

ORIGINAL ARTICLE

Depression and Anxiety in Obstructive Sleep Apnea Syndrome with and without Insomnia

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Background	Obstructive sleep apnea syndrome (OSAS) is a common sleep disorder characterized by repeated upper airway obstruction during sleep. While respiratory pauses followed by loud snoring and daytime sleepiness are the main symptoms of OSAS, most of the patients complain from sleep disruption, mood disturbance, irritability and poor quality of life. Depression and anxiety can be correlated to the different subtypes of insomnia associated with OSAS.
Subjects and Methods	Cases recruited from outpatient clinic in pulmonary department in Mediclinic hospital in Abu Dhabi, UAE. 60 cases collected over 6 months, diagnosed to have obstructive sleep apnea syndrome using The American Academy of Sleep Medicine (AASM, 2014). After which the subjects were subjected to scales to diagnose possible comorbid anxiety and depression in addition to scale to determine presence and absence of insomnia with its type in every case.
Results	This study shows significantly higher prevalence of insomnia among OSAS group versus control. Result showed higher Hamilton depression and anxiety scores in OSAS- insomnia group more than OSAS without insomnia with significant positive correlation between initial insomnia and Hamilton anxiety scores and between maintenance insomnia and Hamilton depression scores.
Conclusions	We conclude that depression and anxiety is a common comorbidity with OSAS and that finding was higher in OSAS with insomnia patient group more than those without insomnia. Which suggested that there is an association between OSAS-insomnia and overall patient quality of life.
Keywords	Anxiety, Depression, Insomnia, Obstructive sleep apnea.

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a common sleep-related breathing disorder with a prevalence of 2-4% among adults in the United States (Yaggi *et al.*, 2005). It is characterized by repeated episodes of partial or complete upper airway obstruction during sleep. Obesity, age, and male gender are the most important risk factors for this syndrome. Patients may complain from difficulty in falling asleep at night, nightmares, morning headaches, and irritability (Kielb *et al.*, 2012). OSAS may cause other consequences like impaired cognition, and psychiatric symptoms including depression, irritability, and anxiety (Galecki *et al.*, 2011; Kielb *et al.*, 2012). While each of these conditions may significantly impair the quality of

life (Partinen and Guilleminault, 1990), many of the patients remain unrecognized with huge medical and economic burden on both themselves and the society (Wiegand and Zwillich, 1994). The delay in diagnosis of OSAS has been partially attributed to the nature of this syndrome, as snoring and nocturnal respiratory pauses may not attract appropriate attention of sufferers. Hence, a better understanding of this condition, its complications, and the presenting symptoms is of great value.

According to International Classification of Sleep Disorders (ICSD-III) published by the American Academy

of Sleep Medicine (AASM), OSAS is diagnosed with either a respiratory disturbance index (RDI) ≥ 15 irrespective of the presence of symptoms, or an RDI > 5 accompanied by any of the following features: 1) sleep attacks, EDS, fatigue, or insomnia; 2) awakening with a choking feeling; 3) loud snoring and/or breathing pauses reported by bed partner (American Academy of Sleep Medicine, 2014).

OSAS with insomnia are associated with significantly greater morbidity functional impairment, and reduced quality of life than either condition alone. Those OSAS patients comorbid with insomnia had moderate to severe symptoms of depression, anxiety, and stress while OSAS-only patients indicated no clinically significant symptoms in these areas. Depression and anxiety can be correlated to the different subtypes of insomnia associated with OSAS, we expect that onset insomnia can be an indicator of high arousal level with more anxiety symptoms, while maintenance insomnia is an indicator of sleep disordered breathing which associated with increased daytime sleepiness and lower anxiety symptoms than the other subtypes of insomnia.

Aim of this study was to evaluate the association of OSAS with anxiety and depression symptoms and to investigate the prevalence of anxiety and depression in OSAS with insomnia versus OSAS without insomnia and if the type of insomnia associated with OSAS can affect the severity of anxiety and depressive symptoms.

SUBJECTS AND METHODS

We conducted this cross-sectional study at the sleep laboratory of Mediclinic Hospital, Abu Dhabi, UAE, from September 2017 to February 2018. We did polysomnography on the patients referred to sleep lab during this period of time, 158 patients were referred from which we select 20 control individuals and 40 patients diagnosed to be Obstructive sleep apnea (OSAS) with help of pulmonary specialist for OSAS according to ICSD-III (American Academy of Sleep Medicine, 2014).

