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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

OBSTRUKTİF UYKU APNESİ HASTALARINDA TİP 2 DİYABETES MELLİTUS PREVALANSI VE BAŞLICA RİSK FAKTÖRLERİ

PREVALENCE OF TYPE 2 DIABETES MELLITUS AND MAIN RISK FACTORS IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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ÖZET

AMAÇ: Obstrüktif uyku apnesi (OUA), obstrüktif tipte apne ve hipopne ile karakterize bir hastalıktır ve çoğu hasta gündüz aşırı uyku halinden şikayetçidir. Aşırı kilo ve obezite OUA için başlıca risk faktörlerdir. OUA'nın tip 2 diabetes mellitus (T2DM) ile ilişkili olduğu bilinmektedir. Bu çalışmanın birincil amacı OUA'lı hastalarda T2DM prevalansını belirlemektir.

GEREÇ VE YÖNTEM: Çalışmamız, Trakya Üniversitesi Hastanesi'nde gerçekleştirilen retrospektif, analitik bir çalışmadır. Ekim 2019 ve Mart 2023 tarihleri arasında polisomnografi ile OUA tanısı konulan yetişkin hastalar çalışmaya dahil edildi. Hastane verilerinden hastaların demografik verileri, Tip 2 DM tanıları ve risk faktörleri tarandı.

BULGULAR: Çalışmaya dahil edilen toplam 244 OUA tanılı hastanın 191'i (%78,3) erkek ve 53'ü (%21,7) kadındı. Hastalarda T2DM prevalansı %31,6 bulundu. Tip 2 DM oranı erkek OUA hastalarında %27,2 kadın OUA hastalarında %47,2 idi. OUA olguları AHİ değeri baz alınarak hastalık şiddetine göre analiz edildiğinde, diyabet ile hastalık şiddeti arasında anlamlı bir ilişki bulunmadı. T2DM prevalansının kadın OUA hastalarında anlamlı olarak daha yüksek olduğunu ve bunun da vücut ağırlığı ve vücut kitle indeksi (BMI) ile doğrudan ilişkili olduğunu bulduk.

SONUÇ: OUA hastalarında T2DM prevalansı yüksektir ve bu yükseklik kadın cinsiyette daha belirgindir. T2DM'li ve OUA'li hastaların komorbiditeleri açısından değerlendirilmesi, her iki hastalığın da erken tanı ve tedavisine katkı sağlayabilir.

ANAHTAR KELİMELER: Obstruktif uyku apnesi, Tip 2 Diabetes Mellitus, Obezite.

ABSTRACT

OBJECTIVE: Obstructive sleep apnea (OSA) is a disorder characterized by obstructive apnea and hypopnea, with most patients complaining of excessive daytime sleepiness. Overweight and obesity are major risk factors for OSA. OSA is known to be associated with type 2 diabetes mellitus (T2DM). The primary aim of this study was to establish the prevalence of T2DM in patients with OSA.

MATERIAL AND METHODS: Our study is a retrospective, analytical study conducted at the Trakya University Hospital. Adult patients diagnosed with OSA by polysomnography between October 2019 and March 2023 were included in the study. Demographic data, Type 2 DM diagnoses and risk factors of the patients were screened from hospital data.

RESULTS: Of the total 244 patients diagnosed with OSA included in the study, 191 (78.3%) were male and 53 (21.7%) were female. The prevalence of T2DM was 31.6% in the patients. The rate of type 2 DM was 27.2% in male OSA patients and 47.2% in female OSA patients. When OSA cases were analyzed according to disease severity based on AHI value, no significant relationship was found between diabetes and disease severity. We found that the prevalence of T2DM was significantly higher in female OSA patients, which was directly associated with body weight and body mass index (BMI).

CONCLUSIONS: The prevalence of T2DM is high in patients with OSA and this prevalence is more pronounced in females. Evaluation of patients with T2DM and OSA in terms of comorbidities may contribute to early diagnosis and treatment of both diseases.

