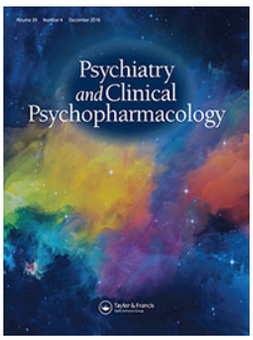

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Evaluation of depression comorbidity in obstructive sleep apnea syndrome

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ABSTRACT

BACKGROUND: Diagnosis and treatment of the comorbid depression in patients with obstructive sleep apnea syndrome could be effective on the reduction of morbidity and mortality.

OBJECTIVES: The present study aimed to investigate the depression comorbidity in OSAS patients grouped by Apnea-Hypopnea Index (AHI). However, the previous studies on the presence of depression in OSAS reported inconsistent findings. It was considered that the differences between the findings could be due to methodological differences and it was planned to investigate the presence of depression with two methodologies in the same patient group and to compare the findings.

METHODS: The study group included 101 individuals who were admitted to the neurology outpatient clinic with the complaints of snoring, diaphoresis history, daytime somnolence, fatigue, and headache and were hospitalized overnight to conduct polysomnography and diagnosed with obstructive sleep apnea syndrome (OSAS). Cases were grouped based on Apnea-Hypopnea Index (AHI) scores. Sociodemographic and Clinical Data Form Hamilton Rating Scale for Depression (HAM-D), Beck Depression Inventory (BDI), Pittsburg Sleep Quality Index (PSQI) and Epworth Somnolence Scale (ESS) were applied to all cases.

RESULTS: Patients with lower than 5 AHI score were considered as the simple snoring group ($n = 20$), those with an AHI score of 5–14.99 ($n = 27$) were considered as the patients with moderate OSAS and those with an AHI score of equal to or greater than 30 ($n = 34$) were considered as severe OSAS patients. The cases included in the study had a wide age range (between 22–61 years) and were mostly male (65.4% male; 34.65% female). Rates of the major depressive disorder according to HAM-D and BDI were 60.4% and 36.6%; respectively. The depression rates were higher in the moderate OSAS group according to the both evaluation methods (HAM-D and BDI), although this was not significant via BDI. Analysis of the ESS scores demonstrated that experienced severe daytime somnolence was seen in 52.5%, and analysis of the PSQI demonstrated that poor sleep quality was seen in 87.1% of the patients. According to the linear regression analysis only PSQI total score ($p = 0.029$) was found to be significant in determining BDI while ESS ($p = 0.44$) and PSQI total scores ($p = 0.003$) were found to be significant in determining HAM-D when ESS, AHI and PSQI were evaluated together.

CONCLUSION: In patients with obstructive sleep apnea syndrome, comorbid depression should be identified in order to achieve better results in treatment. However, the scales used to determine depression in OSAS patients could result in different findings due to methodological differences or the distribution of the tested symptoms. Considering this fact in the diagnosis of comorbid depression in OSAS is important to achieve an accurate diagnosis and commence an effective treatment.

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KEYWORDS
Obstructive sleep apnea syndrome; depression; survey

Introduction

Obstructive sleep apnea syndrome (OSAS) is a sleep-related respiratory disorder characterized by recurrent upper respiratory tract obstructions leading to hypopnea or apnea attacks. It causes a reduction in oxygen saturation and / or awakening from sleep [1]. Older age, male sex, family history and upper airway structural abnormalities are effective on the development of OSAS. Various risk factors such as changes in body fat distribution with age, tissue elasticity and changes in ventilation control facilitate the development of OSAS [2]. OSAS incidence among males is higher than females. The incidence rate increases with increasing age and body mass index (BMI) [3]. OSAS is associated with vascular risk factors including obesity, hyperlipidemia, glucose intolerance, alcohol, and smoking [2]. OSAS is found to be related with some psychiatric disorders like posttraumatic stress disorder, anxiety and depression as well [2,4–8]. However, there are different opinions on OSAS leading to psychiatric disorders like depression. Some researchers reported a comorbid relationship between depression and OSAS, and they claimed that this relationship may be underestimated [9–11], while other studies

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demonstrated OSAS not to be associated with depression [12,13]. Examination of patients with anxiety and depression showed that their sleep patterns were irregular [14]. While it was reported that the incidence of depression in the adult population was between 3% and 10% [15], certain studies demonstrated that the depression incidence was between 20–40% in patients with OSAS [4,16,17]. OSAS may cause depression via sleep loss, sleep disruption, and cognitive changes induced by intermittent hypoxemia, while weight gain and sleep disruption due to depression could cause OSAS [8]. Recent systematic review and meta-analysis showed that the association between OSAS, anxiety, and depression indicates the value of an early diagnosis and treatment of OSAS to improve mental disorders which share a probably bidirectional relationship [4].

