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Original Article

Evaluation of Thyroid Functions and Correlation of Body Mass Index with Apnea-Hypopnea Index in Patients with Obstructive Sleep Apnea Syndrome

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ABSTRACT

Background: Thyroid hormone deficiency and excessive weight, which are considered endocrine disorders, can be easily detected, have low cost, and guide treatment planning in obstructive sleep apnea syndrome (OSAS). We examined thyroid hormone levels in patients diagnosed with OSAS using polysomnography and conducted a study to investigate the correlation between body mass index (BMI) values and apnea-hypopnea index (AHI).

Material and Methods: This study included patients who presented to the Ear, Nose, and Throat Clinic and Sleep Disorders Center of Dicle University Faculty of Medicine Hospital between July 2008 and November 2010, and were diagnosed with OSAS based on polysomnography (PSG) results. The study group consisted of a heterogeneous group in terms of presenting complaints, with most patients reporting complaints of snoring, while others had a history of witnessed apneas by their partners, excessive daytime sleepiness, fatigue, and headaches. From the group diagnosed with OSAS (AHI>5) based on PSG results, the first 100 randomly selected patients were included in the study.

Results: The mean age of the cases diagnosed with OSAS based on PSG results was 48.79±10.70. The age of women ranged from 24 to 76, with a mean age of 55.44±19.25. The age of men ranged from 24 to 77, with a mean age of 46.33±15.48. Among the 100 patients, 33 had mild, 19 had moderate, and 48 had severe OSAS. Among these 100 cases, hypothyroidism was detected in 5 patients (2 with mild OSAS and 3 with severe OSAS) based on serum thyroid hormone levels. Among the patients with hypothyroidism, 2 were female and 3 were male. In all cases, a positive correlation was found between BMI and AHI, with a significance level of 45.9% and a statistically significant correlation.

Conclusion: Based on these findings, it can be concluded that screening for hypothyroidism and measuring BMI should be necessary for all patients presenting to sleep laboratories with suspected OSAS.

Keywords: OSAS, thyroid, BMI, hypothyroidism

INTRODUCTION

Despite sleep being an essential aspect of our lives, occupying approximately one-third of our time and being crucial for a healthy life, the physiology of sleep could only be explained in the 20th century with the application of EEG (1). The effects of sleep on respiration were demonstrated in 1965 by Gastaut through polysomnography, which is now considered the "gold standard" for diagnosing sleep apnea syndrome (2). Initially, sleep apnea syndrome was not recognized as a significant public health issue, but its prevalence, ranging from 1% to 5%, has been shown to be quite high, and it is commonly associated with diseases such as diabetes mellitus and bronchial asthma (3-5). Thus, it has rightfully gained its deserved recognition.

Although there are many diseases that can cause respiratory disorders during sleep, the most significant group is constituted by "sleep apnea syndrome," with "obstructive sleep apnea syndrome" (OSAS) practically being understood when referring to sleep apnea syndrome due to its prevalence, accounting for 90-95% of all cases (6).

The detection of respiratory disorders during sleep is crucial for both the prognosis of the disease and the implementation of appropriate treatment. However, the gold standard for diagnosing this condition, polysomnography, is a costly, time-consuming, and resource-intensive procedure that requires specialized equipment (7). Moreover, the number of laboratories capable of conducting this study at a sufficient level is limited both globally and in our country. Therefore, selective criteria need to be applied when determining who should undergo polysomnographic testing.

The spectrum of symptoms in OSAS is quite broad. These symptoms provide indications of OSAS, but not all of them have diagnostic significance. Among the etiological factors, thyroid hormone deficiency and excessive weight, which are considered endocrine disorders, can be easily detected, have low cost, and provide guidance in treatment planning (8,9).

Based on this premise, we examined thyroid hormone levels in patients diagnosed with OSAS using polysomnography and conducted a study to investigate the correlation between body mass index (BMI) values and the Apnea Hypopnea Index (AHI).

