ORIGINAL ARTICLE

Prevalence of Depression and Anxiety in Patients with Sleep-Disordered Breathing and its Correlation with Disease Severity

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Abstract

Objective: Primary objective of the study was to assess the prevalence of depression and anxiety among obstructive sleep apnoea (OSA) patients presenting to the sleep clinic of Safdarjung Hospital. Secondary aim was to study the correlation between and severity of depression, anxiety and respiratory disturbance index (RDI) and to see any relation with gender.

Study design: Case–control study.

Materials and Methods: One hundred seventy-two patients with OSA were evaluated before treatment and compared with controls by using the Patient Health Questionnaire-9 (PHQ-9) and anxiety on the basis of General Anxiety Disorder Assessment-7 score (GAD-7). Based on these scores, depression and anxiety were categorised as mild, moderate and severe, respectively. OSA was assessed by Epworth Sleepiness Scale, and polysomnography was used for sleep scoring and classified to mild, moderate and severe OSA by RDI.

RESULTS: Depressive symptoms were identified in 14% (25 of 172) of controls, and 36.4% (62 of 172) of patients with OSA by using PHQ-9 screening ($P<0.006$). Anxiety was identified in 19.2% (33 of 172) OSA patients as compared to 6.7% of controls. Evaluation of the patients with OSA compared to the control group showed depression and anxiety to be significantly more common in OSA patients than in controls (*P*-values 0.006 and 0.01, respectively). Overall, 41.9% and 58.1% of men and women, respectively, with OSA had elevated PHQ-9 scores; 05% and 11% of male and female control patients, respectively, exhibited depressive symptoms ($P<0.001$). In all, 75.75% patients were female OSA cases with symptoms of anxiety (25 of 33), while 24.25% were male ($P<0.02$) as screened by GAD-7 scores. Analysis of depression scores by OSA disease severity category found significant difference in depressive symptoms between participants with mild OSA, moderate OSA and severe OSA (*P*-value <0.006). In this study, the association between OSA disease severity (as determined from the RDI) and PHQ-9 on univariate analysis (P ¼ .OO) was significant, with association found (*P*-value<0.003) on multivariable analysis, after controlling for sex. Partial linearity was noted. Analysis of anxiety scores by GAD-7 scores found no significant difference

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in anxiety symptoms between subgroups with mild, moderate and severe OSA (*P*-value <0.23) on univariate analysis, association between disease severity 0f OSA and GAD-7 scores was not significant, however, on multivariate analysis ruling out confounding factors like sex was significant (*P*-value <0.003).

CONCLUSIONS: Patients with OSA and daytime sleepiness are more likely to have depressive and anxiety symptoms as compared with controls. OSA disease severity, as measured with the RDI score, is a predictor of PHQ-9 score, but no correlation was seen between the severity of OSA and GAD-7 scores. These data suggest that OSA patients with symptoms of excessive sleepiness have the highest risk of associated depressive symptoms and may benefit most from depression screening.

Keywords: OSA, Depression, Anxiety, PHQ-9 Score, GAD-7 score, RDI

Introduction

Obstructive sleep apnoea (OSA) is a common disease, characterised by repetitive upper airway obstruction during sleep and associated with increased morbidity and mortality and diminished quality of life. Obstructive sleep apnoea syndrome (OSAS) is a common disease, affecting about 2%–4% of the adult population[1]. Tiredness, daytime sleepiness, headache and obesity are common symptoms of OSAS, which often lead to inactivity and cardiovascular or other organ manifestations. Some of the symptoms of OSAS resemble symptoms associated with anxiety and depressive conditions. However, clinicians may have problems differentiating psychiatric disease from symptoms related to organic diseases. Most case–control studies have reported increased prevalence rates of depression in OSAS compared to controls[2–5], but other studies indicate no differences[6–8]. Further, the relationship between OSAS and depressive symptoms may be moderated by factors such as gender and OSAS severity[9]. The prevalence of depression in people with OSA ranges from 7% to 63%[10–12]. Although many of these rates reflect the variable composition of the clinical populations studied, they are consistently higher than rates of depression found in community samples (3%–5%)[13] or in the primary care setting (5%–10%)[14]. In addition, rates among women appear to be higher than rates in men within the same cohorts[12].

