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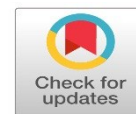*Research Article*

Obesity hypoventilation syndrome in patients with obstructive sleep apnea: prevalence, demographic and clinical characteristics

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Abstract

Background: Obstructive sleep apnea syndrome (OSAS) and obesity hypoventilation syndrome (OHS) are two common syndromes that are associated with obesity. They frequently coexist. Patients with combined OSA-OHS have a higher risk of pulmonary hypertension as well as higher morbidity and mortality. The aim of the study is to estimate the prevalence of OHS in patients with OSA and to compare the demographic and clinical characteristics of patients with pure OSA and those with combined OSA-OHS. **Methods:** Ninety patients with OSAS were enrolled in this study. For all patients, the STOP BANG questionnaire and Epworth scale (ESS) were calculated, body mass index and neck circumference were measured, CBC, arterial blood gases, thyroid function tests and lipid profile were done. Adiponectin level was measured in all patients. PFT and echocardiography were done and a sleep study was done to confirm the diagnosis of OSA. **Results:** Patients were divided into two groups: group I included 74 patients with combined OSA-OHS and group II included 16 patients with pure OSA. BMI (P = 0.04), neck circumference (P = 0.001), and ESS (P = 0.03) were all statistically significantly higher in Group I patients. PASP was found to be elevated in both groups, with a statistically significant increase in group I patients. The AHI (P=0.04) and number of desaturations with Spo2 less than 90% (P= 0.016) were significantly higher in group I patients. **Conclusion:** OHS is a very common association with OSAS. The association of the two syndromes results in a greater increase in comorbidities.

Keywords: obesity, obstructive sleep apnea, apnea hypopnea index, obesity, hypoventilation.

Introduction

Obesity is a serious health condition that affects millions of people all over the world. It is associated with many other medical problems. Sleep-disordered breathing is among the significant medical disorders that are associated with obesity. It is well established that obesity is a significant risk factor for obstructive sleep apnea (OSA) [1.] In two previous studies, more than 80% of severely obese patients were found to have OSA [1,2]

Obesity hypoventilation syndrome (OHS) is another sleep-disordered breathing condition that is related to obesity. The characteristic feature of OHS is the presence of daytime hypoventilation without any other causes of hypoventilation [3].

Although OSA and OHS are two different clinical syndromes, they frequently occur concurrently. When patients with OHS-OSA were compared to obese patients with pure OSA, studies revealed that patients with OHS-OSA had a higher risk of pulmonary hypertension as well as morbidity and mortality [4-6].

The presence of OHS in patients with OSA may pass unrecognized   because the presenting symptoms of both conditions are non-specific and the two syndromes frequently coexist. Therefore, patients with OHS are often underdiagnosed and undertreated, resulting in an increased risk of recurrent hospital admission and an increased risk of death [7].

The prevalence of OHS in patients with OSA varies in different studies, ranging from 11 to 42.1% [8]. When compared to patients with pure OSA, OHS has been linked to a higher economic burden, [9] increased morbidity, [10] and mortality, [11,15]. Therefore, it is of great importance to look for the presence of OHS in patients with OSA.

Aim of study

The primary objective of the study was to estimate the prevalence of OHS in patients with OSA. And to compare the demographic and clinical characteristics of patients with pure OSA and those with OSA in association with OHS.

Methods

It was a prospective observational cross sectional study; ninety patients were enrolled in this study. All the patients were confirmed to have OSAS according to Polysomnographic studies. They were recruited from the polysomnography unit and inpatients ward of our Cardiothoracic University hospital. patients with obstructive or restrictive lung diseases, neuromuscular disorders, chest wall abnormalities were excluded from the study.

OSA is diagnosed according to the standard diagnostic criteria of the international classification of sleep disorders. [12]   The diagnosis of OHS was based on the presence of the classic triad of obesity, diurnal increase in CO_2 tension, and sleep-disordered breathing without any evidence for the presence of other known causes of hypercapnia. [13]

Data collection tools:

1)Thoroughly history taking, general and local chest examination.   All patients provided the following information: age, gender, smoking status and index, comorbidities such as hypertension and diabetes, and OSA symptoms (snoring, daytime sleepiness, witness apnea, nocturia).

2)Two sleep questionnaires: STOP   BANG questionnaire and Epworth scale

3) Anthropometric measurements such as, body mass index and neck circumference measurement

4) Laboratory investigations:

All subject underwent routine investigations including: complete blood count (CBC), renal function test, liver function test, random blood sugar, arterial blood gases, thyroid function tests (TSH, free T3 and free T4) and lipid profile assessment

5) Spirometry: was performed using a spirometer (ZAN 300, Germany).

