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The Relationship Between Sleepiness, Fatigue, Anxiety and Depression Levels and Polysomnographic Variables in Patients with Obstructive Sleep Apnea Syndrome

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Abstract

Background: Obstructive Sleep Apnea Syndrome (OSAS) is not just a limited entity, but is one of the modern age diseases, which is the cause and/or result of several diseases together. The clinical manifestation formed in patients by the interaction of sleepiness, fatigue, anxiety, and depression may cause the development of these diseases. This study aimed to enlighten more of the sleepiness, fatigue, anxiety, and depression with polysomnographic findings in OSAS.

Methods: The study included 95 patients diagnosed with OSAS according to ICSD-3, who presented at the Sleep Centre of Erenkoy Psychiatric and Neurological Diseases Training and Research Hospital. The study group were applied with the Mini International Neuropsychiatric Interview-Clinician Evaluation, the Epworth Sleepiness Scale (ESS), the Chalder Fatigue Scale (CFS), the Motivation And Energy Inventory-Short Form, the Hospital and Anxiety Depression Scale (HADS) and polysomnography.

Results: In the hierarchic multiple linear regression model, apnea/hypopnea index (AHI) was found to be independently related to CFS ($p<0.01$, $\Delta R2:0.03$), the HADS depression scores were related to the mean oxygen saturation (MO_2S) (p:0.01, $\Delta R2:0.03$). HADS anxiety scores were related to REM and N3 duration (p:0.02, $\Delta R2:0.03$; p:0,01, $\Delta R2:0.04$), and there was a relationship between ESS scores and oxygen desaturation index (ODI) ($p<0.01$, $\Delta R2:0.07$), when adjusted for sex, age, BMI and other clinical variables.

Conclusions: The results showed relationships between clinical variables seen in OSAS and the objective sleep variables. Fatigue could be predicted with the polysomnographic variable of AHI and depression with MO_2S and, anxiety with REM and N3 duration, and sleepiness with ODI.

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INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is one of the most frequently encountered sleep disorders that can be seen with repeated episodes of full (apnea) or partial (hypopnea) upper respiratory tract obstruction during sleep with a concomitant fall in oxygen saturation [1-3]. OSAS symptoms may not be noticed by the individual, or late identification may cause an incorrect diagnosis by increasing clinical confusion as some symptoms are similar to those of anxiety and depression [4-6]. As the symptoms of the disease and their consequences can lead to hypertension, cardiovascular and cerebrovascular problems, increased insulin resistance diabetes mellitus, increased disability and accidents, or because of resistance to treatment, there can be a severe financial burden [7-9].

Symptoms of the disease are usually not noticed by the individual, are denied or are noticed late [10]. The clinical structure formed in patients by the interaction of sleepiness, fatigue, anxiety, and depression may cause the development of several different diseases that can affect patient behavior [11-14]. The correct and timely evaluation of complaints such as attention disorder, fatigue, lethargy, irritability, sleepiness, and experiencing problems in work life, which do not have the core symptoms of depression and anxiety, has been shown to increase the rates of correct treatment and consequently increased compatibility with treatments related to somatic disease [15,16]. These individuals then go on to improve both social and professional functionality, and there is no need for long-term, inappropriate psychiatric treatment from which they will not benefit [17]. Disease symptoms lasting throughout the day and a sedentary lifestyle associated with low motivation have been shown to be a risk factor for the development of several diseases and resistance to

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treatment [7].

The aim of this study was to investigate the relationship between the objective variables of sleep and the clinically significant and often seen sleepiness, fatigue, anxiety, and depression dimensions in newly-diagnosed, treatment-naive OSAS patients. In future studies, these relationships could be valuable in the research into the etiopathology of related diseases and the determination of areas for intervention with treatment.

METHODS

Participants and procedure

The study included 95 patients diagnosed with OSAS according to ICSD-3 (International Classification of Sleep Disorders) criteria as a result of polysomnographic tests and clinical evaluations made in the Sleep Centre of Erenkoy Psychiatric and Neurological Diseases Training and Research Hospital (EPNH). The study protocol was approved by the institutional review board and the ethical committee of EPNH. Signed informed consent forms were obtained from all the patients.

Exclusion criteria

1) age <18 years

2) mental retardation preventing verbal and oral communication, low educational level, the presence of any psychiatric, general medical or neurological disorder.