The direction of the association is unclear because there is significant overlap in the symptoms of OSA and depression, including fatigue, decreased libido and poor concentration, which are common to both conditions and not specific for either. The purpose of this study was to determine whether a relationship exists between depression, anxiety and OSA, disease severity, in patients with OSA presenting to our sleep clinic as compared with controls.

Materials and Methods

Methods

Primary aim of the study was to assess the prevalence of depression among OSA patients presenting to the sleep clinic of Safdarjung Hospital. Secondary aim was to study the correlation between respiratory disturbance index (RDI) and severity of depression and anxiety and to see any relation with gender.

Study Design

It was a case–control study involving 172 patients visiting the sleep clinic of Safdarjung Hospital being evaluated for SDB. Depression was assessed on the basis of Patient Health Questionnaire-9 (PHQ-9) and anxiety on the basis of General Anxiety Disorder Assessment-7score (GAD-7).

Epworth Sleepiness Scale (ESS) was used for assessing daytime sleepiness[17,18]. This used self-administered scale with eight items about how easily the respondent would fall asleep in different situations. The items were scored on a 0–3 scale, which were added to give an overall score of 0–24. Higher scores indicate more sleepiness. ESS score 2–10 was considered 'normal' and ≥10 indicative of pathological sleepiness. OSAS was diagnosed with a full night of in-laboratory, clinical polysomnography evaluating the following physiological and respiratory variables: central and occipital EEG, oblique EOG, submental and tibialis EMG activity, ECG, nasal and oral airflow via nasal pressure transducer and thermister, thoracic and abdominal excursions with peizo belts and continuous oxygen saturation. Sleep stage

was scored by trained technicians using standard criteria[19]. Apnoeas and hypopnoeas were scored using recommended guidelines. An apnoea was defined as the cessation of airflow for 10 s or longer. Hypopnoea was defined as a 30% decrease (from baseline) in airflow or chest wall movement for at least 10 s, accompanied by an oxygen desaturation of 4% or greater. This definition also included respiratory effort–related arousals (RERAs), whereby arousals were identified in the setting of heavy snoring without hypoxaemia or discernible reductions in airflow. Thus, SDB severity was measured by the RDI, an index of apnoeas–hypopnoeas and RERAs, divided by the total sleep time. OSA severity was defined according to the criteria of the American Academy of Sleep Medicine, with mild OSA defined as 5–14 events per hour, moderate as >15 to <30 events per hour and severe OSA defined as 30 events per hour[16].

The PHQ-9 scale was used to assess depression. It is a reliable instrument in screening for clinical depression in many different settings and populations[20]. It incorporated DSM-IV criteria questions as a self-report tool. The scale was self-administered and as 10 items scored on a 0–3 scale. Scores on the items were summed to give a score to comprise the depression score. Hence, scores range 0–21, with higher scores indicated more symptoms of depression. A score greater than or equal to 10 correlated with major depression with a sensitivity and specificity of 88%, respectively, hence, patients with a score of more than 10 were assigned to be having depression. Those with scores of 10, 15 and greater than or equal to 20 were classified to be having mild, moderate and severe depression, respectively[20].

The GAD-7 score was calculated by assigning scores of 0, 1, 2 and 3 to the response categories of "not at all," "several days," "more than half the days" and "nearly every day," respectively, and adding together the scores for the seven questions[21]. Scores of 5, 10 and 15 are taken as the cutoff points for mild, moderate and severe anxiety, respectively.

Control population was also chosen among populations attending Outpatient Department in Safdarjung Hospital but with ESS of <10.

