Obstructive Sleep Apnea Syndrome and Sleep Efficiency in Patients With Ankylosing Spondylitis

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ABSTRACT

Objectives: This study aims to determine the prevalence of obstructive sleep apnea syndrome (OSAS) and assess sleep efficiency in patients with ankylosing spondylitis.

Patients and methods: A total of 42 patients (36 males, 6 females; mean age 39.4±9.1 years; range 23 to 63 years) with ankylosing spondylitis were included in this study. Demographic data, spinal mobility measurements, disease activity measurements, and sleep questionnaire results were recorded for each patient. All subjects underwent an overnight polysomnography test and their sleep records were evaluated.

Results: Polysomnography test revealed OSAS in 13 (30.9%) patients. Patients with OSAS had a significantly greater occiput-to-wall distance and neck circumference (p=0.025 and p=0.004, respectively). In addition, there was a positive correlation between apnea hypopnea index and occiput-to-wall distance and neck circumference (r=0.355, p=0.021; r=0.413, p=0.007, respectively) whereas apnea hypopnea index and body mass index did not significantly correlate.

Conclusion: Our study showed that patients with ankylosing spondylitis had higher OSAS prevalence than reported in the general population. Furthermore, OSAS prevalence accordingly increased with the severity of cervical vertebral involvement.

Keywords: Ankylosing spondylitis; obstructive sleep apnea syndrome; polysomnography; sleep efficiency.

Ankylosing spondylitis (AS) is a common inflammatory rheumatic disease involving the axial skeleton with resultant characteristic inflammatory back pain. It has adverse structural and functional consequences and causes reduced quality of life.1 Patients with AS have significant difficulties related to pain, stiffness, fatigue, and disordered sleep.2 It has recently been brought to attention of the medical community that patients with AS experience disordered sleep characterized by reduced sleep quality, sleep onset insomnia, difficulty in awakening, and obstructive sleep apnea syndrome (OSAS).3 These patients characteristically suffer fragmented sleep due to their inflammatory low back involvement that occurs in the form of axial pain and stiffness at night, especially in the second half of the latter.4 Studies have shown that pain aggravates sleep disorders and short sleep duration has been shown to cause emotional stress, attention deficit, and learning difficulties.5

Obstructive sleep apnea syndrome is a prevalent disorder caused by recurrent attacks of the upper airway collapse during sleep. OSAS triggers a series of events including arousals, intrathoracic pressure swings, and repeated cycles of hypoxemia and reoxygenation.6 OSAS is also associated with increased mortality and morbidity, for example excessive daytime sleepiness, hypertension, cardiovascular disease, and fatigue. Similarly, sleep disturbance and fatigue...
are common features of AS.\textsuperscript{7} Polysomnography (PSG) is accepted as the ‘gold standard’ for diagnosing OSAS and measuring sleep.\textsuperscript{8} The contribution of OSAS to sleep disturbances in AS is not well characterized. Studies employing PSG to determine sleep disturbance in AS have either been scarce or studied in limited numbers of patients.\textsuperscript{9,10} Thus, in this study, we aimed to determine the prevalence of OSAS and assess sleep efficiency in patients with AS.

\section*{PATIENTS AND METHODS}

Our study enrolled patients with AS who applied to the outpatient clinics of the Rheumatology and Physical Medicine and Rehabilitation departments of our hospital between November 2013 and September 2014. Patients fulfilled the modified New York criteria for the classification of AS.\textsuperscript{11} Patients who had a severe infection or any systemic disease (cardiac, respiratory, gastrointestinal, neurological, endocrine, etc.), or who used any medication that would potentially alter sleep pattern were excluded. All enrolled subjects underwent an otorhinolaryngology examination and those having any anatomic disorder in upper airways potentially causing OSAS were also excluded. Among the remainders, a total of 44 patients who met the inclusion criteria and accepted to undergo an overnight PSG test in the sleep laboratory were included. Two of them, however, had missing medical records and were thus excluded. Hence, 42 subjects (36 males, 6 females; mean age 39.4±9.1 years; range 23 to 63 years) were included in the final analysis. All participants’ rights were protected, and informed consents were obtained according to the Helsinki Declaration. The study protocol was approved by the local ethics committee.