KEYWORDS: Obstructive sleep apnea, Type 2 Diabetes Mellitus, Obesity.

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INTRODUCTION

Clinical pictures caused by pathologic changes in the breathing pattern during sleep, leading to increased morbidity and mortality, are called "sleep-disordered breathing" (SDB). Obstructive Sleep Apnea (OSA) is a disease condition which occurs as a result of complete (apnea) or incomplete (hypopnea) obstruction in the upper airways for at least 10 seconds during sleep, despite continued respiratory effort, resulting in excessive decrease in blood oxygen levels at night and excessive daytime sleepiness. OSA is the most common sleep-related respiratory disorder. Although it is most common in older men, it can also affect women and children (1). Recent publications point to a dramatic increase in the prevalence of OSA. Studies on the epidemiology of OSA in the literature vary greatly in terms of methodology, diagnostic criteria and severity assessment. A current study reported that the prevalence of OSA varies from 4-30% in different countries (2).

Obesity is one of the most significant risk factors for sleep apnea. Compared to people of normal weight, the odds of developing sleep apnea are 4 to 10 times higher (3, 4). In epidemiological studies, the prevalence of OSA in the population aged 30-49 years ranges from 1.4-7% in those with a body mass index (BMI) <25 kg/m^2, while it increases dramatically to 44.6% (in men) and 13.5% (in women) in those with a BMI of 30-39.9 kg/m^2 (5).

OSA is also very common among patients with type 2 diabetes (T2DM) and it affects 24-86% of patients, which is significantly more than in the non-diabetic population (6). There is information in the literature that the prevalence of OSA is also found to be high in people with type 1 diabetes (7).

In our study, we planned to examine the prevalence of T2DM and prominent associated factors in patients diagnosed with OSA by polysomnography (PSG) in our sleep laboratory.

MATERIALS AND METHODS

Data of patients over the age of 18 who were diagnosed with obstructive sleep apnea between November 2019 and March 2023 in the Sleep Laboratory of Trakya University Hospital were retrospectively evaluated. Nineteen of 263 patients diagnosed with OSA were excluded from the study due to insufficient data. Age, sex, body mass index (BMI), weight, height, apnea hypopnea index (AHI), and diagnosis of diabetes mellitus were investigated from a database based on the patient's own anamnesis, as well as from hospital enrollment and e- nabız® databases in accessible cases.

Polysomnographic (PSG) Examinations:

All patients undergoing polysomnographic examinations gave pre-procedural consent that they agreed to the procedure and to the use of their data for scientific purposes only.

All patients underwent a full-night study PSG. During the night, an Electroencephalogram (EEG), using the electrodes placed according to the international 10-20 system. Electromyogram, electromyography for mentalis, electrocardiogram (ECG), respiratory pattern, pulse rate, nasal air flow, sleeping position and sound of snoring , were all monitored simultaneously. All these data were analyzed by computational analysis as well as manual interpretation.

All recordings were manually scored by a certified sleep physician. Sleep-related abnormal respiratory events were scored according to the American Academy of Sleep Medicine (AASM 2017) criteria. Apnea was defined as the complete cessation of oral and nasal airflow for at least 10 seconds. The criteria for hypopnea scoring was accepted as the decrease in airflow which lasted more than 10 s leading to arousal or oxygen desaturation (represented by a decrease in the oxygen saturation greater than 3%). OSA is classified as : mild (AHI ≥ 5 and <15 events per hour), moderate (AHI ≥ 15 and ≤ 30 events per hour), or severe (AHI> 30 events per hour).

Ethical Committee

Our study was approved by the decision of the Ethics Committee of the Faculty of Medicine of Trakya University on 19.02.2024 under the number 03/09.

