

Evaluation of thyroid functions and obesity in obstructive sleep apnea syndrome

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SUMMARY

OBJECTIVE: Obstructive sleep apnea syndrome is associated with many chronic diseases.

METHODS: Obesity and thyroid function tests were evaluated retrospectively and cross-sectionally for 782 obstructive sleep apnea syndrome patients.

RESULTS: The mean patient age was 49.3 ± 11.5 years, and the majority were obese (67.9%) or overweight (26.6%). The mean age of the patients in Group 2 (moderate/severe obstructive sleep apnea syndrome) was higher than that of Group 1 (simple snoring/mild obstructive sleep apnea syndrome). The rate of severe obstructive sleep apnea syndrome among obese patients (35.2%) was significantly higher than that of normal-weight (11.6%) and overweight (18.3%) patients ($p=0.001$). The oxygen desaturation index/apnea-hypopnea index and levels of leukocytes and C-reactive protein were significantly higher, while mean/minimum saturation values and hemoglobin, hematocrit, and free triiodothyronine levels were significantly lower among obese patients compared with overweight and normal-weight patients ($p=0.001$). Leukocytes, C-reactive protein, and apnea-hypopnea index/oxygen desaturation index values were higher, and mean/minimum saturation values were lower in Group 2 than in Group 1.

CONCLUSION: There were relationships between obstructive sleep apnea syndrome severity and body mass index. Obesity could be a critical predisposing factor for sleep disturbances. The prevention and control of obesity is important while being treated for obstructive sleep apnea syndrome.

KEYWORDS: Body fat distribution. Body mass index. Obesity. Sleep apnea, obstructive.

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a frequent sleep disorder in the middle-aged population¹. Obesity, with increased body fat ratio (BFR), has been associated with numerous chronic diseases¹. OSAS is related to not only primary obesity but also many chronic diseases¹.

Many endocrine and inflammatory parameters are suspected to be associated with obesity and ultimately OSAS². Hypothyroidism and OSAS are both common in the general population and show some clinical overlap^{3,4}. This study investigates the relationships among obesity, thyroid function tests (TFTs), and OSAS using polysomnography (PSG).

METHODS

Study design and ethical approval

In this retrospective cross-sectional study, medical documents of inpatients who underwent PSG in the Polysomnography Unit of Sivas Numune State Hospital, Turkey, in 2012-2018

were evaluated. The study was planned in accordance with the recommendations of the Declaration of Helsinki and good clinical practice guidelines, and the Institutional Ethics Committee for Clinical Research approved the study (Date: 05.05.2021, No.: E-70632468-050.01.04-70430/2021/229).

Study population

The medical records of 960 inpatients who underwent PSG were reviewed. Patients who had active systemic infections or endocrinological and hematological disorders were excluded. These cases were analyzed according to body mass index (BMI) values (i.e., normal weight, overweight, and obese) and OSAS severity (i.e., Group 1: simple snoring/mild OSAS and Group 2: moderate/severe OSAS).

BMI values were calculated as $\text{weight (kg)}/\text{height}^2 \text{ (m}^2\text{)}$ and grouped as follows: BMI <25, normal weight; BMI 25-30, overweight; and BMI >30, obese. BFR was estimated using the Deurenberg equation $[(1.2 \times \text{BMI}) + (0.23 \times \text{years of age}) - (10.8 \times G) - 5.4]$.

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Polysomnography studies

Under the surveillance of a technician, PSG was performed during an overnight stay. An Embla S4500 PSG device was used for visual and auditory recording. Electromyogram (EMG/submental), electromyogram (EMG/right/left tibialis), two-channel electrooculogram (right/left EOG), and four-channel electroencephalogram were used. Pulse oximetry and nasal airflow were monitored overnight for blood oxygen saturation levels. The mean and minimum values of oxygen saturation were calculated from overnight records.

Mean oxygen saturation of at least 4% below the basal value per hour reflects the oxygen desaturation index (ODI). Data were manually scored, and PSG results were classified according to the American Academy of Sleep Medicine guidelines⁵.

The number of total episodes of apnea and hypopnea per hour of sleep constitutes the apnea-hypopnea index (AHI), which was evaluated by PSG and oxygen saturation records. Apnea is defined as a lack of nasal airflow for at least 10 s. The presence of any of the following criteria defines hypopnea: 50% decrease in airflow for at least 10 s, oxygen desaturation of at least 3%, development of arousal, more than 30% reduction in airflow for at least 10 s, or 4% reduction in oxygen saturation. AHI values were classified as follows: AHI <5, simple snoring; 5 ≤ AHI <15, mild OSAS; 15 ≤ AHI <30, moderate OSAS; and AHI ≥30, severe OSAS.