DATA COLLECTİON TOOLS

Sociodemographic data form

This form was prepared to record the sociodemographic variables of the patients, such as age, gender, marital status, years of education and employment status, and body mass index (BMI), alcohol consumption, smoking status, and disease history.

Polysomnography (PSG)

In the PSG examination, a record was made of 6-channel EEG, as C4-A1, C3-A2, O2-A1, O1-A2, F4-A1, F3-A2 electrodes, placed appropriate to the international 10-20 assembly system, 2-channel EOG in the monitorisation of right and left eye movements, jaw EMG, anterior tibialis EMG, oronasal airflow with nasal cannula, arterial oxygen saturation, respiratory effort with chest and abdominal bands, ECG and video monitorization. The RemLogic file method was used as the PSG software in the gathering and examination of the data. The scoring and reporting procedures in this program, which allows the possibility of manual and automatic scoring, were applied as described in the AASM rules. The clinicians in the unit prepared the PSG reports, including the date of the recording, starting and finishing times, sleep latency, total sleep duration, the ratio of sleep stages to total sleep duration, and respiratory parameters. Statistical analysis was made using the data of the PSG parameters of total sleep time (TST), apnea/hypopnea index (AHI), sleep efficacy, REM latency, N3 duration, REM duration, oxygen desaturation index (ODI), mean oxygen saturation (MO_2S) and lowest oxygen saturation (LO_2S).

Epworth Sleepiness Scale (ESS)

This simple questionnaire form was first developed by M.W. Johns in 1991. The ESS is a 4-point Likert-type scale. The tendency to sleepiness during 8 daily activities is questioned, and high scores indicate higher levels of sleepiness. The self-reporting scales developed to measure sleepiness quantitatively and qualitatively target the measurement of the general level of daytime sleepiness rather than sleepiness in particular daytime conditions and in particular time slices [18]. The ESS is a valid and reliable scale in the evaluation of the general sleepiness level, and it has been reported to be a valid and reliable test that can be used in studies in Turkey related to sleep and sleep disorders [19].

Chalder Fatigue Scale (CFS)

This 11-item scale was developed to measure the severity of fatigue in adults. It is applied in both clinical and research settings. The items related to fatigue are answered with one of 4 Likert-type responses as “better than usual,” “no better than usual,” “worse than usual,” and “much worse than usual” [20]. The Turkish version of the CFS was shown to have good validity and reliability [21].

Motivation and Energy Inventory-short form (MEI-SF)

The MEI-SF is an 18-item scale that was developed to evaluate fatigue and lethargy. This self-reported scale was originally developed to evaluate the development of energy and depression in patients. Completion of the form takes 5-10 minutes using pen and paper [22]. Turkish translation of the scale was made by the developer, Sheri Fehnel and Glaxo Smith Kline, and written permission was obtained [22]. In the current study, the Turkish version of MEI-SF was used, and the Cronbach’s alpha coefficient for the MEI-SF was 0.91.

Hospital Anxiety and Depression Scale (HADS)

The HADS is a self-reported scale that aims to determine the risk of the patient in respect of anxiety and depression by measuring the change in level and severity. Turkish validity and reliability studies were conducted by Aydemir et al. [24]. The cutoff scores of the Turkish version of the HADS have been determined as 10 for the subscale of anxiety and 7 for the subscale of depression. The aim of the scale is not diagnostic, but to determine the risk group of patients with a physical disease by screening anxiety and depression in a short period. The scale can also be used in the evaluation of change in the emotional status of the patient. The HADS aims to minimize the effects of physical

disease on the scale results. Therefore, it does not include any physical symptoms. The content of the questions has been designed to reach a result by comparing present and past states related to the pleasure taken from life, feelings of worry and tension, and interest in appearance and surroundings [23,24].

Mini-International Neuropsychiatric Interview (MINI)

This scale was designed in 1998 by Sheehan et al. as a short structured interview evaluating basic first axis psychiatric disorders in the DSM-IV and ICD-10. Turkish version 5.00 was used in the current study [25].