Statistical analysis was made by mean, standard deviation percentages. Independent variables like age at time of survey and sex were included. The Fisher exact test was used to compare demographics between OSA and control patients, and the Mann–Whitney *U*-test was used to compare differences in PHQ-9 and GAD scores between OSA and control patients. Spearman correlation analysis was used to evaluate correlations between factors. Multivariable linear regression analysis was used to examine the data and describe the relationship between OSA, depression, anxiety and sexes. Results of univariate and multivariate analysis are presented as *P*-values and *r*-values. Simple linear regression models were also fitted for each individual factor. Data analyses were conducted using SPSS 11.5 (SPSS, Inc., Chicago, IL). Significance level was set at 0.05 for all analyses.

Results

A total of 172 patients were surveyed. This group was compared with a group of 172 controls who presented to the Department of Respiratory, Critical Care and Sleep medicine for non-sleep-related disease. There was no significant difference between groups with respect to age (Table 1).

The OSA patients differed from controls in that there were less male patients in the OSA group (54.07%) than in the control group (56.3%). Patients with OSA differed significantly from controls in regard to mean PHQ-9 and GAD-7 scores for depression and anxiety, respectively (Table 1).

Depressive symptoms were identified in 14% (25 of 172) of controls, and 36.4 % (62 of 172) of patients with OSA by using PHQ-9 screening (P<0.006). Anxiety was identified in 19.2% (33 of 172) of OSA patients as compare to 6.7% of controls. Evaluation of the patients with OSA compared to the control group showed depression and anxiety to be significantly more common in OSA patients than in controls (P-values=0.006 and 0.01, respectively). Overall, 41.9% and 58.1% of men and women, respectively, with OSA had elevated PHQ-9 scores; 05% and 11% of male and female control patients, respectively, exhibited depressive symptoms (P<0.001). In all, 75.75% patients were female OSA cases having symptoms of anxiety (25 of 33), while 24.25% were male (P<0.02) as screened by GAD-7 scores.

Analysis of depression scores by OSA disease severity category found significant difference in depressive symptoms between participants with mild, moderate and severe OSA (P-value<0.006).

In this study, the association between OSA disease severity (as determined from the RDI) and PHQ-9 on univariate analysis (P< 0.OO) was significant, with association found (P<0.13). But on multivariate analysis,

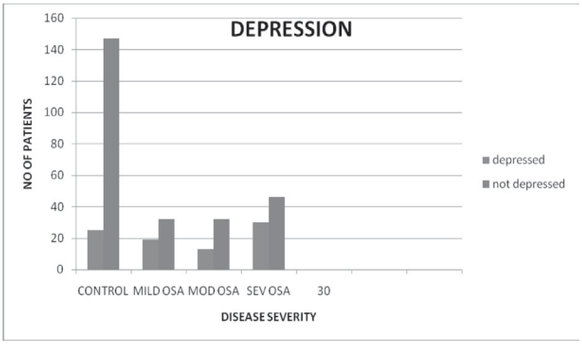
Table 1: Comparison of demographic characteristics of patient and control population

Patient characteristics	OSA (*n*=172)	Control (*n*=172)	*P*-value
Age (years), mean±SD	50.59±10.8	50.12±9.4	0.99
Male, *n* (%)	93 (54.07)	97 (56.3)	
Female, *n* (%)	79 (45.9)	75 (43.6)	
Depression PHQ-9 ≥10	62 (36.4)	25 (14.5)	0.006
Anxiety GAD-7 ≥10	33 (19.2)	12 (6.9)	0.01

GAD-7: General Anxiety Disorder Assessment-7 score; PHQ-9: Patient Health Questionnaire-9; OSA: Obstructive sleep apnoea

after controlling for sex, partial linearity was noted (Figure 6).