Demographic characteristics, disease duration, treatments, physical examination findings (neck circumference, occiput-to-wall distance, Schober’s test, and chest expansion) were documented for each patient. The duration of the morning stiffness (minutes) and pain [10 cm visual analog scale (VAS)] were also recorded. The disease activity and functional statement were evaluated using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Bath Ankylosing Spondylitis Functional Index (BASFI), respectively.\textsuperscript{12,13} The reliability and validity of the Turkish version of BASDAI and BASFI have already been demonstrated.\textsuperscript{14,15}

Pulmonary function parameters (forced expiratory volume in 1 second and forced vital capacity) were measured using a spirometer (Ultima CPX 790705-205; Medgraphics Corporation, St. Paul, MN, USA). The values were interpreted according to the predicted values provided by the European Respiratory Society.\textsuperscript{16} Pulmonary function values were expressed as a percentage of the predicted values.

All of the patients were questioned about complaints of snoring, witnessed apnea, daytime sleepiness, frequent night awakenings, fatigue, and waking up with headache. Sleep quality and excessive daytime sleepiness were evaluated by using the Pittsburgh Sleep Quality Index (PSQI) and the Epworth sleepiness scale, respectively. The reliability and validity of the Turkish versions of these questionnaires have been verified by Agargün\textsuperscript{17} and Izci.\textsuperscript{18}

All of the polysomnographic sleep studies were performed in the sleep disorders laboratory of our hospital. The whole study population underwent full overnight in-laboratory polysomnography with a 44-channel recording system (Compumedics E series, Compumedics Inc., Melbourne, Australia). Polysomnography was performed with simultaneous monitoring of brain activity (electroencephalogram with electrodes placed at C3A2, C4A1, O1A2, O2A1), muscle tone (electromyogram), eye movements (electrooculogram), heart rate (electrocardiogram), oxygen saturation (pulse oximetry), chest and abdominal wall movement (thoracic and abdominal belts), airflow (thermistor and nasal prong pressure transducer), and snoring (microphone).

The recordings were scored according to the standard criteria of American Academy of Sleep Medicine.\textsuperscript{8} Sleep efficiency was defined as total sleep time as percentage of time in bed. Percentage of the various sleep stages [non-rapid eye movement (non-REM) 1, non-REM 2, non-REM 3 and REM] was calculated as the minutes in each stage as the percent of total sleep time. Apnea was defined as a drop in the
peak thermal sensor excursion of ≥90% of the baseline for ≥10 seconds. Hypopnea was defined as a reduced nasal pressure signal of ≥30% of the baseline that lasted ≥10 seconds, resulting in a ≥3% decreased oxygen saturation from the pre-event baseline or an arousal. Desaturation was defined as a reduced oxygen saturation by 3% from the baseline. Mean oxygen saturation was defined as the average oxygen saturation at night. Lowest oxygen saturation was defined as the lowest value of oxygen saturation at night. Arousal index was defined as the number of awakenings per hour. The apnea-hypopnea index (AHI) was defined as the average number of apneic and hypopneic events per sleep hour. An AHI higher than 5/hour was considered as diagnostic of OSAS.

**Statistical analysis**

We used the IBM SPSS Statistical Product and Service Solutions version 21.0 software (IBM Corporation, Armonk, NY, USA). Results were expressed as mean ± standard deviation. A p value less than 0.05 was accepted statistically significant. The chi-square test was used to compare differences between categorical values of two groups. An independent samples t-test was used to compare differences between continuous variables. Correlation analysis between variables was performed using Pearson’s correlation test.

**RESULTS**

The mean body mass index (BMI) was 25.6±3.7 kg/m². The clinical and demographical characteristics of the patients are listed in Table 1.

Thirteen (30.9%) of the 42 AS patients had OSAS according to PSG assessments. No statistically significant difference was found between patients with and without OSAS regarding the age and sex (for age, p=0.219; for sex, p=0.276; Chi square=1.18). Seven patients had mild OSAS (AHI: 5-15/hour) and six had moderate OSAS (AHI: 15-30/hour), whereas none had severe OSAS (AHI higher than 30/hour).

There was no statistically significant difference between the groups regarding mean BMI, disease duration, duration of the morning stiffness, VAS, BASDAI and BASFI scores, Schober’s test, and chest expansion. However, occiput-to-wall distance and neck circumference were significantly greater in patients with OSAS (p=0.025, p=0.004, respectively).

Pulmonary function test was consistent with a restrictive pattern in 12 patients (28.6%) whereas it did not demonstrate an obstructive pattern in any patient. There was no difference between the patients with and without OSAS with respect to forced vital capacity and forced expiratory volume in 1 second levels (Table 1).