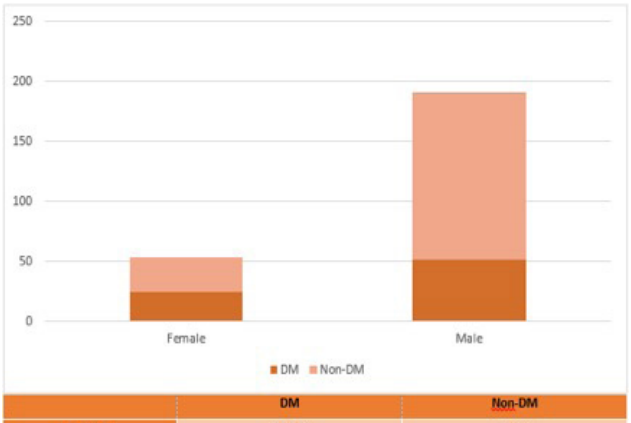
Statistical Analysis

CMS Excel and IBM SPSS (Version 20.0) package programs were used for analysis.

Continuous data following a normal distribution were presented as the mean ± standard deviation (SD). Frequency analysis was used for categorical variables. Comparisons between groups were conducted using the chi-square test and student t-test. A p value <0.05 was considered statistically significant.

RESULTS

Of a total of 244 patients diagnosed with OSA, 191 (78.3%) were male and 53 (21.7%) were female. The mean age was 49.22 ± 10 years. BMI was similar in both sexes with a mean of 34 ± 7 in women and 33 ± 6.5 in men. Of the 244 patients who participated in our study, 77 (31.6%), 52 males and 25 females, were diagnosed with T2DM. Diabetes was diagnosed in 27.2% of men and 47.2% of women **(Figure 1)**.



	DM	Non-DM
Female*	47.2 %	52.8 %
Male*	27.2 %	72.8 %
TOTAL	31.6 %	68.4 %

Figure 1: Type 2 DM rates by sex (*p value was found 0.007)

When evaluated according to gender, the diagnosis of T2DM in OSA patients was statistically significantly higher in the female gender (p= 0.007). When OSA patients were analyzed for disease severity according to AHI value, no significant relationship was found between T2DM and OSA severity. Patients were evaluated in terms of height, body weight and BMI in addition to gender. No significant relationship was found between height and T2DM. When body weight and BMI were compared in both groups, the mean body weight of patients with T2DM was 101.38 ± 23 kg, while the mean body weight of patients without diabetes was 95.18 ± 18 kg (p= 0.033). Mean BMI was 35.5 ± 7 in patients with T2DM and 32 ± 6 in patients without diabetes (p = 0.006). Body weight and mean BMI were significantly higher in T2DM patients compared to those without T2DM **(Figure 2)**.

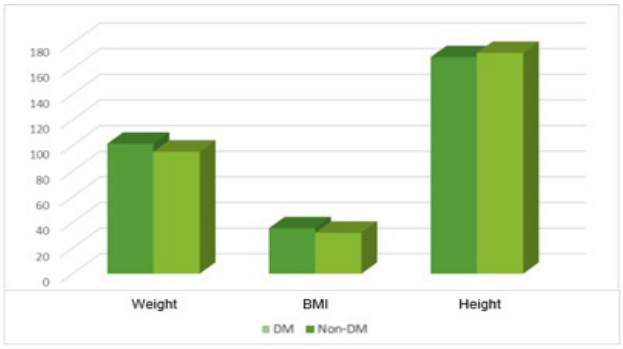


Figure 2: Mean Weight, BMI and Height of the Patients Included in the Study (*p value for weight was found 0.033. **p value for BMI was found 0.006)

DISCUSSION

In our study, the prevalence of DM in adult OSA patients was 31.6%. The prevalence of DM was almost 2 times higher in females than in males. No significant association was found between T2DM and AHI, whereas a significant association was found between body weight and BMI increase and T2DM.