Determination of the presence of comorbid depression may be effective in the reduction of morbidity and mortality in OSAS patients. However, the results of the studies about OSAS and comorbid depression is inconsistent. We speculate that the difference may be due to the methodological differences**.** The scales used to determine depression in OSAS patients could result in different findings due to methodological differences or the distribution of the tested symptoms. The present study aimed to investigate the depression comorbidity in OSAS patients grouped by Apnea-Hypopnea Index (AHI) and if the different methodological instruments used in the same population point out the same results while evaluating the relation between OSAS and depression.

Materials and methods

The study was conducted after the Ethics Committee consent (06.05.2011/no:2011/03) was obtained. It was conducted by the neurology and psychiatry clinic between October 15, 2010 and May 25, 2012. Informed consent of all patients was obtained.

One hundred fifty-two 20–65 years old individuals who were admitted by the neurology outpatient clinic with the complaints of mostly snoring, diaphoresis history, daytime sleepiness, fatigue, and headache and were hospitalized overnight to conduct polysomnography and diagnosed with obstructive sleep apnea syndrome (OSAS) were invited. Participants with severe psychiatric disorders such as Mental Retardation, Schizophrenia, Bipolar Affective Disorder, Psychotic Disorder, and participants with Dementia, Alcohol and Substance Abuse were excluded from the study. Since 4 out of 152 invited patients were diagnosed with a psychiatric disease with psychotic characteristics, intracranial masses were identified in 3 cases, 25 cases did not consent to participate in the study, and 20 cases had missing data, these cases were excluded from the study. A sociodemographic data form that included personal information such as gender, age, marital status, occupation, education level and information on the disease was filled for the cases that met the study criteria. Height and body weight data were recorded for the patients. Hamilton Rating Scale for Depression, Beck Depression Inventory (BDI), Pittsburg Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS) were administered by the psychiatrist.

Polysomnography (PSG)

Polysomnography is the gold standard diagnostic method for OSAS diagnosis [18]. In the present study, PSG exams were conducted in the Sleep Laboratory under the supervision of a trained healthcare worker using a polysomnographic device (Embla S4000, Natus Medical Inc., Denver, U.S.A.) during spontaneous sleep.

Hamilton rating scale for depression (HAM-D)

The scale was developed by Hamilton in 1960 [19]. It is the most frequently used measure to measure depression symptoms by clinicians. It measures the level of depression of the patient and changes in depression severity. It is not a diagnostic tool. It includes 17 questions. The HAM-D scale items are rated between 0–4 or 0–2. In the present study, the 0–2 rating was used. The validity and reliability of the Turkish adaptation of the scale were determined by Akdemir et al. [20].

Beck depression inventory (BDI)

The Beck Depression Inventory was developed by Beck [21]. It aims to measure the severity of the symptoms observed in emotional, cognitive and motivational dimensions of depression. It is a self-reporting scale that includes 21 items. It is a four-point Likert type scale. It is not a diagnostic tool. The validity and reliability of the Turkish adaptation of the scale were conducted by Hisli et al. The scale cut-off point is 17 [22].

Pittsburgh sleep quality index (PSQI)

It is an assessment tool to differentiate individuals with and without sleep disorders, to identify sleep problems, and to determine the sleep quality. The index provides information on the quality of sleep and the type and severity of sleep disorder within the last month. Although it is a self-evaluation scale, there are questions for the partner of the patient to respond. The scale contains 24 questions and 19 are answered by the patient and 5 are answered by the patient's partner. The final 5 questions are used only for clinical information and are not included in the scoring [23].

Epworth sleepiness scale (ESS)

The Epworth Sleepiness Scale is the most commonly used method to determine daytime sleepiness. In this subjective assessment scale, patients are asked about their possibility to fall asleep under certain conditions. Cases with a score of 10 and above are considered positive [24].