MATERIAL and METHODS

This study included patients who presented to the Ear, Nose, and Throat Clinic (ENT) and Sleep Disorders Center of Dicle University Medical Faculty Hospital between July 2008 and November 2010 and were diagnosed with OSAS based on polysomnography (PSG) results. The study group consisted of a heterogeneous group of patients with diverse complaints. Most of them complained of snoring, while others presented with a history of breathing pauses during sleep reported by their partners, excessive daytime sleepiness, fatigue, and headaches. From the group of patients diagnosed with OSAS (AHI>5) based on PSG results, the first 100 patients were randomly selected. No gender distinction was made among the patients.

The study excluded the following cases: Secondary cases who had previously received a diagnosis of OSAS and undergone any surgical intervention in any clinic due to sleep disorders. Cases who presented with other complaints received a diagnosis of thyroid dysfunction and underwent replacement therapy.

Age, body weight, and height measurements were recorded to calculate their BMI, and its correlation with the AHI was evaluated. Thyroid-stimulating hormone (TSH), Free T3 (FT3), and Free T4 (FT4) hormone levels were examined. The prevalence of existing thyroid dysfunction associated with OSAS was determined as a percentage. Changes in symptoms in patients receiving replacement therapy or undergoing surgical treatment were recorded and compared with the reevaluation of thyroid function in subsequent follow-ups.

A detailed medical history was obtained from the patients included in the study, as well as from their spouses. The patients were asked to answer the following questions:

- Frequency, intensity, and association with sleep position of snoring.
- Presence or absence of respiratory irregularities and feelings of suffocation during sleep.
- Frequency of nighttime awakenings.
- Ease or difficulty of waking up in the morning.
- Changes in intellectual functions such as learning, comprehension, management, and memory.
- Sexual problems such as decreased libido or impotence.

These questions aimed to gather information about the patients' symptoms and experiences related to sleep and to assess potential associations with OSAS.

After obtaining the medical history, a routine ENT examination was performed on each patient. The examination included evaluating nasal structure and nasal passage patency, the condition of the soft palate, length of the uvula, epiglottis position, mandibular structure, size of the tongue, presence of craniofacial anomalies, and the size and movement of lymphoid tissues such as tonsils and adenoids.

In this study, PSG recordings were conducted at the Sleep Laboratory of Dicle University Hospital's Chest Diseases Clinic under the supervision of a technician, and during the patients' spontaneous sleep. A video camera system was used to record audio and visual data throughout the night. Patients were admitted to their designated rooms two hours before their usual bedtime and were encouraged to settle into the sleeping environment. After the process of attaching electrodes to the patients, the computer-controlled the status of all electrodes, and then the patients were left alone to sleep. PSG recordings included EEG, mentalis and submental EMG, EMG from the right anterior tibial muscle, airflow measurement from the mouth and nose, chest and abdominal respiratory movements, and pulse oximetry throughout the night. Respiratory monitoring was achieved by integrating a pulse oximeter and oronasal airflow measurement (oronasal cannula) into the main device. Respiratory sounds were recorded using a microphone placed on the neck, and thoracic and abdominal movements were assessed using piezoelectric bands to examine respiratory effort. Body position sensors (back, front, right, left) were used to record patients' sleeping positions. Additionally, heart rhythm was monitored throughout the night using EKG electrodes. All procedures and recordings were conducted under the supervision of a technician.

PSG recordings were scored according to the international sleep disorder criteria (AASM 2007) using the Twin polysomnographic analysis program. The PSG results obtained in the study were compared with anthropometric measurements. The device used in the study was the Compumedics e-series with 44 channels. The recordings were initially scored using computer software and later manually evaluated by the physician for further analysis. The reports were then explained by the responsible physician.

BMI is calculated as Body Weight (kg) divided by Height squared (m^2).