It is estimated that 530 million adults in the world between the ages of 20 and 79 are affected by diabetes, with a global prevalence of 10.5% (8, 9). T2DM represents the highest rate of global diabetes diagnosis (approximately 98%), but this rate may vary greatly among countries (10). Important clinical risk factors for T2DM include obesity, family history, ethnicity, body fat distribution, exercise, lifestyle, smoking, birth and childhood weight and sleep duration (11). The role of lifestyle habits in the management of T2DM has been recognized for many years. Factors such as adopting a healthy diet, regular physical activity and avoiding smoking have an important role in the management of diabetes (12). Apart from these lifestyle habits, the importance of sleep habits has been emphasized recently. In general, 7-9 hours of sleep per day is recommended for adults and it is thought that these periods are ideal in terms of reducing the risk of diabetes. One meta-analysis found that the risk of diabetes was lowest among those who slept 7-8 hours (13). In the same meta-analysis, it was stated that each 1-hour decrease in sleep duration compared to 7 hours per

day was associated with a 9% increase in the risk of T2DM and each one-hour increase in sleep duration was associated with a 14% increase in the risk of T2DM.13 In studies conducted with individuals with T2DM, it has been reported that short or long sleep duration may be negatively associated with HbA1c levels and positively associated with diabetes complications such as retinopathy and albuminuria (14).

In a 16-year follow-up study of OSA patients, there was a significant increase in the incidence of T2DM during follow-up. In addition, the contribution of OSA to the development of DM was found to be gender-dependent and higher in females than in males (15). This result is similar to the result that the rate of T2DM in OSA patients in our study was significantly higher in women than in men.

Studies show that sleep problems are more common in individuals with T2DM than in the general population. In a study conducted in Turkey, the mean Pittsburgh Sleep Quality Index (PSQI) score was found to be 9.14±4.07 points in individuals with diabetes and 5.38±3.30 points in healthy individuals (16). In another study investigating the relationship between diabetes and sleep quality, it was reported that 50.7% of individuals with diabetes had poor sleep quality, while this rate was 31.8% in individuals without diabetes (17).

In most of the studies, the effect of sleep time on glucose metabolism has been investigated. It is observed that changes in sleep time changes cause impairment in glucose metabolism. In studies, it is emphasized that irregular sleep, eating at night and skipping breakfast behaviors due to going to bed late and waking up late negatively affect glucose metabolism and are important in the development of obesity and the pathophysiology of T2DM.

In OSA patients diagnosed by polysomnography and clinical findings, sleep architecture is highly disturbed and deep sleep continuity is disrupted due to arousals caused by apnea-hypopnea episodes and the patients' quality of sleep time decreases. The possible mechanisms of sleep patterns and obesity-related conditions such as OSA on the development of DM are not clear. In our study, T2DM was found in 31.6% of our patients diagnosed with OSA. There are studies supporting that one of the reasons for this high rate may be related to the decrease in melatonin secretion that may be caused by poor quality and short sleep duration (18).

OSA patients are at high risk for many adverse clinical conditions. The main conditions found to be associated with OSA can be listed as drowsy motor vehicle accidents due to excessive daytime sleepiness, neuropsychiatric dysfunctions, cardiovascular and cerebrovascular diseases, pulmonary hypertension-right heart failure, metabolic syndrome and T2DM, nonalcoholic fatty liver disease (NAFLD) (19). An increased risk of gout in OSA patients and, in a large French cohort study, an association between nocturnal hypoxemia and cancer in OSA patients has been suggested (20, 21).

The association between obesity and T2DM has been clearly demonstrated. Indeed, 80% of T2DM patients are obese and 40-60% of markedly obese patients are expected to develop diabetes. Therefore, it can be said that obesity is an important risk factor for T2DM. It is not clear whether obesity itself causes glucose intolerance or whether another factor causes both obesity and diabetes. However, the more widely accepted view today is that obesity aggravates hepatic insulin resistance (IR) present in T2DM (22).