Statistical analyses

The study data were analyzed with SPSS (Statistical Package for Social Sciences) for Windows 15.0 software. The Kruskal Wallis test was used for the comparison of the parameters without normal distribution between the groups and Mann Whitney U-test was used to determine the group that led to a difference. The results were analyzed within the 95% confidence interval and a significance level of $p \leq 0.05$. The data were presented with minimum-maximum-median, mean ± standard deviation or count (%) figures.

Results

Cases were categorized based on the Apnea-Hypopnea Index (AHI). Twenty patients with an AHI of less than 5 were considered in the simple snoring group ($n = 20$, 19.8%), patients with an AHI between 5 and 14.99 ($n = 27$, 27.6%) were considered in mild OSAS group, patients with an AHI between 15 and 29.99 ($n = 20$, %19.8) were considered in moderate OSAS group, and patients with an AHI of 30 or more ($n = 34$, 33.7%) were considered in severe OSAS patient group.

Statistical analysis was conducted on the data collected from a total of 101 cases. The cases included in the study were between the ages of 22 and 61 and there was no statistically significant difference between the groups. Sixty-six patients were male (65.35%) and 35 were female (34.65%). Sociodemographic information about the participants is provided in Table 1.

When the cases were analyzed based on the HAM-D scores, it was determined that a total of 61 patients (60.4%) had depression (HAM-D > 7). Depression rate was significantly higher in the moderate OSAS group ($n = 17$% 85.1). When the BDI scores were assessed, it was determined that BDI scores of 37 (36.6%) cases were greater than 17 (depressive symptoms). The depression rate in the moderate OSAS group was higher when compared to the other groups ($n = 12$, 60%). However, the difference was not statistically significant. There was no significant difference between the groups based on BMI scores. Analysis of the ESS scores that aim to determine daytime sleepiness demonstrated that 53 (52.4%) cases experienced excessive daytime sleepiness. Based on overall PSQI scores, 88 (87.1%) cases had poor sleep quality (PSQI ≥ 5). The highest rate of poor sleep quality was determined in the mild OSAS group, however, the difference was not statistically significant ($p = 0.166$). Analysis of HAM-D, BDI, ESS, PSQI, number of patients, gender, age, BMI parameters is presented based on AHI groups in Table 2.

When linear regression analysis was performed, only PSQI total score ($p = 0.029$) was found to be significant in determining BDI while ESS ($p = 0.44$) and PSQI total scores ($p = 0.003$) were found to be significant in determining HAM-D when ESS, AHI and PSQI were evaluated together.

Discussion

According to our study, while 61 patients were diagnosed with depression based on the HAM-D scores (HAM-D > 7) and the depression rate was significantly higher in the moderate OSAS group; 37 patients were diagnosed with depression (BDI > 17) based on BDI scores and the depression rate was higher in the moderate OSAS group. However, this difference between the groups was not statistically significant. The ESS scores that was applied to determine daytime somnolence demonstrated that 53 cases experienced severe daytime somnolence. Based on the total PSQI scores, it was observed that 88 patients had poor sleep quality.

In the present study, the mean age of patients with OSAS was consistent with the literature and no statistically significant difference was found between the groups. 66 (65.35%) cases were male and 35 (34.65%) were female (M / F = 2/1). It was observed that there was a statistically significant difference between the distribution of gender among the groups. In the severe OSAS group, the ratio of males was significantly higher (F / M; 7/27). In recent studies, OSAS was shown to be more common among males [25,26]. In the present study, the ratio of males was higher consistent with the literature ($p = 0.031$). Due to the androgenic fat distribution in males, the accumulation of fat, especially in the neck region, increases OSAS risk [25] Obesity is among the most important risk factors in OSAS. In the present study, it was determined that 69 cases (68.3%) were obese (BMI ≥ 30). The prevalence of OSAS increases with the increase in body mass index (BMI) and associated markers (e.g. neck circumference, waist-hip ratio) [2]. In the present study, albeit not statistically significant, the majority of the cases were obese. It was demonstrated that a higher level of obesity led to higher OSAS severity and daytime sleepiness [27]. In the present study, the number of obese subjects was higher in the severe OSAS group. Obesity is a correctable OSAS risk factor [28]. The prevalence of snoring was higher among smokers compared to non-smokers. The effect of tobacco smoking is not clearly known; however, it was reported to increase the tendency for OSAS, causing inflammation in the

Table 1. Sociodemographic information about the participants.