Analysis of anxiety scores by GAD-7 scores found no significant difference in anxiety symptoms between subgroups with mild, moderate and severe OSA (*P*-value<0.23) on univariate analysis. However, on multivariate analysis, ruling out confounding factor like sex was significant (*P*-value<0.003; Figure 1).



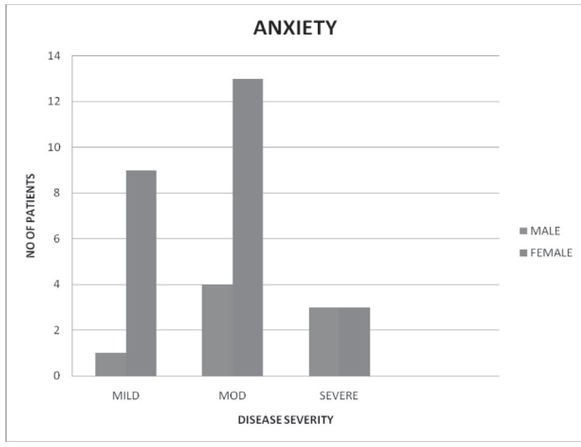
MOD: moderate; SEV: Severe.

Figure 1: Comparison of prevalence of depression according to disease severity in obstructive sleep apnoea (OSA) population and control population.

Table 2: Comparison of prevalence of depression and anxiety according to disease severity in OSA population and control population

Measure	Control	Mild OSA	Mod OSA	Severe OSA	*P*-value
Depressed *n* (%)	25 (14.5)	19 (30.9)	13 (20.9)	30 (48.3)	0.006
Anxious, *n* (%)	12 (6.9)	11 (33.3)	8 (24.2)	12 (36.6)	0.21

OSA: Obstructive sleep apnoea



MOD: moderate.

Figure 2: Comparison of prevalence of anxiety according to disease severity in obstructive sleep apnoea (OSA) population.

On comparing the depression scores between two sexes, no significant difference was seen (*P*-value <0.33). However, on comparing anxiety scores between two sexes, significantly higher scores were seen among females (*P*-value <0.004).

Table 3: Severity of depression and anxiety in male and female sexes of OSA population

Depression

	Mild	Moderate	Severe
Male, *n* (%)	16 (16.2)	6 (6.3)	4 (4.2)
Female, *n* (%)	23 (29.9)	7 (9.1)	4 (5.2)

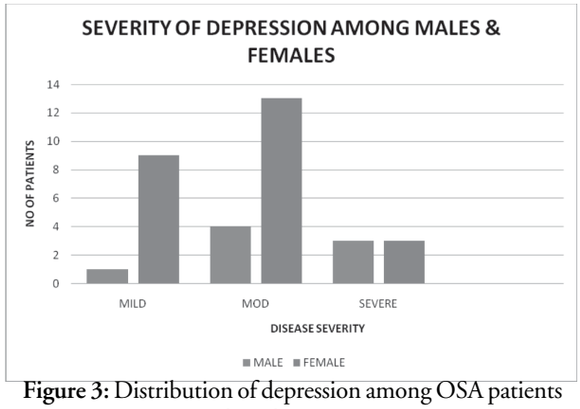
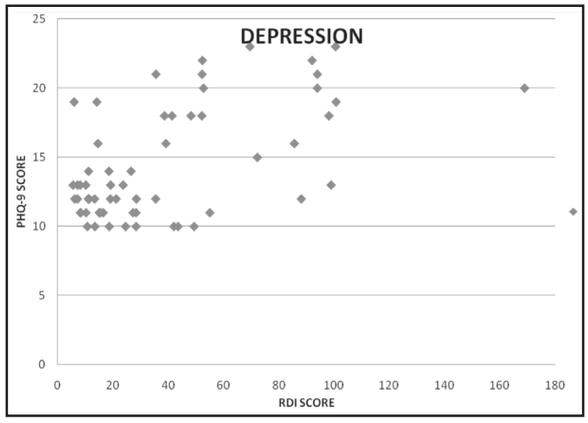