This study was conducted in agreement with the Declaration of Helsinki-Ethical principle for medical research involving human subject

STATISTICAL ANALYSIS

SPSS (Statistical Package for Social Sciences) for Windows 15.0 software was used for data analysis. Descriptive statistical methods (mean, standard deviation, frequency) were employed to evaluate the study data. Student's t-test was used for comparing normally distributed quantitative variables between groups, and a one-way ANOVA test was used for comparing means among more than two groups. The Chi-square test was utilized for evaluating categorical variables, and a two-way ANOVA test was applied when assessing two categorical variables. The Chi-square test was used for comparing qualitative variables. The Pearson correlation test was employed to examine the relationships between variables. The results were presented as mean, standard deviation, and 95% confidence intervals for each variable. Statistical significance was evaluated at $p<0.05$ level.

RESULTS

A total of 100 cases with ages ranging from 24 to 77 years who applied to the ENT Clinic and Sleep Disorders Center of xxxx University Faculty of Medicine were included. Of the cases, 27 (27%) were female and 73 (73%) were male. The characteristics of the participants were given in **Table 1**.

Table 1. The characteristics of patients (n=100)

	Mean (±SD)
Age, year	48.79±10.70
Weight, kg	85.63±12.65
Height, cm	171.0±7.94
BMI, kg/m2	29.09±4.41
AHI	37.66±29.21

BMI; body mass index, AHI; Apnea-Hypopnea Index

All cases underwent routine ENT examinations. Specifically, the nasal passage patency, nasopharynx, soft palate, uvula, palatine tonsils, tonsillar pillars, and posterior pharyngeal wall mucosa were evaluated. Secondary cases who had previously received a diagnosis of OSAS and undergone any surgical intervention, as well as cases with other complaints who had been diagnosed with thyroid dysfunction and received replacement therapy, were not included in the study.

Patients who presented with complaints of snoring underwent polysomnographic examination based on the anamnesis and physical examination findings, leading to a preliminary diagnosis of sleep apnea. The average age of patients diagnosed with OSAS was 48.79 years. The ages of female patients ranged from 24 to 76, with an average of 55.44 years. The ages of male patients ranged from 24 to 77, with an average age of 46.33 years. Serum-free T3, T4, and TSH levels were measured, and body weight and height were recorded to calculate BMI. The apnea-hypopnea indices of the patients were calculated based on the polysomnographic examination. Among the 100 patients, 33 had mild, 19 had moderate, and 48 had severe OSAS. Among these 100 patients, hypothyroidism was found in 5 patients (2 with mild OSAS and 3 with severe OSAS) based on the measured serum thyroid hormone levels. Of the patients with hypothyroidism, 2 were female and 3 were male.

When calculating the average ages of patients according to gender, there was a statistically significant difference between male patients (46.33±8.866) and female patients (55.44±12.473) ($p<0.0001$). According to this result, the average age of females is approximately 9 years higher than that of males. There is no statistically significant difference in the distribution of cases by gender based on the AHİ ($p>0.05$, **Table 2**).

Table 2. The frequency of AHI between genders

	Male	Female	Total
Mild	34.2%	29.6%	33.0%
Moderate	17.8%	22.2%	19.0%
Severe	47.9%	48.1%	48.0%
Total	100%	100%	100%

$x^2=0.33$ and $p>0.05$. No significant difference

The heights of the individuals range between 150 cm and 194 cm, with an average of 171 cm. The weights of the individuals range between 55 kg and 120 kg, with an average of 85.63 kg. The BMI levels of the individuals range between 22.30 and 44.10, with an average of 29.09. When the BMI averages are calculated according to gender, there is no statistically significant difference between the two groups ($p>0.05$). The average BMI for males (n=73) is 28.79±3.95 and for females, the average BMI is 29.92±5.46 ($p>0.05$).

According to the AHI, there is a statistically significant difference in BMI averages among female cases. The BMI levels of female cases with severe AHI are significantly higher than those with mild and moderate AHI. However, there is no statistically significant difference in BMI levels among cases with mild and moderate AHI .

According to the AHI, there is a statistically significant difference in BMI averages among male cases. The BMI levels of male cases with severe AHI are significantly higher than those with mild and moderate AHI. However, there is no statistically significant difference in BMI levels among cases with mild and moderate AHI (**Table 3**).