Statistical Analysis

The findings obtained in the study were analyzed statistically using SPSS for Windows ver. 20.0 software. The conformity of the data to normal distribution was assessed using the Kolmogorov-Smirnov test. In the correlation analyses, the Pearson Correlation tests were applied according to the distribution characteristics of the continuous variables. Hierarchic multiple linear regression analysis was used in the examination of the relationships between the clinical variables and the PSG variables. Results were evaluated in a 95% confidence interval. A value of $p<0.05$ was accepted as statistically significant.

RESULTS

The evaluation was made of a total of 95 OSAS patients, who had no additional medical disease, had not received any psychiatric treatment, and had not received any OSAS treatment. The patients comprised 64 (67.4%) males and 31 (32.6%) females in the age range of 28 – 68 years. The demographic data of the cases are shown in Table 1. The mean of polysomnographic and clinical variables are shown in Table 2.

To investigate the relationships of PSG variables with the clinical variables independent of their effects on each other, first, Pearson correlation was used. A significant negative correlation was determined between the mean HADS depression and MO_2S (r:-.21, p:.04), and the HADS anxiety scores and REM were seen to be significantly negatively correlated (r:-.22, p:.03). Also, a significant positive correlation was determined between the mean HADS anxiety scores and the N3 duration (r:.26, p:.01). It was found a significant negative correlation was determined between the ESS and the and LO_2S (r:-.3, p<.01), and a significant positive correlation was determined between the ESS and the Apne/Hypopnea Index (AHI), Sleep Efficacy and Oxygen Desaturation Index (ODI) (r:0.32, p<.01; r:.21, p:.04; r:.36, p<.01) (Table 3). Then, separate models were created in the hierarchic multiple linear regression analysis, as age, sex, BMI (step 1-enter), clinical variables (step 2-enter), and PSG variables (step 3-stepwise). In the hierarchic multiple linear regression model, AHI was found to be independently related to CFS (p<.01, ΔR^2:.03). There was no relationship between MEI-SF and PSG variables. The HADS depression scores were related to the MO_2S (p:.01, ΔR^2:.03), HADS anxiety scores were related to REM and N3 duration (p:.02, ΔR^2:.03; p:.01, ΔR^2:.04), and there was a relationship between ESS scores and ODI (p<.01, ΔR^2:.07) (Table 4), when adjusted for sex, age, BMI and other clinical variables.

Table 1. Demographic characteristics

		Mean + SD
Age (year) (N=95)		48.02±9.38
Education (year) (N=95)		8.67±3.89
		N %
Sex	Male	64 (67.4)
	Female	31 (32.6)
Marital status	Married	75(78.9)
	Single	10(10.5)
	Other	10(10.5)
Employment	Employed	62 (65.3)
	Unemployed	33 (34.7)
Alcohol use	Yes	11 (11.6)
	No	84 (88.4)
Smoking	Yes	52 (54.7)
	No	43 (45.3)

SD=standart deviation

Table 2. Polysomnographic variables, and mean ESS, CFS, MEI-SF, HADS-A, HADS-D scores (N=95)

	Mean+ SD
BMI (kg/m^2)	30.1±3.6
MEI-SF	54.8±18.6
HADS anxiety score	7.8±4.2
HADS depression score	7.3±4.1
ESS	7.8±4.9
CFS score	16.1±5.9
AHI (/h)	35.6±25.3
Mean SpO2 (%)	93.2±3.2
Lowest SpO2 (%)	80.4±8.1
ODI (/h)	31.6±25.2
Total sleep time (min)	381.1±43.0
Sleep Efficacy (%)	85.1±11.8
REM latency	143.5±94.
N3 duration	94.5±50.6
REM	38.1±22.7

SD=standart deviation, AHI= Apnea-hypopnea index, BMI= body mass index, ODI= oxygen desaturation index, SpO2= pulse oximeter oxygen saturation, CFS= Chalder Fatigue Scale, MEI-SF= Motivation And Energy Inventory-Short Form, HADS-D= Hospital Anxiety And Depression Scale Depression Subscale, HADS-A= Hospital Anxiety And Depression Scale Anxiety Subscale, ESS= Epworth Sleepiness Scale.