Parameter	Simple snoring	Mild OSAS	Moderate OSAS	Severe OSAS	Total case count	*p*
Gender (F/M) (n)	12/8*	10/17	6/14	7/27*	35/66	$p < 0.05$
(F/M) (%)	(34.3/12.1)	(28.6/25.8)	(17.1/21.2)	(20.0/40.9)	(100/100)	
Marital Status						
Married n (%)	17 (17.9)	27 (28.4)	19 (20.0)	32 (33.7)	95 (100)	**
Unmarried n (%)	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)	
Widowed n (%)	2 (40)	0 (0)	1 (20)	2 (40)	5 (100)	
Education level						
n(%)	0 (0)	2 (66.7)	0 (0)	1 (33.3)	3 (100)	**
Illiterate	3 (30)	1 (10)	5 (50)	1 (10)	10 (100)	
Literate	7 (23.3)	6 (20)	6 (20)	11 (36.7)	30 (100)	
Primary School	3 (27.3)	3 (27.3)	1 (9.1)	4 (36.4)	11 (100)	
Middle School	3 (13.6)	9 (40.9)	2 (9.1)	8 (36.4)	22 (100)	
High School	4 (16.0)	6 (24.0)	6 (24.0)	9 (36.0)	25 (100)	
College						
Residence n(%)						
Village	1 (25.0)	2 (50)	0 (0)	1 (25.0)	4 (100)	**
Town	0 (0)	1 (20)	2 (40)	2 (40)	5 (100)	
City	19 (20.7)	24 (26.1)	18 (19.6)	31 (33.7)	92 (100)	
Abuse						
(Yes) n%	4 (9.3)	13 (30.2)	12 (27.9)	14 (32.6)	43 (100)	$p > 0.05$
Tobacco	1 (3.2)#	10 (32.3)	8 (25.8)	12 (38.7)#	31 (100)	$p < 0.05$
Drugs	3 (18.8)	3 (18.8)	5 (31.3)	5 (31.3)	16 (100)	$p > 0.05$
Alcohol	0 (0)	1 (20.0)	3 (60.0)	1 (20.0)	5 (100)	$p > 0.05$
Diseases						
(Yes) n(%)	10 (22.2)	12 (26.7)	11 (24.4)	12 (26.7)	45 (100)	**
DM	2 (14.3)	4 (28.6)	4 (28.6)	4 (28.6)	14 (100)	
HT	6 (20.7)	9 (31.0)	7 (24.1)	7 (24.2)	29 (100)	
Coronary	2 (25.0)	3 (37.5)	2 (25.0)	1 (12.5)	8 (100)	
Other	8 (25.8)	5 (16.1)	10 (32.3)	8 (25.8)	31 (100)	
Age min-max	(24–56)	(30–59)	(29–61)	(22–59)		$p > 0.05$
Median	42.50	40.00	45.50	43.50		
BMI min-max	(18–49)	(23–40)	(26–48)	(26–44)		$p > 0.05$
Median (kg/m^2)	(30.00)	(31.00)	(31.00)	(34.00)		
AHI n (%)	20 (19.8)	27 (26.7)	20 (19.8)	34 (33.7)	101 (100)	

*F gender was higher in SS group when compared to severe OSAS group.
**The data were not calculated statistically.
#Smoking rate was higher in SS group when compared to severe OSAS group.
SS: Simple Snoring.

respiratory tract [29]. In the present study, consistent with the literature, the prevalence of smoking was significantly higher in the severe OSAS group when compared to the simple snoring group ($p < 0.05$). In the simple snoring group, the smoking rate was lower when compared to the other groups (5% were smokers).