<p>| Table 1. Clinical and demographical characteristics of ankylosing spondylitis patients with and without obstructive sleep apnea syndrome |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Age (years) | No OSAS (n=29) | OSAS (n=13) | Total group (n=42) | p |</p>
<table>
<thead>
<tr>
<th>n</th>
<th>%</th>
<th>Mean±SD</th>
<th>n</th>
<th>%</th>
<th>Mean±SD</th>
<th>n</th>
<th>%</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>38.2±8.5</td>
<td>26</td>
<td>89.6</td>
<td>10</td>
<td>76.9</td>
<td>42.2±10.0</td>
<td>36</td>
<td>85.7</td>
<td>39.4±9.1</td>
</tr>
<tr>
<td>25.08±4.1</td>
<td>9.0±3.5</td>
<td>8.9±6.9</td>
<td>42.4±74.2</td>
<td>4.1±3.1</td>
<td>15.3±12.7</td>
<td>3.5±4.2</td>
<td>3.7±2.9</td>
<td>3.3±2.6</td>
</tr>
</tbody>
</table>

OSAS: Obstructive sleep apnea syndrome; SD: Standard deviation; BASDAI: Bath ankylosing spondylitis disease activity index; BASFI: Bath ankylosing spondylitis functional index; FVC: Forced vital capacity; FEV1: Forced expiratory volume in 1 second.
An analysis of the study population with respect to the most common OSAS symptoms revealed that OSAS patients had a significantly higher prevalence of snoring and witnessed apnea compared to the subjects without OSAS whereas the rates of daytime sleepiness, weakness, headache upon awakening, and insufficient-fragmented sleep were similar in both groups. Although there was no significant difference between the groups in terms of total PSQI scores, the OSAS patients had higher scores in the Epworth sleepiness scale (p=0.001) (Table 2).

An analysis of the study population with regard to signs of PSG demonstrated that the two groups did not differ significantly with respect to total sleep time, sleep efficiency, number of awakenings, distribution of sleep stages, and mean saturation during sleep. The OSAS group, however, had a significantly greater number of desaturation and lowest saturation. The arousal

### Table 2. Symptoms, sleep questionnaires and polysomnographic results in ankylosing spondylitis patients with and without obstructive sleep apnea syndrome

<table>
<thead>
<tr>
<th>Symptoms of OSAS, (%)</th>
<th>No OSAS (n=29)</th>
<th>OSAS (n=13)</th>
<th>Total group (n=42)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Snoring</td>
<td>62.1%</td>
<td>100%</td>
<td>73.8%</td>
<td>0.01</td>
</tr>
<tr>
<td>Witnessed apnea</td>
<td>0%</td>
<td>46.2%</td>
<td>14.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Daytime sleepiness</td>
<td>41.4%</td>
<td>61.5%</td>
<td>47.6%</td>
<td>0.227</td>
</tr>
<tr>
<td>Daytime fatigue</td>
<td>65.5%</td>
<td>92.3%</td>
<td>73.8%</td>
<td>0.068</td>
</tr>
<tr>
<td>Waking up with headache</td>
<td>51.7%</td>
<td>61.5%</td>
<td>54.8%</td>
<td>0.555</td>
</tr>
</tbody>
</table>

**Polysomnographic results**

<table>
<thead>
<tr>
<th>Stage 1, (%)</th>
<th>No OSAS (n=29)</th>
<th>OSAS (n=13)</th>
<th>Total group (n=42)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 2, (%)</td>
<td>3.9±4.1</td>
<td>2.7±1.6</td>
<td>3.5±3.6</td>
<td>0.177</td>
</tr>
<tr>
<td>Stage 3, (%)</td>
<td>56.8±13.3</td>
<td>58.9±6.3</td>
<td>57.5±11.5</td>
<td>0.481</td>
</tr>
<tr>
<td>Stage REM, (%)</td>
<td>24.6±10.1</td>
<td>23.9±7.2</td>
<td>24.4±9.2</td>
<td>0.805</td>
</tr>
<tr>
<td>Total sleep time (minute)</td>
<td>330.3±95.5</td>
<td>383.5±67.7</td>
<td>346.8±90.5</td>
<td>0.057</td>
</tr>
<tr>
<td>Sleep efficiency, (%)</td>
<td>65.2±16.4</td>
<td>75.6±9.4</td>
<td>68.4±15.3</td>
<td>0.075</td>
</tr>
<tr>
<td>Number of awakenings</td>
<td>10.8±6.4</td>
<td>8.6±4.1</td>
<td>10.1±5.8</td>
<td>0.201</td>
</tr>
<tr>
<td>AHI events h-1</td>
<td>1.5±1.5</td>
<td>13.5±5.4</td>
<td>5.2±6.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean SaO2, (%)</td>
<td>92.7±1.4</td>
<td>91.5±2.3</td>
<td>92.3±1.8</td>
<td>0.093</td>
</tr>
<tr>
<td>Lowest SaO2, (%)</td>
<td>88.5±2.4</td>
<td>82.9±5.2</td>
<td>86.8±4.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Desaturation number</td>
<td>41±4.9</td>
<td>66.8±36.1</td>
<td>23.5±35.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arousal index</td>
<td>9.5±8.5</td>
<td>13.2±6.3</td>
<td>10.6±7.8</td>
<td>0.121</td>
</tr>
<tr>
<td>Epworth sleepiness scale</td>
<td>5.1±2.8</td>
<td>9.0±3.2</td>
<td>6.4±3.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Pittsburgh sleep quality index</td>
<td>7.1±4.2</td>
<td>8.2±3.2</td>
<td>7.5±3.9</td>
<td>0.359</td>
</tr>
</tbody>
</table>