OSA is frequently comorbid with cardiovascular, cerebrovascular and metabolic diseases and is commonly seen in populations with these comorbidities (23). The relationship of OSA to these multisystem disorders may be bidirectional. OSA may independently contribute to insulin resistance (IR) and glucose dysmetabolism through intermittent hypoxia, sympathetic activation, oxidative stress and inflammation (24). Intermittent hypoxia and repeated stimulation adversely affect autonomic nervous system function, leading to catecholamine secretion. Increased secretion of epinephrine, norepinephrine and cortisol further contributes to b-cell dysfunction due to impaired glucose metabolism and insulin sensitivity, as well as increased gluconeogenesis and decreased glucose uptake (25). Conversely, pre-exis-

ting T2DM accelerates the progression of OSA by impairing upper airway neural control and leading to peripheral neuropathy (26). Furthermore, abnormalities in autonomic nervous system activity, oxidative stress and activation of inflammatory pathways observed in T2DM may further trigger sleep-disordered breathing.

Obesity is now well known to be the most important risk factor for OSA. The risk of OSA correlates with increasing BMI (27). One study revealed that a 10% increase in weight was associated with a 6-fold increase in the risk of OSA (28). Moderate and severe OSA (AHI ≥ 15) was found in 11% of normal weight men, 21% of overweight men (BMI: 25-30kg/m^2), and 63% of obese men (BMI: > 30kg/m^2) in another study. Similarly, it was found to be 3% in normal weight, 9% in overweight and 22% in obese women (29). In our study, similar to the literature, the mean BMI was found to be >30 in both groups with and without T2DM diagnosis (35.5 ± 7 in patients with DM and 32±6 in those without DM).

Leptin and ghrelin release are associated with sleep. Therefore, irregularities in appetite regulation, eating behaviour and energy balance occur in sleep disorders. In sleep deficiency;, leptin, which is a satiety hormone, is suppressed and ghrelin release, which is an appetite stimulant, increases. Thus, an increase in weight may occur due to increased hunger and food intake (30).

A 12-year cohort study conducted in the UK aimed to determine the role of T2DM as a risk factor for OSA and the determinants of OSA in T2DM patients. In all cohorts stratified by age and BMI, except for patients aged 16-29 years, a significant increase in the incidence of OSA was found in patients with T2DM compared to those without. A statistical increase in the incidence of OSA was observed in T2DM patients regardless of the presence or absence of comorbid conditions. When our study was evaluated in terms of sex, the incidence of DM was significantly higher in female OSA patients (47.2%) compared to male patients (27.2%). In the mentioned study, insulin treatment and diabetes-related foot disease, in addition to known predictors of OSA, were identified as risk factors for OSA in patients with T2DM (31).

The rapid increase in type 2 diabetes mellitus (T2DM) and associated complications is associated with clinically important gender differences. T2DM is more frequently diagnosed in men of lower age and body mass index, while obesity, the most prominent risk factor, is more common in women. In general, large sex ratio differences are also observed between countries. Differences in biology, culture, lifestyle, environment and socioeconomic status influence the differences between men and women. Genetic influences and epigenetic mechanisms, nutritional factors and sedentary lifestyles affect risks and complications differently in both sexes. Furthermore, sex hormones have a significant impact on energy metabolism, body composition, vascular function and inflammatory responses. Both biological and psychosocial factors are responsible for sex differences in diabetes risk and outcomes. In general, psychosocial stress seems to have a greater impact on women than on men (32). In our region, the fact that female gender OSA patients are less frequently referred to sleep laboratories and diagnosed later may explain the high rate of T2DM.

In the follow-up of 1206 subjects who underwent an all-night sleep study, 152 of the subjects developed T2DM at a median of 7.3 years, and the risk of developing T2DM was found to be higher in untreated moderate and severe OSA. This plateaus in patients with severe OSA (2.01 and 2.62 times). The risk of T2DM decreased from 3.41 to 1.61 cases per 100 persons in one third of moderate and severe OSA patients who regularly used CPAP (33).

The most important limiting feature of our study is that it was planned as a retrospective file review.

In conclusion, this study provides further evidence that OSA is closely associated with diabetes risk. This risk is more pronounced in and in those with higher body mass index. Gender difference is one of the results that should be investigated in particular. Evaluating patients with T2DM and OSA for comorbidities may contribute to early diagnosis and treatment of both diseases. In addition, prospective and long-term studies are needed to investigate the effects of positive airway pressure therapy on T2DM control in patients with OSA.

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