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RESEARCH ARTICLE  
KLİNİK ÇALIŞMA

# Coexistence of obstructive sleep apnea syndrome and fibromyalgia

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## ABSTRACT

### Coexistence of obstructive sleep apnea syndrome and fibromyalgia

**Introduction:** Fibromyalgia is characterized by pain all over the body, whose diagnosis and treatment are not fully understood. Obstructive sleep apnea syndrome (OSAS) is a disease that causes apnea, hypopnea and oxygen desaturation due to collapse in the upper respiratory tract and is characterized by excessive daytime sleepiness, fatigue and lack of attention. Symptoms and signs of OSAS and fibromyalgia are similar. In our study, we aimed to compare the association of fibromyalgia in female OSAS patients in terms of polysomnography and laboratory parameters.

**Materials and Methods:** We aimed to examine the association of fibromyalgia in patients with female OSAS. A total of 190 female OSAS patients were included in the study. The patients were divided into two groups according to the presence of fibromyalgia: 88 (46.3%) patients in the fibromyalgia group and 102 (53.7%) patients in the control group. Statistical Package for the Social Sciences (SPSS) program was used for the evaluation of demographic data, polysomnography parameters and laboratory tests of the patients, and values with  $p < 0.05$  were considered statistically significant.

**Results:** Mean age of the patients was  $52.1 \pm 11.9$  years and mean body mass index (BMI) was  $35.1 \pm 7.2$ . There was no difference between age and BMI ( $p = 0.971$ ,  $p = 0.716$ , respectively). Periodic leg movements (PLMS) were higher in the fibromyalgia group ( $p = 0.02$ ). The desaturation index (CT90) was found to be high in the fibromyalgia group ( $p = 0.043$ ). The minimum SaO<sub>2</sub> value was found to be low in the fibromyalgia group ( $p = 0.022$ ). Sleep latency was found to be higher in the fibromyalgia group ( $p = 0.031$ ). Hemoglobin and hematocrit values were found to be statistically significantly higher in the fibromyalgia group ( $p = 0.020$ ,  $p = 0.027$ , respectively). Triglyceride level was found to be high in the fibromyalgia group ( $p = 0.043$ ).

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**Conclusion:** We recommend clinical evaluation of female patients with fibromyalgia and we suggest polysomnography, especially in patients with excessive daytime sleepiness. Early diagnosis and treatment of concomitant OSAS will contribute to quality of fibromyalgia patients' life.

**Key words:** OSAS; fibromyalgia; nocturnal desaturation; excessive daytime sleepiness; minimum SaO<sub>2</sub>

## ÖZ

### Obstrüktif uyku apne sendromu ile fibromiyalji birlıklığı

**Giriş:** Fibromiyalji, tanısı ve tedavisi tam olarak anlaşılmayan tüm vücutta ağrı ile karakterize bir hastalıktır. Obstrüktif uyku apne sendromu (OSAS), üst solunum yolları kollapse sonucu apne, hipopne ve oksijen desatürasyonuna neden olan, gündüz uyku hali, yorgunluk ve dikkat eksikliği ile karakterize bir hastalıktır. Obstrüktif uyku apne sendromu ve fibromiyaljinin semptom ve bulguları benzerdir. Çalışmamızda kadın OSAS'lı hastalarda fibromiyalji birlıklığını polisomnografi ve laboratuvar parametreleri açısından karşılaştırmayı amaçladık.

**Materyal ve Metod:** Kadın OSAS'lı hastalarda fibromiyalji ilişkisini incelemeyi amaçladık. Çalışmaya toplam 190 kadın OSAS hastası dahil edildi. Hastalar fibromiyalji varlığına göre iki gruba ayrıldı: Fibromiyalji olan grupta 88 (%46.3), fibromiyaljinin olmadığı kontrol grubunda ise 102 (%53.7) hasta vardı. Hastaların demografik verileri, polisomnografi parametreleri ve laboratuvar testlerinin değerlendirilmesinde SPSS programı kullanıldı,  $p < 0.05$  olan değerler istatistiksel olarak anlamlı kabul edildi.