In OSAS, characterized by hypoxia and interrupted sleep that develop as a result of recurrent upper respiratory tract collapse, it was reported that the factors that could be responsible for depression symptoms were interrupted sleep and oxygen desaturation during sleep. Sleep interruption is the primary cause of daytime sleepiness in OSAS patients [16]. It was reported in the literature that daytime sleepiness might lead to mood disorders in OSAS patients [30]. In the present study, it was demonstrated that 52.4% of all cases experienced excessive daytime sleepiness. Analysis of the individuals with depression and anxiety demonstrated that their sleep patterns were significantly irregular [14]. The serotoninergic system plays a central role in the individual's mood, sleep cycle, and the control of the muscle tonus in the upper respiratory tract during sleep. Depression is associated with the reduced serotoninergic neurotransmitter functions. The said reduction in functions is often associated with altered sleep cycles [31]. Different theses drew attention to the association of OSAS with depression. The first these argued that OSAS patients experienced a high level of depression, while the latter claimed that the depression comorbidity was coincidental and not significant. The third stated that OSAS was not associated with depression [32]. There are even studies which reported that there was a negative correlation between

Table 2. Analysis of the HAM-D, BDI, ESS, PSQI, number of patients, gender, age, BMI parameters for study cases based on AHI groups.

Parameter	Simple snoring	Mild OUAS	Moderate OUAS	Severe OUAS	Total
HAM-D > 7 n (%)	7 (35)	16 (59.3)	17 (85.1)	21 (61.8)	61 (60.4)
BDE > 17 n (%)	5 (25)	10 (37)	12 (60)	10 (29.4)	37 (36.6)
EUS ≥ 10	10 (50)	13 (48)	9 (45)	21 (61.7)	53 (52.4)
PSQI ≥ 5	17 (85)	26 (96)	18 (90)	27 (79.4)	88 (87.1)
# of patients n (%)	20 (19.8)	27 (26.7)	20 (19.8)	34 (33.7)	101 (100)
Gender n F/M (%)	12/8 (34.3/12.1)	10/17 (28.6/25.8)	6/14 (17.1/21.2)	7/27 (20.0/40.9)	35/66 (100/100)

total depression scores and OSAS [33,34]. It is widely accepted that depressive mood is significantly high in OSAS [33–35]. Certain studies reported that obstructive sleep apnea syndrome is an independent risk factor in depression [36]. Millman et al. [37] found that 45% of the patients with OSAS had higher depressive symptom scores and there was no correlation between the severity of the disease and depression score, and the use of nasal CPAP application reduced the scores up to normal levels. Based on this finding, the researchers considered that OSAS itself could lead to depression symptoms, which could improve with treatment [37]. Different researchers also demonstrated that there was a reversible correlation between OSAS and depression [13]. In a study by Pillar and Lavie [38] where the psychiatric symptoms in 2271 individuals with OSAS, it was determined that there was no correlation between the presence or severity of OSAS and depression and anxiety in males, while the correlation between depression and anxiety was higher in females independent of other factors. Furthermore, females with severe OSAS had higher anxiety and depression scores when compared to those with mild OSAS. Certain studies reported no correlation between OSAS and psychiatric symptoms. Bliwise et al. [12] found no significant correlation between depression and OSAS in 336 adult patients. Asghari et al. [39] conducted BDI-II and BAI with 685 patients with OSAS. The study demonstrated that depressive symptoms and anxiety were present in half of the patients, but OSAS was not associated with depression or anxiety. The DSM 5 criteria used for the diagnosis of depression include psychological and somatic symptoms and certain depression and OSAS symptoms are consistent [40]. Symptoms such as insomnia, distractibility, fatigue, and psychomotor retardation are among the consistent symptoms. Negative affect, depressive thoughts and anhedonia are the depression specific symptoms. In a recent study, 357 patients with OSAS were analyzed with HAM-D at baseline, followed by CPAP and monitored for 12 weeks [37]. At the end of the period, HAM-D scores demonstrated a rapid improvement in overlapping symptoms after CPAP, however, the same finding was not obtained in non-overlapping symptoms. Thus, it was claimed that analysis of non-overlapping symptoms would be more realistic in the diagnosis of comorbid depression in OSAS patients [37,41]. In a study by Nanthakumar et al. [42] that was a review of thirteen studies, the prevalence of depression in OSAS was investigated. Use of the scales that utilized overlapping symptoms in both cases led to a higher depression prevalence. However, it was found that depression prevalence was lower when the scales, where overlapping symptoms were less significant, and the rate of anhedonia symptoms was high, were utilized. Thus, it was stated that current scales were not suitable to evaluating depression in chronic diseases with comorbid symptoms such as OSAS, chronic kidney disease, heart disease and diabetes. In a study conducted by Ye L. et al. [27], it was reported that complaints associated with OSAS could coincide with somatic symptoms associated with a depressive mood disorder and that this comorbidity might partially explain the high mood disorder rate observed in the OSAS population.

