in the overlap syndrome (OSA and COPD) when compared to patients with COPD without OSA (17). In the current study OSA increases with increasing COPD severity (either obese or non-obese) with total prevalence 60%. OSA prevalence in non-obese COPD was 28% and 70% in obese patients. Anisa et al., demonstrated that COPD patients with severe degree are 4.39 times greater risk to suffer from OSA than mild to moderate COPD patients and each centimetre increase of waist circumference has higher risk of OSA (18). Patil et al**.,** found that out of 30 COPD patients 23 had OSA, of which 4 patients (17.33%) had normal BMI and 19 patients (82.6%) were overweight (19). In a study done by Wan et al., on 106 stable COPD patients. Portable monitoring, echocardiography and questionnaires (ESS and mMRC) were done. They had found a high prevalence of OSA in patients with COPD with total prevalence 52.8% (20). Also, Solar et al had found a prevalence of OSA of 65.9% in patients with confirmed diagnosis of moderate to severe COPD (14). On the other hand in the study done by Narasimhan et al., on 66 COPD patients who were subjected to overnight Polysomnography and questionnaires (ESS and mMRC). They found that total prevalence of OSA was 53% (21). In the current study OSA severity (represented by AHI) was significantly correlated BMI, FEV1, smoking index, sleep questionnaire and polysomnographic parameter. Also, McNicholas had found that patients with COPD were overwhelmingly smokers or ex-smokers. Smoking can lead to inflammation of the upper airway which in turn could lead to swelling, narrowing, and thus increasing the propensity to airway closure. Indeed OSA was reported to be approximately three times more prevalent in ever- smokers than never-smokers (22).

On the other hand in a similar new study done by Philippe and Ali on 225 COPD patients. They reported that there was no significant association observed between severity of airflow limitation and AHI ($P = .31$). This result did not match the one obtained from the current study and this may be explained by smaller number of patients included in the current study which may be non representative (23). Multivariate logistic regression analysis which revealed that BMI, Post FEV1, smoking index and baseline oxygen were independent predictors of OSA in COPD patients with with no impact of pulmonary hypertention on OSA (reflected by AHI) in COPD patients. A cohort study on south indian patients, Sreedharan et al., enrolled 152 patients and polysomnography was done to study demographic, clinical, and polysomnographic predictors of OSA severity. They had found that in multivariate analysis among the PSG parameters, longer apnea duration and more severe nocturnal hypoxemia as evidenced by higher desaturation index and nocturnal desaturation occupying >10% of total sleep time correlated independently with OSA severity. They had showed a positive correlation of OSA severity with nocturnal hypoxemia (24). Also, Sun et al., performed a study on 106 patients with COPD who performed home portable nocturnal sleep monitoring and echocardiography. They found that median pulmonary artery pressure (PAP) were similar in the COPD with OSA group and the COPD without OSA group. They did not find significant correlation between AHI and PAP (25). Another study done by Izabella et al., on 1566 patients with suspected OSA. In the univariate regression analysis gender, age, BMI, neck circumference(NC), hip circumference(HC), waist circumference, ESS and smoking index were associated with OS. In the multiple logistic regression analysis, BMI, NC, HC, ESS and smoking index were only the

independent variables for OSA (26). Also, Jing et al., from the 766 COPD patients enrolled in their study had found that (overlap syndrome) OS patients had a higher BMI than patients with COPD only. Moreover, their multiple regression analysis had found that the BMI had a positive correlation with the AHI in OVS patients, which suggested that the BMI seems to be a significant predictor for OSA in COPD patients (27). In the study done by Sharma et al., on 206 COPD patients who underwent polysomnography and pulmonary function test. They demonstrated that BMI, male gender, relative-reported snoring index and choking index were independent predictors of OSA. BMI, as a continuous variable, was a significantly independent predictor of OSA, suggesting thereby that the risk of developing OSA rises in a continuous fashion with increasing BMI (28).

6. Conclusions

From this study, it can be concluded that:

- High prevalence of sleep disordered breathing in patients with moderate to severe COPD.
- Obese COPD more susceptible to develop OSA.
- AHI increased with increase COPD severity leading to more complication and exposed COPD patient to nocturnal hypoxaemia which decrease quality of life.

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Author contributions

All authors were involved in the study design, analysis, interpretation of the data and revising its content. All authors agree to be accountable for all aspects of the work.

Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Ethical approval

The Research Ethics Committee at the Faculty of Medicine, Benha University has approved the study. Informed consent was obtained from every single individual member incorporated into the study.

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