**Bulgular:** Hastaların yaş ortalaması  $52.1 \pm 11.9$ , ortalama vücut kitle indeksi (VKİ)  $35.1 \pm 7.2$  idi. Yaş ve VKİ açısından iki grup arasında fark yoktu (sırasıyla  $p = 0.971$ ,  $p = 0.716$ ). Periyodik bacak hareketleri (PLMS) fibromiyalji grubunda daha yüksek ve istatistiksel olarak anlamlıydı ( $p = 0.02$ ). Fibromiyalji grubunda desatürasyon indeksi (CT90) yüksek ve istatistiksel olarak anlamlı bulundu ( $p = 0.043$ ). Fibromiyalji grubunda minimum SaO<sub>2</sub> değeri düşük ve istatistiksel olarak anlamlı bulundu ( $p = 0.022$ ). Uyku latansı fibromiyalji grubunda daha yüksek ve istatistiksel olarak anlamlı bulundu ( $p = 0.031$ ). Hemogloblin ve hematokrit değerleri fibromiyalji grubunda yüksek ve istatistiksel olarak anlamlı bulundu (sırasıyla  $p = 0.020$ ,  $p = 0.027$ ). Fibromiyalji grubunda trigliserit düzeyi yüksek ve istatistiksel olarak anlamlı bulundu ( $p = 0.043$ ).

**Sonuç:** Fibromiyalji kadın hastaların klinik olarak değerlendirilmesini ve özellikle gündüz aşırı uyku hali olan hastalarda polisomnografi yapılmasını öneriyoruz. Fibromiyaljiye eşlik eden OSAS'ın erken tanı ve tedavisi, fibromiyalji hastalarının yaşam kalitesine katkı sağlayacağı gibi OSAS'a eşlik eden fibromiyaljinin tedavi edilmesi de OSAS tedavisine uyumu dolayısıyla hasta konforunu artıracaktır.

**Anahtar kelimeler:** OSAS; fibromiyalji; noktürnal desaturasyon; gündüz aşırı uykululuğu; minimum SaO<sub>2</sub>

## INTRODUCTION

Fibromyalgia is a common health problem characterized by pain all over the body, whose diagnosis and treatment are not fully understood. In addition to chronic pain, conditions such as joint tenderness, muscle fatigue, sleep problems, cognitive impairment and depression may also be seen. It affects 2-4% of the population, 80-90% of the patients are women, and it is often seen between the ages of 30-50 (1,2).

Obstructive sleep apnea syndrome (OSAS) is a disease that causes apnea, hypopnea and oxygen desaturation due to collapse in the upper respiratory tract and is characterized by daytime sleepiness, fatigue and lack of attention (3). Symptoms and signs of OSAS and fibromyalgia are similar. Treatment efficacy is limited in fibromyalgia, and these patients often live with sleep problems, fatigue and pain symptoms (4). Sleep disturbance is typically seen in 80% of fibromyalgia patients. Patients with fibromyalgia usually report complaints such as frequent sleep interruptions, restless sleep, and daytime sleepiness.

Musculoskeletal pain, fatigue, and sleep disturbance were first described by Moldofsky et al. as fibrositis syndrome (5). Most sleep research in fibromyalgia patients focuses on sleep quality because the amount of sleep does not differ between fibromyalgia patients and healthy individuals (6,7). Sleep disorders may increase pain complaints in musculoskeletal disorders (8). Presence of similar sleep patterns, feeling of restlessness and daytime sleepiness in OSAS and fibromyalgia suggest that these two conditions may be related. Pathophysiological causes such as central sensitization and serotonin deficiency in fibromyalgia and OSAS have been held responsible for sleep disturbance. In addition, it was determined that sympathetic activity increased during sleep in both cases.

Mutlu et al. have evaluated female patients with fibromyalgia using polysomnography according to the results of the daytime sleepiness questionnaire and found that simultaneous OSAS is seen in 65.9% of the patients (9). Sepici et al. have performed polysomnography on a 55-year-old female patient with fibromyalgia for 10 years because she had complaints

of waking up tired in the morning, restless sleep, and daytime sleepiness, and they detected severe OSAS (10). Based on these assumptions, we aimed to examine the association of fibromyalgia in patients with OSAS, to whom we applied polysomnography.

## MATERIALS and METHODS

Female OSAS patients aged 18-75 years with a sleep efficiency of 75% and above that applied to our sleep laboratory between January 2017 and December 2019 were evaluated retrospectively.

Patients with chronic diseases (such as neurological and psychiatric disorders, drug and substance use), degenerative joint diseases and lung diseases that could cause sleep disorders were excluded from the study.

Among the patients diagnosed with OSAS after polysomnography, patients with fibromyalgia were included as the study group, and patients without fibromyalgia were included as the control group.

When the patient file was examined, patients with a history of fibromyalgia were evaluated in a group. The control group was formed among the patients without a history of fibromyalgia by simple random sampling. Polysomnography and laboratory data between the two groups were compared.