6) Echocardiography: Echocardiogram was performed to assess pulmonary artery systolic pressure (PASP).

7) Polysomnography: The following parameters were obtained from the sleep study:

a. AHI (numbers of apnea and hypopnea per hour of sleep duration).

b. ODI (numbers of oxygen haemoglobin saturation drops of 3% or more per hour of sleep duration).

c. RDI is the number of respiratory events per hour of sleep.

d. Minimum O_2 value: the lowest oxygen level recorded during the polysomnogram.

e. The number of desaturations below 90%.

f. During the polysomnogram, the average SpO2 [%] was recorded

Ethical approval:

The study was approved by the ethics committee of Minia University Faculty of Medicine with approval no. 226-2022. Informed consent was taken from all participants.

Statistical Analysis:

Using Microsoft Excel software, data gathered throughout time, basic clinical examinations, laboratory investigations, and outcome measures were coded, tabulated, and analysed. The Statistical Package for the Social Sciences (SPSS software version 25.0) programme was then used to input the data and perform analysis.

Results

Ninety patients were enrolled in this study from the polysomnography unit and inpatient ward of Cardiothoracic University Hospital during the period from July 2019 to January 2020. 30 (33.3%) males and 60 (66.67%) females. Their age ranged from 32 to 72 years old. Out of the ninety patients, 16 patients had a diagnosis of pure OSA without hypercapnia and 74 patients had a diagnosis of combined OSA-OHS syndrome. Demographics, spirometric measurements, ESS scores, pulmonary artery pressure and ABG analysis results of the OSA-OHS

patient group (Group I) and pure OSA patient group (Group II) are given in table (1).

A significant statistical difference was observed between both groups regarding BMI, neck circumference, ESS, and arterial blood PH, PCO2, PO2 and HCO3 with statistically significant higher BMI (P = 0.04), neck circumference (P= <0.001) and ESS (P= 0.03) in group I patients. Regarding ABG measurements, there were significantly higher PCO2 (P <0.001) and HCO3 (P <0.001) in group I patients, while PO2, SO2 and PH were significantly lower in this group (P = 0.018, 0.003 and <0.001 respectively).

Among comorbidities, hypertension was found in 62.2% and 37.5% of group I and group II patients respectively, with no statistically significant difference between them. Also, DM was found in group I and group II patients in 18.9% and 25% of patients respectively, without a statistically significant difference. Pulmonary artery systolic pressure was found to be elevated in both groups,

with a statistically significant increase in group I patients.

Table (2) represents the laboratory data among the 2 studied groups. Hemoglobin level was significantly higher in group I patients than in group II patients (P = 0.005*). Serum bicarbonate level was found to be higher in OHS group (P <0.001*). Lipid profile values elucidated significantly higher TC and LDL levels in group I patients (P = 0.030* and 0.005* respectively).

Polysomnography data for the OHS and pure OSA groups are given in table (3). The AHI (P =0.04) and the number of desaturations with Spo2 less than 90% (P = 0.016) were significantly higher in group I (OHS) patients. The mean Spo2 (P =0.021) and minimal Spo2 (P = 0.032) were significantly lower in group I patients.

Table (1) Demographic, spirometric measurements, ESS scores, Pulmonary artery pressure and ABGs analysis results of OSA-OHS patient group (Group I) and pure OSA patient group (Group II)

Variable	Group I N=74	Group II N=16	P -value
Age: Range (mean±SD)	37-72 (57.4± 8.5)	32-69 (56.1 ±11.1)	0.47
Gender(freq.) Male Female	26 (35%) 48 (65%)	4(25%) 12 (75%)	0.69
Smoking history: No (%)	40 (54%)	8 (50%)	0. 53
BMI (mean±SD)	48± 6.9	42± 5.3	0.04*
Neck circumference (mean±SD) cm	46.7±3.9	41.3 ± 6.1	<0.001*
Comorbidity: No (%) HTN DM	46 (62.2%) 14(18.9%)	6 (37.5%) 4(25%)	0.25 0.65
FEV1 (mean±SD) % predicted	56.4± 15.3	64.9 ±15	0.16
FVC (mean±SD) % predicted	51.9±11.9	59±10.8	0.12
FEV1/FVC (mean±SD)	78.1±13.9	78.1±12.2	0.99
ESS score (mean±SD)	19.3± 2.7	15.2± 2.6	0.03*
PASP (mean±SD)	59.1± 11.3	47.4 ± 12.5	0.04
ABG **PH** (mean±SD) **PaCO2**(mean±SD) mmHg **PaO2**(mean±SD)mmHg **HCO3 (**mean±SD) mmol/ l	7.4± 0.04 51.2± 9.8 49.1 ±10.6 35.4± 4	7.4 ±0.1 34.8± 8.7 59.9± 14 24.8 ±4.5	<0.001* <0.001* 0.018* <0.001*