Table 3. Pearson correlations between polysomnographic variables, and mean ESS, CFS, MEI-SF, HADS-A, HADS-D scores (N=95)

	CFS		HADS-D		HADS-A		MEI-SF		ESS	
	r	p	r	p	r	p	r	p	r	p
AHI (/h)	-.160	.122	-.022	.835	.073	.483	-.056	.588	**.319**	**.002** *
ODI (/h)	-.124	.232	.051	.620	.075	.469	-.084	.421	**.364**	**.000** **
Mean SpO2 (%)	.102	.324	**-.209**	**.042** *	-.030	.775	.060	.562	-.115	.268
Lowest SpO2 (%)	.078	.453	-.059	.571	-.111	.283	.139	.178	**-.295**	**.004** *
Sleep Efficacy (%)	-.031	.768	-.046	.657	.043	.677	.016	.881	**.208**	**.043** *
REM latency	-.006	.954	.129	.213	.079	.445	-.034	.745	-.053	.612
N3 duration	.184	.075	.045	.663	**.260**	**.011** *	-.148	.153	.067	.516
REM	-.083	.426	-.109	.292	**-.219**	**.033** *	.105	.309	.048	.645
Total sleep time (min)	-.069	.507	-.130	.210	.030	.775	.055	.595	.049	.637

*p <.05; **P≤.01 AHI= apnea-hypopnea index. BMI= body mass index, ODI= oxygen desaturation index, SpO2= pulse oximeter oxygen saturation, CFS= Chalder Fatigue Scale, MEI-SF= Motivation And Energy Inventory-Short Form, HADS-D= Hospital Anxiety And Depression Scale Depression Subscale, HADS-A= Hospital Anxiety And Depression Scale Anxiety Subscale, ESS= Epworth Sleepiness Scale.

Table 4. Multiple linear regression analysis

Dependent variable		Independent variables included	B	t	F	adjR2	ΔR^2	Sig.
CFS	*Step1*	*Age, Gender, BMI*						
	Step2	*Age, Gender, BMI, HADS-D, HADS-A, MEI-SF, ESS*						
	Step3	**AHI**	-.047	-2.752	-2.752	.636	.029	**.007** *
MEI-SF	*Step1*	*Age, Gender, BMI*						
	Step2	*Age, Gender, BMI, HADS-D, HADS-A, CFS, ESS*						
	Step3	No variable						
HADS-D	*Step1*	*Age, Gender, BMI*						
	Step2	*Age, Gender, BMI, HADS-A, CFS, MEI-SF, ESS*						
	Step3	**Mean SpO2 (%)**	-.225	-2.577	14.749	.539	.033	**.012** *
HADS-A	*Step1*	*Age, Gender, BMI*						
	Step2	*Age, Gender, BMI, HADS-D, CFS, MEI-SF, ESS*						
	Step3	Rem	-.031	-2.373	16.278	.565	.026	**.020** *
	Step4	**Rem** **N3 duration**	-.039 .017	-2.986 2.886	16.628	.599	.035	**.004** * **.005** *
ESS	*Step1*	*Age, Gender, BMI*						
	Step2	*Age, Gender, BMI, HADS-D, HADS-A, CFS, MEI-SF*						
	Step3	**ODİ**	.061	3.202	7.321	.350	.071	**.002** *

*p <0.05; AHI= apnea-hypopnea index, BMI= body mass index, ODI= oxygen desaturation index, SpO2= pulse oximeter oxygen saturation, CFS= Chalder Fatigue Scale, MEI-SF= Motivation And Energy Inventory-Short Form, HADS-D= Hospital Anxiety And Depression Scale Depression Subscale, HADS-A= Hospital Anxiety And Depression Scale Anxiety Subscale, ESS= Epworth Sleepiness Scale.

DISCUSSION

OSAS, together with its complications, is a serious public health problem [7]. The interaction of the sleepiness, fatigue, and psychological problems such as anxiety and depression, which are often seen in OSAS, causes the development of other problems [26-28].

There is a positive relationship between sleepiness and OSAS disease, and this relationship is known to be related to the variables obtained in PSG [29]. However, this relationship has not been shown in studies [30]. Mediano et al. [31] showed that in patients with daytime sleepiness, sleep latency was shorter, sleep efficacy was higher, and there was poor nocturnal oxygenation compared to those without daytime sleepiness. In the same study, it was suggested that nocturnal hypoxemia was the most important determinant of daytime sleepiness in OSAS patients. Daytime sleepiness and snoring affect the cognitive functions and work performance of patients. In a study by Tasbakan et al. [27], there was found to be a relationship between sleepiness and low quality of life in females. However, not all OSAS patients complain of daytime sleepiness. Two patients with the same demographic and AHI values may not have complaints of daytime sleepiness at the same level. There may not be a relationship between the severity of sleepiness and the severity of the disease [32]. Karakoç et al. [33] conducted a study on 264 patients and found a positive relationship between mean ESS scores and AHI. The results of the current study support the findings of several studies in the literature [29]. The results of the current

study demonstrated a positive correlation between the mean ESS scores and AHI and ODI, which are determinants in particular of OSAS severity.