According to the AHI, there is a statistically significant difference in BMI averages among all cases. The BMI levels of cases with severe AHI are significantly higher than those with mild and moderate AHI. However, there is no statistically significant difference in BMI levels among cases with mild and moderate AHI (**Table 4**).

DISCUSSION

There are some risk factors for obstructive sleep apnea syndrome (OSAS) including male gender, advanced age, and family history. Diabetes mellitus, hypothyroidism, acromegaly, and obesity are endocrine disorders believed to be associated with OSAS. Various cellular-level changes in hypothyroidism contribute to an increased susceptibility to OSAS. Although this relationship has been clearly established, the exact prevalence of hypothyroidism in OSAS patients is not fully known.

According to the literature, the coexistence of OSAS and hypothyroidism is reported to be between 1.2% and 11% (8,10,11). In investigations exploring the connection between thyroid dysfunction and OSAS, Mickelson et al. conducted a study involving 842 cases and found that the prevalence of clinical hypothyroidism was 1.2%. Among these cases, 5 out of 10 patients exhibited simple snoring (2 with a previous history, 3 diagnosed through PSG). The frequency of hypothyroidism among OSAS patients did not differ significantly from the general population (12). Similarly, Winkelman et al. reported a prevalence of 2.9% for hypothyroidism among 255 cases diagnosed with OSAS using PSG (13). Skjodt et al. conducted a study on 200 patients diagnosed with OSAS and observed a prevalence of 1.5% for hypothyroidism among individuals tested via PSG, while suspects of OSAS showed a prevalence of 2.4%. They emphasized the importance of screening for hypothyroidism to prevent misdiagnosis of primary sleep apnea and unnecessary expenses on sleep studies (14). Furthermore, Popovici et al. observed a high coexistence rate of 11% between the two diseases in a group of 95 patients diagnosed with OSAS (15). Another crucial aspect to consider regarding the association between OSAS and hypothyroidism is the similarity in symptoms shared by both conditions. Symptoms and findings such as daytime sleepiness, fatigue, apathy, lethargy, decreased libido, depressive mood, headache, obesity, and snoring, which are commonly seen in hypothyroidism, are frequently encountered in patients with OSAS as well (16). Orr et al. emphasize the importance of recognizing myxedema and obstructive sleep apnea syndrome as potential life-threatening complications in hypothyroid patients experiencing excessive daytime sleepiness (17).

Looking at studies conducted in Turkey, Guven et al. diagnosed OSAS in 111 out of 134 cases (82%) who presented to the sleep center with suspicion of OSAS and underwent overnight PSG. Among these patients, hypothyroidism was detected in 5 cases (4.5%). This finding is similar to our study (18).

In our study of 100 cases, 33 had mild OSAS, 19 had moderate OSAS, and 48 had severe OSAS. Among these 100 patients, hypothyroidism was detected in 5 cases (2 with mild OSAS, 3 with severe OSAS) based on their serum thyroid hormone levels. Of the patients with hypothyroidism, 2 were female and 3 were male. After hormone replacement therapy, there was an improvement in the symptoms of patients with mild OSAS, while no changes were observed in the symptoms of the 3 patients with severe OSAS. The co-occurrence rate of OSAS and hypothyroidism in our study was found to be 5%, which is consistent with the literature.

Table 4. Mean BMI according to OSAS severity levels in all cases.

Mild	27.50±0.85
Moderate	28.06±1.03
Severe	31.08±0.68

There are three important physiological factors involved in the development of upper airway obstruction and collapse. These are the anatomy of the upper airway, the

Table 3. Descriptive statistics of the BMI variable according to Gender and OSAS groups

OSAS	BMI, Male, n=77	BMI, Female, n=23
Mild	27.67 ± 1.83, CI 95% 26.009 - 29.343	27.32 ± 1.48, CI 95% 24.379 - 30.271
Moderate	27.19 ± 1.16, CI 95% 24.881 - 29.503	28.93 ± 1.71, CI 95% 25.532 - 32.335
Severe	30.18 ± 1.70, CI 95% 28.774 - 31.591	31.98 ± 1.16, CI 95% 29.674 - 34.296

OSAS; obstructive sleep apnea syndrome, BMI; body-mass index

negative pressure generated during inspiration, and the loss of muscle activity that dilates the pharyngeal airway (19,20). Various risk factors for OSAS facilitate these physiological conditions and increase the susceptibility to OSAS. Age, gender, obesity, neck circumference, smoking, alcohol, and sedative use, and certain accompanying diseases are among the major proposed risk factors (19).