Laboratory studies

Laboratory values of free thyroxine (FT4), free triiodothyronine (FT3), thyroid-stimulating hormone (TSH), C-reactive protein (CRP), and complete blood count (CBC) were obtained from the medical records of patients.

Statistical analysis

Kolmogorov-Smirnov and Shapiro-Wilk tests were used to determine normality. Descriptive data were evaluated as percentage (%), number (n), and mean ± standard deviation (minimum-maximum). For mean values of data with and without normal distribution, independent-samples t-tests and Mann-Whitney U tests were used, respectively. The comparison of more than two normally distributed groups was performed using one-way ANOVA. Differences between more than two groups without normal distribution were analyzed using the Kruskal-Wallis test. Mann-Whitney U tests and Bonferroni correction were performed for post-hoc analysis. Numerical data were analyzed using Spearman correlation tests. Correlations (r) were accepted as weak at r=0.05-0.30, weak to moderate at 0.30-0.40, moderate at 0.40-0.60, strong at 0.60-0.70, very strong at 0.70-0.75, and perfect at 0.75-1.00. The results were evaluated using SPSS 16.0 (SPSS Inc., Chicago, IL, USA). Values of p<0.05 were accepted as statistically significant.

RESULTS

The mean age of the 782 patients in this study was 49.3±11.5 years, and most of them were males (55.2%). The number of patients with OSAS (83.1%) was greater than the number of patients with simple snoring (16.9%). The majority of patients were either overweight (26.6%) or obese (67.9%). Flowchart of OSAS patients with their BMI is shown in Figure 1. Laboratory results of all patients are shown in Table 1.

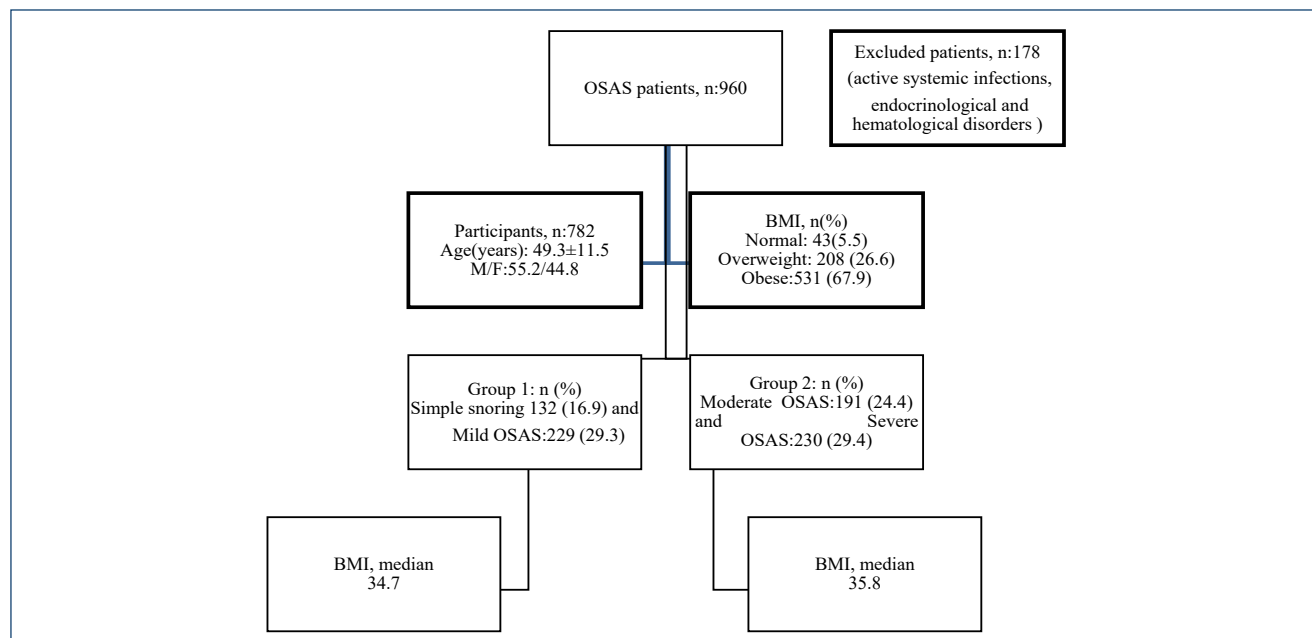


Figure 1. Flowchart of obstructive sleep apnea syndrome patients with their body mass index.