Laboratory parameters consisted of routine laboratory tests (hemogram, lipid panel, vitamin B12, Vitamin D, ferritin) that were examined in terms of differential diagnosis (cardiovascular diseases, thyroid dysfunctions, restless legs syndrome, etc.) at the time of admission to the sleep laboratory.

## Polysomnographic Evaluation

Patients were evaluated using a 55-channel polysomnograph (Alice 6<sup>®</sup> Sleepware, Philips Respironics, PA, USA) system. Sleep recordings were analyzed in 30-second epochs and staged according to the guidelines published by the American Academy of Sleep Medicine (AASM) criteria version 2.4 (11). Apnea-hypopnea index (AHI): It was obtained by dividing the sum of the hypopnea and apnea numbers by the sleep duration in hours. Sleep stages were scored as N1, N2, N3, and REM sleep. Leg movements were evaluated in accordance with AASM recommendations. The desaturation index (CT90) was defined as a 3% reduction in SaO<sub>2</sub> from baseline, with the minimum SaO<sub>2</sub> being the lowest SaO<sub>2</sub> recorded overnight.

## Statistical Analysis

SPSS (IBM SPSS Statistics 25, NY, USA) program was used. Obtained values were given as mean  $\pm$  standard deviation. Demographic, polysomnographic and laboratory parameters of the patients were compared with independent sample t-test. ANOVA was used to compare more than two categorical variables. Values with  $p < 0.05$  were considered statistically significant.

## RESULTS

A total of 190 female OSAS patients were included in the study. The patients were divided into two groups according to the presence of fibromyalgia. Fibromyalgia group consisted of 88 (46.3%) patients, and the control group consisted of 102 (53.7%) patients. The power of the study with this sample size was 96.14%. Mean age of the patients was  $52.1 \pm 11.9$ . Mean body mass index (BMI) of the patients was  $35.1 \pm 7.2$ . There was no difference between the two patient groups in terms of age and BMI ( $p = 0.971$ ,  $p = 0.716$ , respectively). Of the patients, 39 (20.5%) had mild, 51 (26.8%) had moderate, and 100 (52.6%) had severe OSAS. There was no statistical difference between the two groups in terms of the degree of OSAS ( $p = 0.757$ ).

Among the polysomnography parameters, AHI, arousal index and sleep efficiency were found to be similar in both groups, and no statistical difference was found ( $p = 0.766$ ,  $p = 0.308$ ,  $p = 0.955$ , respectively). There was no statistical difference between the two groups in terms of the distribution of sleep stages (N1, N2, N3, REM) ( $p = 0.492$ ,  $p = 0.923$ ,  $p = 0.626$ ,  $p = 0.170$ , respectively). Periodic leg movements (PLMS) were higher in the fibromyalgia group and difference was statistically significant ( $p < 0.001$ ). CT90 was found to be high in the fibromyalgia group and it was statistically significant ( $p = 0.043$ ). Minimum SaO<sub>2</sub> value was found to be low in the fibromyalgia group and it was statistically significant ( $p = 0.022$ ). Sleep latency was found to be higher in the fibromyalgia group and the difference was statistically significant ( $p = 0.031$ ). Demographic and polysomnographic parameters of the patients are shown in Table 1.

While there was no difference in hematological parameters in terms of leukocyte, thrombocyte, lymphocyte and neutrophil counts; hemoglobin and hematocrit values were found to be statistically sig-

**Table 1.** Comparison of the demographic and polysomnography parameters of the groups with and without fibromyalgia

	Fibromyalgia (+) OSAS (+) (n= 88)	Fibromyalgia (-) OSAS (+) (n= 102)	p
Age years (mean ± SD)	52.2 ± 11.7	52.1 ± 12.1	0.971
BMI kg/m <sup>2</sup> (mean ± SD)	34.9 ± 7.9	35.3 ± 6.6	0.716
AHI (events/h)	39.2 ± 24.6	38.0 ± 28.4	0.766
CT90 (%)	31.5 ± 32.2	22.6 ± 26.3	<b>0.043</b>
Minimum SaO <sub>2</sub> (%)	78.3 ± 7.6	80.8 ± 7.6	<b>0.024</b>
Arousal index (events/h)	10.5 ± 12.6	8.7 ± 9.7	0.308
PLM index (events/h)	33.1 ± 23.7	13.6 ± 17.8	<b>&lt;0.001</b>
N1 (%)	8.7 ± 9.6	9.9 ± 14.4	0.492
N2 (%)	54.0 ± 16.0	53.8 ± 15.3	0.923
N3 (%)	23.9 ± 14.2	24.9 ± 14.4	0.626
REM (%)	12.6 ± 7.7	11.1 ± 7.3	0.170
Sleep activity (%)	76.3 ± 15.9	76.2 ± 12.8	0.955
Sleep latency (min)	16.09 ± 9.8	13.27 ± 7.7	<b>0.031</b>