Age, gender, and obesity are the most significant risk factors. Aging is associated with changes in body fat distribution, tissue elasticity, and control of ventilation, which increase the tendency for OSAS (21). It has been reported that OSAS is most commonly observed in the 40-65 age group and its prevalence decreases after the age of 65 (22).

Comparisons conducted on the elderly show a higher rate of detection of disorders based on the AHI, but the clear relationship between this and the development of morbidity and mortality due to daytime sleepiness is not known. In a study conducted in a nursing home, the prevalence of OSAS in individuals aged 65 and above was reported to be 62% (23). However, whether age alone increases the risk of OSAS has not been fully clarified. The increase in the disease with age is not as significant in individuals over the age of 65 as it is in those under the age of 65 (24). This can be explained by the possibility of more deaths in OSAS or a decrease in the disease with age. However, there is no definitive evidence to suggest that OSAS causes death or declines with age. It has been observed that reports of snoring decrease in the elderly compared to the middle-aged group, and this has been attributed to a decrease in the survival of bed partners who can witness the snoring in elderly patients and an increase in the frequency of central apnea in the elderly (25). The complexity of the relationship between age and OSAS prevalence can be explained by cohort effects and difficulties in detecting OSAS in the elderly. The lack of sufficient information on OSAS incidence and mortality rates specific to age groups makes it difficult to make definitive conclusions on the subject.

Male gender is also an important risk factor for OSAS. The frequency of OSAS has been reported to be higher in men than in women during middle age. The accumulation of fat, particularly in the neck area, due to androgenic fat distribution in men increases the risk of OSAS. Epidemiological studies in the 1980s found high male-to-female ratios of 10/1 to 7/1 (26,27). However, recent studies have reported that the gender difference is not as high, with a female-to-male ratio of 1/3 for every age group (27). The gender-related difference may be attributed to women reporting OSAS symptoms such as apnea, snoring, and waking up choking less frequently, seeking medical help less often for these symptoms, and doctors considering the diagnosis of OSAS less frequently in female patients presenting with the same complaints compared to male patients. Bed partners may also report less snoring and choking-like symptoms in women. The lower prevalence of OSAS in premenopausal women compared to men has been attributed to differences in fat distribution due to sex hormones (28). However, administration of sex hormones (estrogen and progesterone) did not lead to a decrease in AHI in male and postmenopausal female OSAS patients (29). Occupational and environmental factors, upper airway structure, and differences in fat distribution have been proposed to explain the gender-related differences in OSAS prevalence, but there is no definitive evidence regarding these factors.

In a screening study conducted by Nieto et al. (30) with 6,132 individuals, it was reported that approximately 37% of diagnosed OSAS cases were women. In our study, 73% of our OSAS patients were male and 27% were female. Our findings are consistent with the literature.

Obesity plays an important role in the pathophysiology of OSAS (31,32). In fact, improvement in the OSAS clinic can be observed with weight loss (31,32). When defining obesity as an increase in body fats, the most important determinant factor of the health risks posed by obesity is the distribution of fat in the body. Male-type obesity is generally characterized by central fat deposition, particularly in the abdomen and neck regions. Female-type obesity, on the other hand, is characterized by fat deposition around the hips. Numerous studies have shown that android fat distribution, which is centered around the neck and abdominal organs, leads to more complications. Güven et al. found that 69% of mild OSAS patients and 77% of moderate and severe OSAS patients were obese (BMI >29) among 67 OSAS cases (18).