We exclude from the study incomplete and unreliable cases, those patients with AHI < 5 event/hour or with periodic limb movements > 15 /hour, patients with substance abuse or psychotic or cognitive disorders, and patients under hypnotics.

OSAS Patients group included 19 men and 21 women of mean age 47.9 ± 11.2 years, ranging from 25 to 60 years, while control group included 8 men and 12 women of age 49.8 ± 12.1 years without OSAS manifestations, aged from 25 to 60 years.

Before to data collection, informed consent was obtained from all participants.

To assess associated psychiatric symptoms and quality of life for participants we used Hamilton depression scale to assess depressive symptoms (Hamilton, 1960). Similarly, anxiety level was also evaluated by Hamilton anxiety (Hamilton, 1959; Maier *et al.*, 1988). Short Form-36 health survey predicting quality of life (Ware *et al.*, 1996). It is one of widely used generic measures of health-related quality of life and has been shown to discriminate between subjects with different chronic conditions and between subjects with different severity levels of the same disease. Data for absence or presence of Insomnia and type of detected insomnia collected from polysomnography and ICSD.

For assessment and analysis of insomnia Participants underwent overnight polysomnography. Based on the Manual of AASM criteria, sleep apneas were ascertained as ≥ 10 seconds of air flow pauses (American Academy of Sleep Medicine, 2014). A 50% decrement in the amplitude of baseline airflow followed by $\geq 3\%$ of oxygen desaturation was considered as hypopnea (Baharmam *et al.*, 2012). The severity of OSAS was determined by apnea-hypopnea index (AHI; mean number of apnea + hypopnea per hour of sleep).

Stages of sleep, total recording time, sleep latency (time until first falling asleep), total sleep time, and sleep efficiency (sleep time in relation to total time in bed) were calculated. WASO (wakefulness after sleep onset, indicates sleep fragmentation), WASF (wakefulness after sleep offset, indicates insomnia), AHI, and early awakening insomnia were also determined and finally to evaluate the severity of insomnia, insomnia severity index (ISI) was calculated (Bastien *et al.*, 2001).

Statistical Analysis

Data was analyzed using SPSS (Statistical Package for Social Sciences) version 15. Qualitative data was presented as number and percent. Comparison between groups was done by χ^2 test. Quantitative data was tested for normality by Kolmogorov-Smirnov test. Normally distributed data was presented as mean \pm SD. Student *t*-test was used to compare between two groups. Non parametric data was presented as min – max and median. Mann-Whitney test was used for comparison between groups. Spearman's correlation coefficient was used to test correlation between variables. $p < 0.05$ was considered to be statistically significant.

RESULTS

Table 1 shows the demographic data of groups OSAS and without OSAS. There was a significantly higher mean BMI in OSAS group as compared with without OSAS group ($p = 0.001$).

The mean age in OSAS group was 47.93±11.21 while in without OSAS group was 49.85±12.17. Female sex was predominant in studied groups. Results showing high BMI in OSAS group as compared to without OSAS group ($p=0.001$), no significant difference in residence in studied groups ($p=0.576$).

Table 2 showing the prevalence of insomnia in both groups according to ICSD-3, there was higher prevalence of insomnia among OSAS group 90% versus without OSAS group 15% $p=0.001$. Correspondingly, the severity of insomnia was significantly higher in OSAS group as shown by insomnia severity index (Table 3), ($p\leq 0.001$).

Table 3 insomnia subtypes were evaluated among both groups and it was observed that the most common insomnia subtypes were “maintenance insomnia” and “more than one subtype insomnia” (85% each) followed by “initial insomnia 82.5%” and “early awakening insomnia” (waking up before desired time) which showed the lowest frequency (40%) in OSAS group. The prevalence of these subtypes in OSAS group was significantly different than in without OSAS group, where the most common insomnia subtypes were initial insomnia (10%) followed by maintenance insomnia (5%).

Polysomnographic variables related to insomnia were analyzed in OSAS and without OSAS groups. The results showed that mean sleep efficiency and mean maintenance sleep efficiency were significantly lower in OSAS group ($p<0.001$). As regards WASO, the median value was higher in OSAS group versus without OSAS ($p=0.001$). Also, there was a significant difference between both groups as regards AHI ($p=0.001$) and there was a statistically significant higher mean value of total sleep time in OSAS versus without OSAS groups ($p=0.01$). Median value of sleep latency was significantly higher in OSAS group compared to without OSAS ($p=0.031$) (Table 4).