*significant (P value < 0.05). SI: Smoking Index. BMI: Body Mass Index. ESS=Epworth Sleepiness Score. ABGs=Arterial Blood Gases. Kg/m2=Kilogram per square meter. Cm=Centimeter. DM= Diabetes Mellitus. FVC=Forced Vital Capacity. FEV1= Forced Expiratory Volume in first second. Paco2=Partial pressure of Carbon dioxide tension. Pao2= Partial pressure of Oxygen tension. HCO3= Bicarbonate. *significant if P <0.05

Table (2) laboratory data of the study groups

Variable	Group I N=74	Group II N=16	P -value
Hemoglobin(mean±SD)	12.9±1.7	11±1.5	0.005*
TLC	7.4±1.7	8.4±3.6	0.486
Bicarbonate level (mean±SD) mmol/L	36.2±3.0	25.1±4.2	<0.001*
TC median (IQR)	275 (214.5-334)	193.5 (131.5-240)	0.030
TG median (IQR)	130(89.5-212.5)	140.5 (92-233.3	688.0
HDL(mean±SD)	46.3±10.4	40±10.4	0.126
LDL median (IQR)	186 (141.5-222)	108.5 (75-144.5)	0.005*

SD= standard deviation, TLC= total leucocytic count, IQR= interquartile range, mmol/L= millimol per liter, TC= total cholesterol, TG= triglycerides, HDL= high density lipoproteins, LDL= low density lipoproteins. *significant if P <0.05

Table (3) Polysomnographic data of the study groups

Variable	Group I N=74	Group II N=16	P -value
AHI median(IQR)	55 (27-86)	27 (12-55.5)	0.04*
Mean Spo2 median(IQR)	81 (74-86)	90 (82.8-92.8)	0.021*
Minimal Spo2 median(IQR)	50 (45-62)	82.5 (52-85)	0.032*
Sleep time spent with Spo2less than 90% median (IQR)	94 (90-96.5)	86 (60-97.8)	0.988
Number of desaturation with Spo2less than 90% median (IQR)	173 (77-216.5)	81.5 (40.5-109.5)	0.016*

AHI= Apnea Hypopnea Index, IQR= Interquartile Range, Spo2= Arterial Oxygen saturation, *significant if P <0.05

Discussion

In this study, we evaluated ninety patients with OSA whose diagnosis was confirmed with polysomnography. OHS was found to be present in 74(82%) of the patients.

The prevalence of OHS in our patients was markedly higher than the reported prevalence in other studies. It was reported that the prevalence of OHS in patients with OSA varied in different studies, ranging from 11 to 42.1%. [8] This could be attributed to the different studies' populations, different numbers and different study designs.

When the demographic data from both groups were compared, there were no significant differences in terms of age, gender, or smoking history. (P= 0.74, 0.699 and 0.20 respectively). These data agree with Bingol et al.,[8] as they found that OSA-OHS patients were insignificantly older than pure OSA patients (P = 0.27) and they also found an insignificant difference between both groups regarding gender and smoking history (P = 0.059 and 0.20 ,respectively). Similarly, a study of Elsayed et al.,[14] found non-significant difference between OSA and OHS patients regarding age and gender (P = 0.382 & 0.430 respectively).

Our subjects with OSA-OHS had significantly higher BMI and neck circumference than pure OSA patients (P =0.04 and < 0.001*

respectively). Supporting these results, a study of patro etal., [15] showed significant increase in BMI and neck circumference in OHS than OSA patients (38.01±6.91 and 42.1±3.82 vs 32.20±5.46 and 38.92±3.77, P = 0.004 and 0.015 respectively).

Similar to our results, Bingol et al., [8] found that OHS patients had significantly higher BMI mean ± SD (41.3 ± 6.2) than pure OSA group patients (39.2 ± 5.0) with (P= 0.02) and also higher neck circumference in the OHS group than the pure OSA group (42.2 ± 4.1 vs 40 ± 3.7 respectively) with (P < 0.001). Also, Tarkada et al., [16] reported that subjects with OHS were more obese and had a higher neck circumference. Liu et al., [17] also documented that OHS patients had greater neck circumference and BMI than pure OSA patients.

Elsayed et al., [14] found that OHS patients were significantly more obese than OSA patients measured by mean ± SD of BMI (P = 0.002), while the increase in neck circumference in their study was insignificant (P = 0.136) and this may be due to change in the number of patients.