Chervin wanted to determine symptoms in OSAS patients at the same time by objectively identifying excessive daytime sleepiness with multiple sleep latency test [33]. The complaints of the patients were determined subjectively as fatigue, exhaustion, reduced energy, and sleepiness. No significant relationship was found between disease severity and sleepiness severity and the frequency of these symptoms. Similarly, no significant relationship was found between mean fatigue scores and AHI and LO_2S [33,34]. The current study results are not consistent with these findings. From the starting point that fatigue in OSAS patients could also be a symptom of depression, Bardwell et al. found that depression scores were an independent predictive factor of fatigue rather than of OSAS severity [35]. In the same study, no significant relationship was determined between fatigue scores and AHI and LO_2S. That the fatigue seen in OSAS patients could predict the severity of depression independently of disease severity has been supported in several studies [36]. In the current study, the relationship with AHI could be related to fatigue, indicating more severe clinical OSAS symptoms. The AHI, the ''gold standard'' of obstructive sleep apnea severity, was not notably related to symptoms of depression or anxiety. Psychological symptoms occurring as a complication of OSAS may not be at the level of psychiatric disease. These results suggest that fatigue seen in OSAS patients could be considered as a dimension independently of other clinical variables.

Depression may lead to increased perceived fatigue in OSA patients and impaired quality of life by impairing functionality. Although some population-based and clinical studies have found a positive relationship between the severity of OSA and depression, others have not found such a link. An observational study using country-wide data has shown that OSA is associated with an increased incidence of depression and anxiety [37]. Previous studies have shown that there is inconsistency in the relationship between OSA severity and depression/anxiety levels. In the current study, a correlation was found between depressive symptoms and MO_2S, and anxiety symptoms were found to be related to N3 and REM duration.

In contrast, a previous study that investigated the relationship between OSAS and anxiety and depression found a negative relationship between AHI and anxiety and depression scores [38]. In another study, no relationship was determined between the presence or severity of OSAS and depression and anxiety scores, whereas depression and anxiety scores were determined to be independently higher than other factors [39]. It may be problematic to identify some mood disorder symptoms, such as depression, independent of OSAS, as they contain symptoms similar to OSAS, such as sleep problems. HADS, which does not include physical symptoms such as fatigue, minimizes the effects of physical diseases on scale results. HADS may better assess the relationship between depression and anxiety symptoms in patients with newly diagnosed and untreated OSA without psychiatric disorders. In the present study, no relationship has been found between depression/anxiety levels and PSG variables, which are determinants in particular of OSAS severity. The relationship found between the mean anxiety-depression scores and the MO_2S, N3, and REM duration was non-specific and could have been associated with the day on which the PSG was conducted. The present study demonstrates that there is no relationship between OSA severity and depression/anxiety beyond fatigue and excessive daytime sleepiness. The results of the current study showed that depression and anxiety were not independently associated with OSAS severity. Many psychiatric clinical manifestations are associated with sleep disorders, and screening for the presence of sleep disorders, including OSAS, is essential. Focusing on the improvement of depressive/anxiety symptoms could be a strategy to improve OSAS treatment efficacy.

Interpretation of the current study results is limited by the low number of the sample, the self-reporting nature of the clinical scales, that there was no comparison of the patients with the control group. The present study was a cross-sectional study, and causality could not be addressed. Our inverse correlation between the PSG variables and the clinical symptoms could not be generalized. However, the results can be considered as pioneering for shedding light for further controlled clinical studies. The results of the current study are essential in terms of independently showing the relationship between frequent symptoms of treatment-naive OSAS patients and PSG variables. Further extended studies with broader samples that examine other related disorders would be able to make a significant contribution to the available data.

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Conflicts of interest: There are no conflicts of interest.

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