Data in table 5 showing scores of Hamilton anxiety and depressive scales in addition to Short Form Health survey-36 in both groups, those cases with OSAS and the

control group without OSAS. The differences between both groups were statistically significant as regards Hamilton anxiety scale, SF-36 (p values of 0.025 and 0.001 respectively) while there was no statistically significant difference between both groups as regards Hamilton depression scale ($p=0.099$).

Depression and anxiety level then compared among OSAS patients with and without and without insomnia it was observed that mean Hamilton depression scale, and Hamilton anxiety scale in OSAS with insomnia group was higher (although nonsignificant) than in OSAS without insomnia group. However there were a statistically significant differences in both groups as regard SF-36 which suggested that there is an association between OSAS-insomnia and quality of life (Table 6).

Table 7 showed impact of insomnia on quality of life as that there were positive correlation between insomnia severity index and SF-36, Hamilton depression scale without statistically significance as ($p=0.185, 0.247$). There was significant positive correlation between insomnia severity index and Hamilton anxiety scale ($r=0.433$ and $p=0.030$).

Table 8 showed that there was significant positive correlation between initial insomnia and Hamilton anxiety scale as ($r=0.466$) and ($p=0.002$). There was positive correlation between maintenance insomnia and Hamilton depression scale, Hamilton anxiety scale, SF-36 as ($r=0.307, 0.181, 0.212$ respectively) without statistically significance ($p=0.064, 0.283, 0.207$ respectively) while there was positive correlation between early awakening insomnia (before desired time) and Hamilton anxiety scale, Hamilton depression scale and SF-36 as ($r=0.286, 0.196, 0.291$ respectively) without statistically significance ($p=0.236, 0.422, 0.227$ respectively).

Table 9 showed positive correlation between SF-36, Hamilton depression scale, Hamilton anxiety scale with AHI of OSAS group but without statistically significance.

Table 1: Demographic data of studied Groups:

Variables	OSAS (N=40)		Without OSAS (N=20)		Statistical Test	P
Age	47.93±11.21		49.85±12.17		$t=0.609$	0.545
BMI	35.63±6.46		26.80±2.26		$t=13.001$	<0.001
	No	%	No	%		
Male	19	47.5%	8	40.0%	$\chi^2=0.303$	0.582
Female	21	52.5%	12	60.0%		
Rural	25	62.5%	11	55.0%	$\chi^2=0.313$	0.576
Urban	15	37.5%	9	45.0%		

Table 2: Prevalence of insomnia in OSAS group versus controls according to ICSD-3:

Variables	OSAS (N=40)		Without OSAS (N=20)		Statistical test	P
	No	%	No	%		
Insomnia	36	90%	3	15%	32.667	<0.001
without insomnia	4	10%	17	85%		

Table 3: Prevalence of insomnia subtypes is OSAS group versus without OSAS group according to ISI:

Variables	OSAS (N=40)		Without OSAS (N=20)		Statistical test	P
	No	%	No	%		
Insomnia subtypes						
1. Initial insomnia	33	82.5%	2	10%	32.35	<0.001
2. Maintenance Insomnia	34	85%	1	5%	31.25	
3. Early awakening insomnia (before desired time)	16	40%	0	0	27.5	
4. More than one subtype insomnia	34	85%	0	0	30.4	

Table 4: Polysomnographic data suggestive of insomnia in OSAS group versus without OSAS group:

Variable	OSAS (N=40)	Without OSAS (N=20)	Statistical test	P
Sleep latency (min)	10 (1–60)	7.25 (1–33)	$z=1.932$	0.031
WASO (% of TST)	0.16 (0–12)	0.02 (0–0.08)	$z=-4.181$	<0.001
Total sleep time (min)	365.25±60.6	462±75.6	$t=2.711$	0.01
Sleep efficiency (%)	66.10±7.43	83.10±8.99	$t=7.783$	<0.001
Maintenance sleep efficiency	69.38±7.75	84.15±7.29	$t=7.095$	<0.001
AHI / hour	23.5 (5.4–104)	3.3 (0.1–4)	$z=6.244$	<0.001

Table 5: Depression and anxiety levels in OSAS group versus without OSAS group:

Variables	OSAS (N=40)	Without OSAS (N=20)	Statistical test	P
Hamilton depression scale	28.45±5.82	26.00±4.14	1.678	0.099
Hamilton anxiety scale	29.30±6.45	25.60±4.44	2.301	0.025
SF-36	50.45±21.62	89.60±5.19	10.846	<0.001

Table 6: Depression and anxiety scales in OSAS patients with insomnia versus without insomnia group:

Variables	OSAS with insomnia (N=36)	OSAS without insomnia (N=4)	Statistical test	P
Hamilton depression scale	29.25±7.83	28.36±5.69	0.286	0.776
Hamilton anxiety scale	29.67±6.58	26±4.55	1.08	0.287
SF- 36	48.42±21.3	68.75±16.52	1.838	0.074

SF-36 (Short Form Health survey-36).