The present study showed that hypertension and DM were common in both groups, with 62.2% and 18.9% in group I versus 37.5% and 25% in group II respectively without statistically significant differences between both groups (P = 0.254 & 0.651 respectively). Galal and Kamal [18] also found insignificant difference between both groups regarding the occurrence of DM and hypertension (P = 0.052 and 0.262 respectively). Moreover, in agreement with our results, Bingol et al., [8] found hypertension in 50% and 47.7% of OHS and pure OSA respectively and DM in 31.2% and 29.5% in both groups respectively, with no significant difference (P = 0.46 for both hypertension and DM). Basoglu et al., [19] Macavei etal., [20] also supported the present results as they documented that the most common comorbidities in OHS are hypertension, DM, hyperlipidemia, congestive heart failure and gastroesophageal reflux disease. Near to the current results regarding comorbidities in OHS, a study of Alzaabi etal.,[10] showed DM to be found in 44.4% of patients and arterial hypertension in 55.6%.

The severity of pulmonary hypertension in OHS is variable. In a series of 27 patients with OHS, Kessler etal., [22] found an average PVR of 4 Wood units and mPAP of 23 mmHg. This is in contrast with the much higher PAP and PVR reported in the study of Held et al. [23].

In the current study, pulmonary artery systolic pressure was found to be higher in both groups of patients. However, in patients with combined OSA-OHS the elevation was significantly more than in patients with pure OSA. (P=0.04). Naeije [21] reported that up to 50% of OHS patients present with pulmonary hypertension, as compared with a small percentage of patients with pure OSA. Alzaabi et al., [10] also found pulmonary hypertension to be found in 33.3% of OHS patients.

The current study results showed significantly higher levels of TC and LDL in the OSA-OHS group than in the pure OSA group (P = 0.030 & 0.005 respectively), while there are no significant differences in the level of TGs or HDL. Macavei et al., [20] found hyperlipidemia in 45% of OHS patients and 41.7% of pure OSA patients. Borel et al. [24] found an insignificant difference between levels of TC and LDL in OHS compared to pure OSA.

Some laboratory tests were investigated during the current study. Serum hemoglobin was found to be significantly higher in the OHS group than in the pure OSA group (P= 0.005). Elsayed et al., [14] discovered a non-significant increase in hemoglobin levels in the OHS group (P = 0.153). This difference may be due to difference in number of patients or more pronounced hypoxia in OSA-OHS patients in the current study causing increase in hemoglobin level.

In the current study, spirometric parameters showed restrictive pattern as evidenced by lower FEV1% and FVC% with a normal FEV1/FVC% ratio. This is supported by the findings of kaw et al., [25] who discovered restrictive pattern in their subjects.

Our data revealed non-significant difference between both groups of patients in regard to the spirometric parameters. Our finding is supported by the results of Bingol et al., [8] as they showed insignificant differences between OHS and pure OSA group patients as regards FVC, FEV1 and FEV1/FVC (P= 0.25, 0.59 and 0.27 respectively).

Basoglu et al., [19] reported that Epworth sleepiness scores were higher
(14.0 vs 11.9, respectively, p = 0.021) in OHS than OSAS patients.

This matches with the current study that revealed also that ESS was significantly higher in OSA-OHS group than pure OSA group (19.3± 2.7 and 15.2 2.6 respectively, P= 0.03). When looking at ABG values, the study of Bingol et al.,[8] showed that subjects with OHS had significantly lower PaO2 (P <0.001), higher PaCO2 (P= <0.001) and HCO3 (P= <0.001) than pure OSA patients. The same results were found with Basoglu et al.,[19] (P= <0.0001 for all). Both studies found that serum HCO3 ≥ 27mmol/L is useful to determine OHS. These results are in agreement with the current study that also elucidated lower PaO2 (P = 0.018), higher PaCO2 (P <0.001) and HCO3 (P <0.001) in OSA-OHS patients. The current results also revealed a lower PH in this group (P <0.001) that is mostly due to increased PaCO2. Resta et al., [26] also found significantly lower PaO2 and higher PaCO2 in OHS patients (P <0.0001).

Polysomnography values showed significantly higher AHI, numbers of desaturation with Spo2 less than 90% and lower mean and minimal SaO2 in OSA-OHS patients than pure OSA group (=0.04, 0.016, 0.021 and 0.032 respectively). In concordance with these results, Bingol etal., [8] found the same difference between both groups of patients with P= 0.01 for AHI and < 0.01 for the other 3 values. In agreement with our results, Galal etal., [26] study also revealed significantly higher RDI, and lower mean and minimal SaO^2.

Conclusion
OHS is a very common association with OSAS. The association of the two syndromes results in more increase in comorbidities, which could in turn affect morbidity and mortality. Because the treatment of pure OSAS differs from the OSA-OHS syndromes, it is crucial to look for the presence of OHS in patients with OSAS.
The study is limited by the small number of patients with pure OSAS, and it is recommended to have more studies with a large number of patients to validate our results.

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