Table 1. Demographics and clinical characteristics of patients grouped according to the severity of obstructive sleep apnea syndrome.

Parameters	All patients	Group 1	Group 2	p
Age (years)	49.3±11.5	46.4±11.4	51.8±11	0.001*
Hemoglobin (g/dL)	14.7 (8.2-19.7)	14.3 (8.2-18.5)	14.3 (10.6-19.7)	0.810
Hematocrit (%)	43.4±5.2	42.4±5.7	43±5.3	0.260
Leukocyte (K/UL)	7.9 (0.5-20.5)	7.8 (3.9-16.6)	8.5 (0.5-20.5)	0.002^a
CRP (mg/L)	0.5 (0.0-23.1)	0.5 (0.0-11.8)	0.6 (0.0-23.1)	0.001^b
TSH (mU/L)	1.7 (0.0-11.3)	1.7 (0.1-10.8)	1.7 (0.0-10.3)	0.772
FT4 (ng/dL)	1.2 (0.1-5.5)	1.2 (0.8-2.7)	1.2 (0.1-3.7)	0.143
FT3 (ng/dL)	3.1±0.5	3.1±0.5	3.0±0.5	0.159
Body mass index	32.6 (20.1-57.8)	34.7 (30.0-51.1)	35.8 (30.0-57.8)	0.002^v
Body fat ratio	40.0±11.8	43.5±10.3	46.2±10.1	0.003^{ff}
AHI	16.5 (0.0-109.8)	6.4 (0.0-15)	32.0 (15.0-109.8)	0.001^s
Mean saturation	91.6 (61.4-97.6)	92.5 (66.3-97.6)	90.3 (61.4-96.5)	0.001^μ
Minimum saturation	80.0 (50.0-95.0)	85.0 (50.0-95.0)	75.0 (50.0-89.0)	0.001^e
ODI	18.9 (0.1-113.9)	7.8 (0.1-58.6)	36.3 (5.7-113.9)	0.001^γ

Data are shown as Mean±SD or median (minimum–maximum). *p<0.05: significant; BMI: body mass index; CRP: C-reactive protein; TSH: thyroid-stimulating hormone; FT3: free triiodothyronine, FT4: free thyroxine AHI: apnea-hypopnea index; ODI: oxygen desaturation index; OSAS: obstructive sleep apnea syndrome; Group 1: simple snoring and mild OSAS; Group 2: moderate and severe OSAS. *Age was significantly higher in group 2 than group 1; ^aleukocyte count was significantly higher in group 2 than group 1; ^bCRP was significantly higher in group 2 than group 1; ^vBMI was significantly higher in group 2 than group 1; ^fBFR was significantly higher in group 2 than group 1; ^sAHI was significantly higher in group 2 than group 1; ^μmean saturation was significantly lower in group 2 than group 1; ^eminimum saturation was significantly lower in group 2 than group 1; ^γODI value was significantly higher in group 2 than group 1.

Age, BMI, BFR, leukocyte, CRP, AHI, and ODI values were higher, and mean/minimum saturations were lower in Group 2 compared with Group 1 (Table 1).

Estimated BFR values were significantly higher in obese patients (p=0.001), as was the incidence of severe OSAS (35.2%), in comparison with normal-weight and overweight patients (p=0.001). ODI and AHI values (18.4 and 22.6, respectively) were significantly higher, while mean and minimum saturation values (90.6 and 77, respectively) were significantly lower in obese patients (p=0.001) (Table 2).

Obese patients had significantly lower hemoglobin and hematocrit than the overweight and normal-weight patients (p=0.001). In addition, mean leukocyte and CRP levels were significantly higher, and mean FT3 was lower in obese patients than in overweight and normal-weight patients (p=0.001) (Table 2).