OSAS: Obstructive sleep apnea syndrome; SD: Standard deviation; REM: Rapid eye movement; AHI: Apnea-hypopnea index; SaO2: Oxygen saturation.

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**Figure 1.** (a) Correlation between apnea-hypopnea index and occiput-to-wall distance and (b) neck circumference in patients with ankylosing spondylitis. AHI: Apnea-hypopnea index.
frequency was higher in the OSAS group, albeit statistically non-significant (Table 2).

When all patients were analyzed, there was a positive correlation between AHI and occiput-to-wall distance and neck circumference ($r=0.355$, $p=0.021$ and $r=0.413$, $p=0.007$, respectively) (Figure 1) and also a positive correlation between occiput-to-wall distance and neck circumference ($r=0.420$, $p=0.006$). There was, however, no significant correlation between AHI and BMI. There was also no correlation between disease duration and AHI, occiput-to-wall distance, and neck circumference.

The BASDAI score measuring the disease activity had a positive correlation with the PSQI score and the number of awakenings ($r=0.419$, $p=0.006$ and $r=0.517$, $p<0.001$, respectively) and a negative correlation with sleep efficiency ($r=-0.474$, $p=0.002$) (Figure 2). Similarly, the BASFI score indicating the functional state of the disease was significantly correlated with PSQI score and the number of awakenings ($r=0.445$, $p=0.003$ and $r=0.563$, $p<0.001$, respectively), while it had a significant negative correlation to sleep efficiency ($r=-0.530$, $p<0.001$) (Figure 3). Additionally, significantly positive correlations between the BASDAI and BASFI scores and VAS scores were observed ($r=0.742$, $p<0.001$ and $r=0.761$, $p<0.001$, respectively).

**DISCUSSION**

Our study showed that the prevalence of OSAS was higher (30.9%) in AS patients than general population. Furthermore, sleep quality deteriorated as the disease worsened.

Ankylosing spondylitis is an inflammatory systemic disorder predominantly affecting the
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axial skeletal and thoracic cage. It has recently been reported that AS patients have a variety of sleep disorders such as impaired sleep quality, sleeplessness, difficulty in awakening, and OSAS. However, the majority of studies on OSAS have used questionnaires. In a multicenter, large-scale study, Jiang et al. found impaired sleep quality in 37.3% of 683 patients with AS. Similarly, a study that compared 80 AS patients and 52 healthy controls demonstrated worse sleep quality and efficiency and higher PSQI scores in patients with AS. Another study showed that 58.6% of 314 AS patients were at high risk for developing sleep disorders and reported a strong correlation between PSQI score and the BASDAI and BASFI scores. Our study showed a significant correlation between the BASDAI and BASFI scores and PSQI scores; these patients also had reduced sleep efficiency and increased number of awakenings in accordance with the increased disease activity. However, no such correlation was observed with disease duration. Hence, our results suggest that increased number of awakenings and reduced sleep efficiency were not correlated to disease duration, but rather severity. This may be due to increased pain sensation in these patients. Increased disease severity and worsened dysfunction lead to increased pain sensation, resulting in frequent awakenings and reduced sleep efficiency. Hence, we observed a strong correlation between the BASDAI and BASFI scores and VAS scores.