Table 7: Correlation between scales of quality of life and insomnia severity index:

Variables	Insomnia severity index	
	r	P
SF-36	0.214	0.185
Hamilton depression scale	0.187	0.247
Hamilton anxiety scale	0.433	0.009

FSS (Fatigue Severity Scale). SF-36 (Short Form Health survey-36).

Table 8: Correlation between scales predicting quality of life and insomnia subtypes:

Variables	Initial insomnia (No=33)		Maintenance insomnia (No=34)		Early awakening insomnia (No=16)	
	r	P	r	P	R	P
Short Health survey 36 (SF36)	0.069	0.674	0.212	0.207	0.291	0.227
Hamilton depression scale	-0.004	0.981	0.307	0.064	0.196	0.422
Hamilton anxiety scale	0.466	0.002	0.181	0.283	0.286	0.236

Table 9: Correlation between scales predicting quality of life and AHI of OSAS group:

Variables	AHI	
	r	P
SF-36	0.287	0.072
Hamilton depression scale	0.165	0.309
Hamilton anxiety scale	0.208	0.197

DISCUSSION

The association between mood disturbances and anxiety disorder with OSAS has been shown in a large body of epidemiological studies (Akashiba *et al.*, 2002; Azargra-Calero *et al.*, 2012; Velasco-Rey *et al.*, 2012). Nonetheless, there are studies that show contrary results to such a correlation (Wiegand and Zwillich, 1994). Moreover, overlapping symptoms as lack of initiation, and slowed psychomotor function which can found in both OSAS (as a result of diurnal drowsiness) and depression, may make it difficult to distinguish between these conditions (Asghari *et al.*, 2012). The purpose of this study is to determine the prevalence of depression and anxiety in patients diagnosed with OSAS. Also, this study investigated the association of depression and anxiety with other factors related to OSAS severity in these patients.

In the current study there were no significant differences in OSAS group vs. without OSAS as regard demographic data age, sex, and residence. This indicates that the studied groups were comparable. Accordingly, there was high BMI in OSAS group as compared to without OSAS group. High BMI is a well-known risk factor for OSAS. This was supported by Glidewell *et al.*, (2012).

According to our study, OSAS patients group presented a higher prevalence and severity of insomnia, as indicated by AASM insomnia criteria, polysomnogram, and ISI assessment (90% in OSAS group while in without OSAS group prevalence was 15%). Our results were higher than Krell and Kapur, (2005); Lee *et al.*, (2014); Smith *et al.*, (2014), as the prevalence of insomnia in these studies ranged from 7 to 84%.

The co-morbidity of OSAS and insomnia had already been described in the study of Luyster *et al.*, (2010). Jawder and BaHammam, (2012), suggested that there are

two hypotheses explaining this co-morbidity. First suggests that the OSA develops first and the repeated respiratory events serve as a precipitating factor that, if left untreated, becomes a perpetuating factor for insomnia. Second suggest prolonged awakenings and sleep loss from an insomnia disorder could have a negative effect on the tone of the pharyngeal muscles, thus leading to the development or exacerbation of apneas and hypopneas.

Regarding polysomnographic data, there were significantly lower mean value of sleep efficiency, maintenance sleep efficiency and total sleep time in OSAS group versus without OSAS was shown. Moreover data reported significant higher median value of WASO and sleep latency, in OSAS versus without OSAS group.

Regarding the prevalence of insomnia subtypes in OSAS group versus without OSAS, maintenance insomnia and more than one type of insomnia were the most predominate insomnia subtype in OSAS group (85%), whereas initial insomnia was the most predominant in without OSAS group (10%). The results were in line with Chung (2005), who studied the prevalence of insomnia and its subtypes in 157 patients with OSAS, and maintenance insomnia was seen in 40% of cases. On the contrary, our results were against Bjorvatn *et al.*, (2014) who showed that nonrestorative sleep is the most predominant insomnia subtype among OSAS group. This may partially be because the study by Bjorvatn *et al.*, (2014), used Bergen insomnia scale to assess insomnia and ICSD-2 as diagnostic criteria of insomnia.