In the past, OSAS used to be associated with obesity as a prevalent condition. However, recent studies have revealed that approximately 40% of OSAS patients are not classified as obese (33,34). When considering AHI, there is a noteworthy difference in average BMI among female cases. Specifically, females with severe AHI (48.1%) exhibited significantly higher BMI levels (31.9) compared to those with mild (29.6%) and moderate (22.2%) AHI levels (27.3-28.9). No statistically significant difference was found in BMI levels between cases with mild and moderate AHI. Similarly, among male cases, a statistically significant variance in average BMI was observed. Males with severe AHI (47.9%) had significantly higher BMI levels (30.1) than those with mild (34.2%) and moderate (17.8%) AHI levels

(27.6-27.1). Again, no statistically significant difference was detected in BMI levels between cases with mild and moderate AHI. Moreover, there is a statistically significant discrepancy in the average BMI across all cases. Cases with severe AHI demonstrated higher BMI levels (31.0) compared to those with mild and moderate AHI levels (27.5-28.0). No statistically significant difference was found in BMI levels between cases with mild and moderate AHI. Notably, a significantly positive correlation exists between BMI levels and AHI in females, with a correlation coefficient of 57.2% and statistical significance (r(AHI, BMI)=0.572, p= 0.002). Similarly, a positive and statistically significant correlation was observed between BMI levels and AHI in males, with a correlation coefficient of 38.3% (r(AHI, BMI)=0.383, p=0.001). Overall, there is a positive correlation between BMI and AHI across all cases, with a correlation coefficient of 45.9% and statistical significance (r(BMI, AHI) = 0.459, p<0.001).

When calculating the average BMI according to gender, there was no statistically significant difference between the two groups. İbrahim et al. observed that OSAS females had significantly higher BMI values compared to males and there was no significant difference in average BMI values among different OSAS categories (35).

It is known that PSG is the gold standard test for diagnosing OSAS, but it is expensive, time-consuming, requires a specialized team and the number of laboratories capable of conducting sufficient studies is limited. Therefore, although they do not provide a definitive diagnosis, it is important to interpret obesity, which plays an important role in the etiology of OSAS, in determining cases to be referred for polysomnographic examination. However, it should not be concluded that every obese patient needs to be referred for PSG. Because patients with obesity constitute a large population, and not all obese patients have OSAS. We believe that the Epworth Sleepiness Scale should be evaluated before referring to PSG. According to our results, showing that BMI is an important determinant of AHI, there is a relationship between obesity and OSAS.

CONCLUSION

The association between Obstructive Sleep Apnea Syndrome (OSAS) and hypothyroidism has been established in the literature, although the exact prevalence of hypothyroidism in OSAS patients remains uncertain. The reported coexistence rate of OSAS and hypothyroidism ranges from 1.2% to 11% in various studies. Both conditions share similar symptoms, such as daytime sleepiness, fatigue, apathy, and obesity, making it crucial to consider the possibility of hypothyroidism in OSAS patients. Screening for hypothyroidism in individuals suspected of having OSAS can prevent misdiagnosis and unnecessary expenses for sleep studies. Thyroid replacement therapy has been shown to improve OSAS symptoms in patients with hypothyroidism.

Several risk factors contribute to the development of OSAS, including male gender, advanced age, and obesity. Aging is associated with changes in body fat distribution and ventilation control, increasing the susceptibility to OSAS. The male gender has a higher prevalence of OSAS, possibly due to androgenic fat distribution, while women may underreport symptoms and seek medical help less often. Obesity, particularly with android fat distribution around the neck and abdomen, plays a significant role in OSAS pathophysiology. BMI is commonly used to evaluate obesity and higher BMI levels are associated with more severe OSAS.

While PSG is the gold standard for diagnosing OSAS, it is expensive and requires specialized facilities. Considering the relationship between obesity and OSAS, BMI can be used as a screening tool to determine which patients should be referred for PSG. However, not all obese individuals have OSAS, so careful assessment, including the Epworth Sleepiness Scale, is necessary to determine the need for PSG.

Overall, understanding the relationship between OSAS and hypothyroidism, as well as the impact of risk factors like gender and obesity, can contribute to more accurate diagnoses and effective treatment strategies for patients with OSAS.

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