Sleep efficiency and quality in AS patients have been studied by various questionnaire studies to date. Nevertheless, there is a limited number of studies objectively exploring sleep quality and OSAS frequency in AS. One of the reasons of the scarcity of studies on this subject may be that a PSG examination is required for diagnosing OSAS and monitoring sleep, and patients may be reluctant to sleep overnight in a sleep laboratory. Our literature scan revealed only two studies on this subject. One of them reported an OSAS prevalence of 12% in AS patients, a figure that was considerably lower than ours. However, the OSAS definition in that study had some differences compared to ours, i.e., only apnea periods were analyzed but hypopnea periods were completely ignored. Furthermore, this study considered patients with 10 or more apnea periods per hour as OSAS and was conducted in a very small group. Finally, it assumed an OSAS prevalence of 1-4% in healthy subjects. Considering all these factors, OSAS prevalence was still high in AS patients in that study. The other study found an OSAS prevalence of 22.6% based on PSG examination in AS patients. Considering that the OSAS prevalence is 2-7% in the normal population, OSAS prevalence is substantially high in our study as well as in both of the other studies.

Possible mechanisms for the cause of OSAS in AS were suggested by Erb et al. including restriction of the oropharyngeal airway by compression from cervical spine involvement or temporomandibular involvement, restrictive pulmonary disease, or cervical spine disease causing compression of the respiratory centers found in the medulla. As the disease progresses and the vertebral anatomy changes, the occiput-to-wall distance increases which results in an increased neck thickness. Despite similar BMI values in patients with and without OSAS, the occiput-to-wall distance and neck thickness were increased in the OSAS group, supporting our hypothesis. In addition, we observed a positive correlation between AHI scores and these two parameters. These findings suggest that OSAS prevalence increased in patients with advanced cervical vertebral disease (increased occiput-to-wall distance and neck thickness) causing oropharyngeal airway obstruction and tracheal compression. In fact, Solak et al. also found a greater occiput-to-wall distance and neck thickness in patients with OSAS even though their results could not reach statistical significance, most probably due to the limited sample size. This was overcome by a larger sample size in our study. Moreover, none of the patients had central sleep apnea syndrome or increased central apnea frequency, suggesting that the compression of the respiratory center in medulla by cervical vertebra disease is not influential on the OSAS pathophysiology. Lack of any significant difference between pulmonary function test results in patients with and without OSAS does not support the hypothesis that apnea/hypopnea occur as a result of restrictive pulmonary disease, either. Use of steroids with attendant increase in neck circumference and body weight in conjunction to upper airway muscle atrophy has also been proposed as other
Both reduced sleep efficiency and quality, and the OSAS result in fatigue and reduced productivity. Erb et al.\(^9\) stressed that alternative causes like OSAS should be explored when disease activity fails to explain fatigue in patients with AS. In our study, none of the 13 patients diagnosed with OSAS had an AHI higher than 30 (severe OSAS) and the majority of the subjects had mild OSAS (AHI 5-15/hour). Thus, it is likely that these patients are not aware of their sleep problems and have not been investigated for that indication. Moreover, the arousal index was higher in OSAS patients compared to those without OSAS, although this difference did not reach statistical significance. An analysis of sleep stages and sleep quality revealed no significant difference between the two groups although both groups had a reduced sleep efficiency (<80%) and the duration of REM sleep and an increased duration of stage 2 sleep with respect to the normal population.\(^{23}\) It was suggested that whether or not they had OSAS, AS patients experience frequent arousals most likely due to back pain and stiffness resultant reductions in sleep quality. Likewise, a study comparing 20 AS patients and 10 healthy controls found reduced sleep quality and efficiency, prolonged time to progress to sleep, reduced low wave sleep, and increased stage 1 and 2 sleeps and number of arousals in AS patients.\(^{24}\)

As expected, the number of desaturations and the lowest saturation were significantly higher in OSAS patients. On the other hand, mean saturation during sleep was not significantly different between the groups. This may be due to two reasons. First, all OSAS patients had mild or moderate disease in which apnea and hypopnea episodes may not have significantly altered mean saturation levels. Second, hypoventilation secondary to pain or restriction may affect mean saturation to a similar extent in all AS patients independent of the presence of OSAS.

Our study has some limitations. First, we enrolled patients who agreed to spend a night in a sleep center for PSG procedure and these patients may inevitably be the patients with more severe sleep-related symptoms; therefore, a selection bias may have occurred. This may also lead to a higher OSAS prevalence in AS patients. Moreover, PSG is a time-consuming procedure with whole-night monitorization requirement for which a relatively limited number of patients could be enrolled. Our results should be confirmed by further studies with larger sample sizes.

In conclusion, our study demonstrated that OSAS was more prevalent in AS patients than the normal population, disease activity rather than disease duration played an important role in OSAS development, and sleep quality was low in this group of patients. To our knowledge, our study is the first demonstrating the relationship between OSAS and spinal changes in patients with AS.

**Declaration of conflicting interests**

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