BMI: Body mass index, AHI: Apnea-hypopnea index, CT90: Cumulative percentage of time spent at saturation below 90%, SaO<sub>2</sub>: Peripheral capillary oxygen saturation, PLM: Periodic limb movement.

nificantly higher in the fibromyalgia group ( $p= 0.020$ ,  $p= 0.027$ , respectively). While there was no difference in terms of biochemical parameters B12, vitamin D, ferritin, HDL, LDL, and thyroid function tests, the triglyceride level was found to be high in the fibromyalgia group and was statistically significant ( $p= 0.043$ ). The laboratory parameters of the patients that were evaluated for our study are shown in Table 2.

## DISCUSSION

Impaired sleep quality in fibromyalgia increases IL-1, IL-6 and TNF- $\alpha$  levels, resulting in the worsening of pain symptoms (6). Another problem identified in patients with fibromyalgia is the decrease in growth hormone (GH) and insulin-like growth factor 1 (IGF-1) secretion (12).

Some clinical findings such as fatigue, low exercise capacity and cold intolerance in fibromyalgia can be explained by GH deficiency. In addition, GH is thought to decrease further as fibromyalgia progresses (13). Approximately 70% of daily GH is released during N3 and REM sleep. Therefore, sleep disturbance is one of the most important factors affecting GH release (14). Hayta et al. have found that serum IGF-1 levels of patients with fibromyalgia decreased according to age and The Pittsburgh Sleep Quality Index (PSQI) parameters, but were not affected by the severity of OSAS (15).

Approximately 70-80% of fibromyalgia patients have fatigue that continues throughout the day, being more intense in the morning. Although there is a general lack of energy, there is no loss of objective muscle strength. Most of them have paresthesia complaints such as numbness and tingling in any part of the body, especially in the extremities. Fibromyalgia patients may also have restless legs syndrome. Consistent with all these, in our study, PLMS was found to be significantly higher in the group with fibromyalgia.

In our study, sleep latency was found to be higher in the group with fibromyalgia.

This shows that with the decrease in the pain threshold, it becomes more difficult to fall asleep. Similarly, in the study of Köseoğlu et al. a negative and significant relationship was observed between pain threshold and sleep delay, and it was shown that patients had difficulty falling asleep as their pain thresholds decreased (16). Studies have shown that pain sensitivity in women differs between those with and without OSAS, and that pain sensitivity is higher in women with OSAS (17,18).

In our study, there were severe oxygen desaturations in the fibromyalgia group, and the minimum SaO<sub>2</sub> was found to be lower in the fibromyalgia group. This result shows the effect of muscle dysfunction resulting from increased tissue hypoxia and it may also

**Table 2.** Comparison of laboratory parameters of the groups with and without fibromyalgia

	Fibromyalgia (+) OSAS (+) (n= 88)	Fibromyalgia (-) OSAS (+) (n= 102)	p
Hemoglobin, g/dL	14.0 ± 1.7	13.4 ± 1.4	<b>0.020</b>
Hematocrit, %	42.4 ± 4.8	40.9 ± 4.1	<b>0.027</b>
Leucocyte, 10 <sup>3</sup> /L	7.9 ± 2.0	8.1 ± 1.7	0.611
Lymphocyte, 10 <sup>3</sup> /L	3.0 ± 3.4	3.4 ± 5.0	0.524
Neutrophil, 10 <sup>3</sup> /L	5.1 ± 6.3	4.5 ± 1.3	0.433
Platelet, 10 <sup>3</sup> /L	269.4 ± 64.1	262.9 ± 63.5	0.490
MPV (fL)	11.5 ± 10.6	10.2 ± 1.0	0.268
MCV (fL)	80.8 ± 14.6	81.7 ± 11.3	0.634
TSH (mU/L)	3.1 ± 7.3	3.0 ± 8.5	0.980
T3 (pg/mL)	3.2 ± 0.5	3.3 ± 0.4	0.218
T4 (ng/mL)	1.2 ± 0.2	1.2 ± 1.1	0.366
LDL (mg/dL)	125.4 ± 34.4	125.4 ± 33.9	0.999
HDL (mg/dL)	46.1 ± 17.4	45.4 ± 9.3	0.445
VLDL (mg/dL)	36.6 ± 20.1	33.5 ± 16.2	0.348
Triglyceride (mg/dL)	161.7 ± 45.6	146.6 ± 35.1	<b>0.043</b>
Vitamin B12 (pg/mL)	378.3 ± 127.5	400.4 ± 77.2	0.555
Vitamin D (ng/mL)	15.7 ± 9.0	13.6 ± 7.6	0.232
Ferritin, ng/mL	46.2 ± 33.7	65.4 ± 77.2	0.291