Our results suggested that the group of patients with OSAS exhibited higher levels of anxiety as shown by Hamilton anxiety scale especially in those with insomnia, this result different from Park *et al.*, (2015) who reported no statistically significant difference in anxiety levels among OSAS with or without insomnia, assessed by Beck anxiety index.

In contrast, we found a significant positive correlation between severity of insomnia and anxiety levels as shown by ISI and Hamilton anxiety scale. These results were in agreement with those reported by Taylor *et al.*, (2005).

Particularly, the results indicated that OSAS patients presented higher levels of depression as shown by Hamilton

depression scale, however, the results were not significantly different from patients without OSAS depression score, but the p value was as low as 0.09, suggesting a tendency to show higher score levels in OSAS group. The comparison between OSAS with insomnia and OSAS without insomnia did not show a significant difference between depression scores ($p=0.776$). Previous studies confirmed our findings regarding depression score in OSAS vs. without OSAS groups with statistical significance (Bjorvatn *et al.*, 2014). However, the authors did not perform a depression assessment, but merely asked whether the patients had been previously diagnosed with depression. Additionally, Hayley *et al.*, (2015) demonstrated that OSAS patients with insomnia exhibited higher scores of depressions. The authors recruited more than 4500 subjects with a higher percentage of subjects of more than 65 years old who present more depressive symptoms. Also, they assessed depression symptoms by using a partial health questionnaire which aims to assess common mental disorder. These differences might explain why we were not able to detect a statistical difference among OSAS with insomnia and OSAS without insomnia groups.

In this study we described a positive correlation between initial insomnia and Hamilton anxiety scale and positive correlation between Hamilton depression scale and maintenance and early awakening insomnia before desired time, but the latter comparison without statically difference ($p=0.064$, 0.422 respectively). In agreement, Taylor *et al.*, (2005), also suggested that the type of insomnia might relate to depression as they found that people with combined insomnia (like both onset and maintenance insomnia) had greater depression levels than people with onset, maintenance and mixed insomnia.

Moreover, the study showed positive correlation between Hamilton depression scale, Hamilton anxiety scale and AHI without statistically differences, suggesting that apnea and hypopnea events would relate to the presence of higher levels of depression and anxiety. Our result agreed with Bjorvatn *et al.*, (2014), who showed that there was higher depression score among OSAS group than non OSAS group but he was not able to correlate with AHI. This difference might be explained by previous literature that showed that OSAS had a greater impact on life. Many people with OSAS are excessively sleepy during the daytime. This can make it difficult to work, and can even lead to job loss. OSAS can have a major impact on family and friends. Depression makes it hard to maintain relationships, and people with OSAS are less likely to engage in social activities, especially physical exercise, because they are too tired. Because of the loud, bothersome snoring associated with OSAS, spouses or bed partners might choose to sleep in separate bedrooms.

In regard of quality of life impact, we observed that there was a lower score of SF-36 in OSAS group respect to without OSAS group, indicating a lower quality of life and higher levels of fatigue among OSAS patients. Also, our study showed that there was a significantly low score of SF-36 in OSAS with insomnia vs. OSAS without insomnia, suggesting that patients with OSAS that present insomnia would exhibit lower quality of life and higher levels of fatigue than those without insomnia. This might suggest more disability in OSAS with insomnia than OSAS without insomnia, however, statistical analysis did not show a significant difference. These results were similar to Wong *et al.*, (2015); Hayley *et al.*, (2015); Gupta and Knapp (2014); Zwi *et al.*, (2005). These studies showed that quality of life had a higher impact in OSAS with insomnia than OSAS without insomnia.

CONCLUSION

We concluded in this study that depressive and anxiety symptoms are common to be associated with obstructive sleep apnea, additionally insomnia related to OSAS increase the prevalence of anxiety more than depression scores. Further investigations in this area, particularly large-scale studies, are necessary to understand this relationship and the nature of these conditions.

LIMITATIONS OF THE STUDY:

The limitations of this study were that the sample size was limited, that the questionnaires were sometimes more advanced than the educational level of the participants, and that the answers to the questionnaires are subjective. A confirmation by an objective method such as actigraphy for insomnia would be more accurate. Finally, the study is limited to the Mansoura University Hospitals, and did not include other universities or hospitals of our locality, thus the results of the study cannot be generalized.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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