No significant correlations between laboratory tests and AHI, ODI, or mean and minimum saturations were found (r<0.05). AHI was weakly positively correlated with age (r=0.262), BMI (r=0.267), and BFR (r=0.233), and ODI and age were also weakly positively correlated (r=0.285). Weak to moderate positive correlations existed between ODI and BMI (r=0.363) and BFR (r=0.324). Mean saturation was moderately negatively correlated with age (r=-0.451), BMI (r=-0.457), and BFR (r=-0.447). Minimum saturation was weakly-moderately

negatively correlated with age (r=-0.365) and moderately negatively correlated with BMI (r=-0.449) and BFR (r=-0.451) (p=0.001 for all correlations).

DISCUSSION

In this study, relationships between obesity, TFTs, and OSAS were investigated. Severe OSAS was more common, and mean/minimum oxygen saturation levels were lower in obese patients.

Obesity is known to increase the risk of systemic disease, and there are various studies of its effects on surgical outcomes^{2,6}. BMI is a risk factor for complications in the perioperative and postoperative periods of abdominal surgery⁶. However, the relationships between obesity and thoracic surgery outcomes remain unclear. Lung cancer is the most common cause of cancer-related deaths worldwide, and surgical resection is important in its treatment^{6,7}. Obese patients who underwent lung lobectomy due to lung cancer were found to have longer operative times compared with non-obese patients and higher rates of postoperative morbidities⁶. However, the rates of perioperative and postoperative complications and postoperative mortality were similar between the groups and higher BMI did not affect the chosen surgical approach⁶. In another study comparing patients undergoing thoracoscopic anatomic lung cancer surgery, the differences between

Table 2. Clinical characteristics of patients grouped according to body mass index.

	Normal weight (n=43)	Overweight (n=208)	Obese (n=531)	p
Hemoglobin (g/dL)	15.1 (11.3-17.4)	15.3 (10.5-18.5)	14.3 (8.2-19.7)	0.001*
Hematocrit (%)	44.7 (34.1-53.8)	45.0 (33.7-55.0)	42.8 (0.0-60.6)	0.001^α
Leukocyte (K/UL)	7.7 (1.0-12.4)	7.5 (0.0-19.0)	8.2 (0.5-20.5)	0.001^α
CRP (mg/L)	0.2 (0.0-6.7)	0.3 (0.0-14.7)	0.5 (0.0-23.1)	0.001^γ
TSH (mU/L)	1.8 (0.6-4.8)	1.8 (0.0-11.3)	1.7 (0.0-10.8)	0.338
FT4 (ng/dL)	1.2 (1.0-1.5)	1.2 (0.3-5.5)	1.2 (0.1-3.6)	0.065
FT3 (ng/dL)	3.1±0.4	3.3±0.6	3.1±0.5	0.001^η
AHI	3.0 (0.0-45.4)	14.5 (0.3-87.5)	18.4(0.0-109.8)	0.001^ς
Mean saturation	94.2 (79.7-96.8)	92.5 (63.9-96.4)	90.6 (61.4-97.6)	0.001^μ
Minimum saturation	89.0 (51.0-94.0)	84.0 (50.0-92.0)	77.0 (0.0-95.0)	0.001^ε
ODI	3.8 (0.1-60.4)	14.3 (0.3-97.8)	22.6 (0.2-114)	0.001^ν
Simple snoring, n (%)	25 (58.1)	43 (20.7)	64 (12.1)	0.001[†]
Mild OSAS, n (%)	10 (23.3)	68 (32.7)	151 (28.4)	
Moderate OSAS n (%)	3 (7.0)	59 (28.4)	129 (24.3)	
Severe OSAS, n (%)	5 (11.6)	38 (18.3)	187 (35.2)	
Body fat ratio	22.3 (14.4-38)	29 (20.0-46.0)	44.9 (25.1-74.8)	0.001*

Data are shown as Mean±SD or median (minimum–maximum). BMI: body mass index; CRP: C-reactive protein; TSH: thyroid-stimulating hormone; FT3: free triiodothyronine; FT4: free thyroxine; AHI: apnea-hypopnea index; ODI: oxygen desaturation index; OSAS: obstructive sleep apnea syndrome; SD: standard deviation. p<0.05: significant. *Obese patients had significantly lower hemoglobin than the overweight and normal-weight patients; ^αobese patients had significantly lower hematocrit than the overweight and normal-weight patients; ^βmean leukocyte was significantly higher in obese patients than overweight and normal-weight patients; ^γCRP levels were significantly higher in obese patients than overweight and normal-weight patients; ^ηmean FT3 was lower in obese patients than overweight and normal-weight patients; ^ςAHI values were significantly higher in obese patients; ^μmean saturation values were significantly lower in obese patients; ^εminimum saturation values were significantly lower in obese patients; ^νODI values were significantly higher in obese patients; [†]severe OSAS was higher in obese patients than overweight and normal-weight patients; *BFR values were significantly higher in obese patients than overweight and normal-weight patients.

intraoperative transfusions, conversion rates, and postoperative outcomes were not significant, although higher rates of intraoperative hypoxemia and new-onset arrhythmias were reported among obese patients compared with non-obese patients⁸.