Scales such as the Beck Depression Inventory, Minnesota Multiphasic Personality Inventory (MMPI), Zung Self-Rating Scale, Geriatric Depression Scale were used to assess depression in patients with obstructive sleep apnea syndrome. Based on the scale used, the results could differentiate within the same patient group [9,41]. It has been reported in the literature that the prevalence of depression symptoms ranged between 16% and 55% based on different BDI versions [42]. In a study by Beutler et al. [43] where the MMPI was used to assess depression, it was determined that the depression scores of 20 patients with OSAS were high, however, the use of Profile of Mood States in the same population did not reveal the presence of significant depression. Bardwell et al. [44] utilized the validated Center for Epidemiological Studies Depression Scale in their study and reported a significant level of depression in one-third of the individuals examined for OSAS. In the evaluation of mood disorders, clinician administered, and self-administered questionnaires could produce different results [44]. In the present study, it was determined that 61 cases (60.4%) had depression based on the HAM-D scores and depressive symptoms were identified in 37 cases (36.6%) (BDI > 17) based on the BDI scores. HAM-D is a scale implemented by the interviewer [20]. BDI is a self-rating scale [22]. The difference between the depression rates determined by these two scales in the same patient population was noteworthy in reflecting the difference between the methods. Depression is positively and significantly correlated with alexithymia, and it is known that cognitive functions are also affected in depression [2,45]. It could be possible that the patients could not have rated themselves adequately due to the above-mentioned negative factors, leading to the observed low BDI scores. In the present study, the highest depression scores were observed in the moderate OSAS group. A lower incidence of depression was observed in patients with severe OSAS when compared to those in the moderate OSAS group, which could be related to the higher cognitive function rates in the latter group. A previous study that demonstrated consistent findings with the present study was conducted by Fidan F. et al. [46]. In that study conducted with 204 patients who underwent PSG, the Beck Anxiety Inventory (BAI), BDI and a questionnaire that inquired symptoms and the ESS were applied. When the control group was compared with the groups with mild, moderate and severe

OSAS, the highest depression score was observed in the moderate OSAS group, followed by the control and mild OSAS groups. The lowest depression score was determined in the severe OSAS group. There was a negative correlation between anxiety and depression scores and OSAS severity. It can be suggested that this could be due to the impact on cognitive functions in patients with severe OSAS, and the scales that evaluated anxiety and depression could have affected the findings. In the present study, depression was observed in 60.4% of the cases using HAM-D, however, depressive symptoms were determined in 36.6% of the cases with BDI in the same patient population. The difference between the findings obtained with different methods was significant. In the present study, it was found that the depression rate among OSAS patients were higher when compared to the control group (Simple Snoring Group). Depression was observed in 60.9% of all patients. Similar to the findings reported by Ye et al. [27], it is suggested that the above mentioned high rates could be related to the comorbidity of OSAS and the somatic symptoms of depression. In the current study, according to linear regression analysis, PSQI total score was found to be significant in determining both BDI and HAM-D; and ESS was found to be significant in determining BDI. It was showed in a systematic review and meta-analysis that excessive day time sleepiness which is self-evaluated with the ESS appeared to be associated with depressive symptoms in 11 studies in the literature, and, sleep disruption and fatigue could be better predictors of depression in OSAS patients [4]. It was also demonstrated that affective disorders appeared to be closely related to sleep quality and the PSQI had the strongest correlations with the BDI and BAI [47].

The present study has certain limitations. The current study is a cross-sectional study, and prospective studies could contribute further in this field. The fact that somatic complaints were questioned in the item 8 in HAM-D when the depression symptoms were identified could have led to higher rates of depression. Comparisons with a control group that includes a healthy population may strengthen the study.

The incidence of depression is high among patients with obstructive sleep apnea syndrome. To achieve better results in treatment, the presence of a comorbid depression should be identified. However, the scales used in the investigation of comorbid depression may lead to different results based on methodological differences or the prevalence of the symptom that they inquire. Considering the above-mentioned condition in the determination of comorbid depression in OSAS is important to achieve an accurate diagnosis and initiate an effective treatment. However, further studies that would be conducted with larger sample sizes are required.

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No potential conflict of interest was reported by the authors.

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