MPV: Mean platelet volume, MCV: Mean corpuscular volume, TSH: Thyroid stimulating hormone, T3: Triiodothyronine, T4: Thyroxine, LDL: Low-density lipoprotein cholesterol, HDL: High-density lipoprotein cholesterol, VLDL: Very low density lipoprotein cholesterol.

explain the increase in pain complaints in fibromyalgia. This suggests that intermittent hypoxia from OSAS supports the possible effects on patients' functional status. In the study of Köseoğlu et al. It has been found that the mean SaO<sub>2</sub> value during sleep showed a negative correlation with the subjective symptoms of fibromyalgia (16). Nocturnal desaturation was associated with self-reported pain and awakening during sleep in OSAS patients. Indeed, chronic pain appears to be associated with changes in respiratory parameters.

When evaluated in terms of laboratory parameters in our study, hemoglobin and hematocrit values were found to be significantly higher in the group with fibromyalgia. This may be associated with the higher CT90 and lower minimum oxygen saturation in the fibromyalgia group. Sagmen et al. have also found that mean erythrocyte distribution width (RDW) was negatively correlated with minimum SaO<sub>2</sub> and mean SaO<sub>2</sub> in their study on OSAS patients (19). The diurnal decrease seen in serum erythropoietin levels during sleep in normal individuals is not observed in

patients with OSAS, and it is suggested that this may be a sufficient reason for the development of secondary polycythemia.

One of the laboratory results of our study was a higher triglyceride levels in the fibromyalgia group. Similar to our study, Ünübol et al. have found higher serum triglyceride levels in patients with fibromyalgia compared to the control group (20). There are limited studies evaluating the increased risk of atherosclerosis in patients with fibromyalgia. Lee et al. have suggested that there is a relationship between fibromyalgia and endothelial dysfunction (21). We also think that decreased physical activity may affect serum triglyceride level and BMI in this painful syndrome. Concomitant fibromyalgia may pose a significant risk for atherosclerotic heart diseases, especially in the OSAS patient population with high BMI. In addition, cardiac arrhythmias are common in both fibromyalgia and OSAS due to increased sympathetic activity (22).

Sleep disorders are an important factor in the persistence of pain in fibromyalgia, and studies have

shown that improving sleep quality can reduce pain in patients with fibromyalgia (23). CPAP therapy is the mainstay of treatment for OSAS. In a study evaluating 14 patients with sleep-disordered breathing, it has been shown that there was a significant improvement in fibromyalgia symptoms after three weeks of CPAP treatment (24). In addition, opioids and benzodiazepines used in the treatment of fibromyalgia may worsen OSAS and result in an increased perception of pain (25). Therefore, determining the prevalence of OSAS in fibromyalgia patients and early treatment (CPAP) can prevent unnecessary treatments.

Our study had some limitations that should be considered. Since our sample group is small and consists of women, it may not be representative of the entire population.

## CONCLUSION

Although the symptoms of fibromyalgia and OSAS overlap in female patients, there is little data in the literature regarding the prevalence of OSAS in female patients with fibromyalgia and these patients are rarely referred to a sleep physician by rheumatology, physical therapy and algology outpatient clinics. We recommend clinical evaluation of female patients with fibromyalgia and we suggest polysomnography, especially in patients with excessive daytime sleepiness. Early diagnosis and treatment of concomitant OSAS will contribute to quality of fibromyalgia patients' life.

**Ethical Committee Approval:** The ethical approval for this study was obtained from Malatya Clinical Researches Ethical Committee (Decision No: 2021/80).

## CONFLICT of INTEREST

The authors declare that they have no conflict of interest.

## AUTHORSHIP CONTRIBUTIONS

Concept/Design: AAG, RAB

Analysis/Interpretation: AAG, RAB

Data acquisition: RAB

Writing: AAG

Clinical Revision: AAG, RAB

Final Approval: AAG, RAB

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