Obesity is also related to sleep disturbances, particularly OSAS. OSAS can lead to obesity due to increased appetite by affecting the levels of obesity-related hormones⁴. Male gender and advanced age are associated with OSAS⁹, and abdominal obesity was shown to be associated with increased AHI^{10,11}. However, no studies of the relationships between OSAS and BFR as a measure of obesity were found in the literature. In this study, severe OSAS was more common, and mean/minimum oxygen saturation levels were lower in obese patients. Furthermore, increased AHI and decreased mean/minimum saturation levels were found in relation to increased BFR.

Leukocytes are the main elements of inflammatory processes. Adipose tissue is a source of inflammatory proteins, and a positive correlation was shown between adipose tissue and inflammatory markers^{12,13}. In this study, levels of CRP and leukocytes were found to be higher in obese patients than in normal-weight and overweight patients. The increased frequency

of OSAS with obesity, which eventually leads to hypoxia, triggers systemic inflammation. Vascular diseases, especially coronary artery and cerebrovascular diseases, are commonly seen in obese patients with OSAS, and this situation was shown to be associated with sympathetic activation, systemic inflammation, and endothelial dysfunction. These findings suggest that OSAS is not a simple obesity-related phenomenon^{1,14,15}. The finding of increased CRP and leukocytes among obese patients with severe OSAS in this study supports the previous results.

Thyroid dysfunction is closely related to many systemic diseases, particularly obesity. It was reported that the TFT values of patients with OSAS were not different from those of the general population¹⁶. Moreover, no difference in TSH levels was detected in healthy populations with and without obesity. Resta et al.¹⁷ reported that OSAS prevalence and severity were not affected by thyroid hormone treatment or subclinical hypothyroidism. However, an increase in sleepiness was shown in the absence of treatment of subclinical hypothyroidism¹⁷. On the other hand, some researchers have shown differences in T3 and T4 levels, mainly due to low T4, and decreased serum FT4 or increased serum TSH levels may increase the risk of obesity in women¹⁸.

Thyroid functions may also be affected by estrogen. In a study conducted on rats, it was reported that conjugated equine estrogens and tamoxifen increased T4 and T3 levels and had a proliferative effect on thyroid follicular cells¹⁹. Another study found lower FT4 and higher FT3 among euthyroid postmenopausal women with more visceral adipose tissue²⁰. The effect of adipose tissue on the 5'-deiodinase enzyme was suggested as the source of that difference²¹. However, in this study, there were no associations of obesity with the levels of TSH, FT4, or BMI, but FT3 levels were lower in obese patients. These variations among studies might be due to different BMI values being accepted for obesity criteria. Differences in T3 and T4 levels can also be explained by the effect of adipose tissue on the 5'-deiodinase enzyme.

The association between obesity and anemia was suggested to be due to increases in hepcidin, shown to impair iron absorption^{22,23}. Our results, which demonstrate a relationship between increased obesity and decreased hemoglobin and hematocrit levels, support the previous studies in this regard^{24,25}.

Limitations of the study

Participants were divided into three groups in terms of BMI values, but obese patients were not classified into further subgroups. While investigating the relationship of OSAS with obesity, relationships with underlying diseases should also be examined at the same time.

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CONCLUSION

This study has shown associations between OSAS severity, BMI, and BFR. Therefore, obesity could be a critical predisposing factor for sleep disturbances. FT3 levels were significantly lower in obese patients in this study, but no significant relationships were found between FT4 or TSH and obesity. Based on these results, the relationship between obesity and OSAS seems to be more complicated than previously believed. Patients should be informed about the prevention and control of obesity while being treated for OSAS. These results may offer a valuable contribution to the literature due to the large number of patients included in the study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

AUTHORS' CONTRIBUTIONS

DF: Conceptualization, Data curation, Investigation Methodology, Formal Analysis, Writing—original draft, Writing—review & editing. **EF:** Data curation, Formal Analysis, Writing—review & editing.

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