Figure 3: Distribution of depression among OSA patients based on sexes

Anxiety

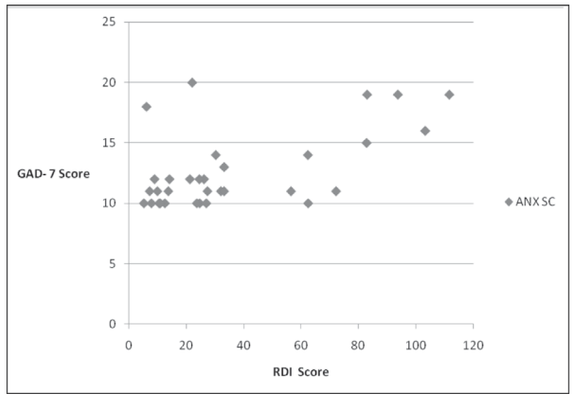
	Mild	Moderate	Severe
Male, *n* (%)	1 (1.1)	4 (4.2)	3 (3.2)
Female, *n* (%)	9 (11.7)	13 (16.9)	3 (3.9)

MOD: moderate; OSA: obstructive sleep apnoea.



PHQ-9: Patient Health Questionnaire-9

Figure 5: Depression score as a function of obstructive sleep apnoea as measured by respiratory disturbance index (RDI) score, partial correlation seen (*P*-value <0.05, *r*-value=0.12)



GAD-7: General Anxiety Disorder Assessment-7 score; RDI: respiratory disturbance index

Figure 6: Partial correlations between apnoea severity and depression and anxiety in depression with obstructive sleep apnoea (*P*-value <0.05, *r*-value=0.12)

On comparison with anxiety and OSA, *P*-value >0.05 and *r*-value=0.69 implies absence of any colinearity.

Discussion

Depression in OSA patients was much more common in this study (36%) than in a recent report by Chandra *et al*. looking at the prevalence of depression in patients with sleep apnoea seen in the general practice setting (14%)[12].

To better understand the relationship between sleepiness and mood disorders, researchers have evaluated the effects of acute sleep deprivation (24 h) on healthy adults without pre-existing mood disorders and have found that depression and anxiety are elevated after acute sleep deprivation[25]. Correlation has also been seen between increased levels of sleepiness and increasing depressive symptoms, a finding which suggests that there may be a causal relationship between the two conditions[26]. Although little is known about the effects of chronic sleep deprivation or sleep restriction on the incidence of mood disorders, several studies have suggested that the relationship between the two is complex and that sleepiness may in fact be more than a symptom of depression; rather, sleepiness instead may contribute to the development of depression[27,28]. In addition, recent studies have looked at the effect of chronic sleep restriction/deprivation on the brain chemistry of rats and found that the changes in neurotransmitter receptor systems and neuroendocrine reactivity are similar to those seen in depression[29]. OSA is associated with elevated levels of the cytokines IL-6 and tumour necrosis factor[30,31]. These cytokines have been proposed as the mediators of daytime sleepiness in this condition. Administration of a tumour necrosis factor antagonist has been shown to dramatically reduce the level of daytime sleepiness in patients with OSA[32]. Major depression has also been shown to be associated with an immune response involving proinflammatory cytokines IL-1, IL-6[33]. While these studies involve small numbers of subjects and do not imply causation, they do suggest a possible shared pathway between abnormalities in central and peripheral neurotransmission of serotonin[34]. Serotonin is also thought to be involved in the sleep dependant reduction in output to the upper airway dilator muscles, particularly, the hypoglossal nucleus, although this pathway is extremely complex, with multiple receptor subtypes[35]. The exact role of serotonin in the hypoglossal nucleus has also not been characterised. Again this may suggest a shared pathway. A further possibility is an as yet uncharacterised underlying causal mechanism for both OSA and depression. Overall, similar factors may be causative for both OSA and depression, with links between the two still uncertain. In our study also we could not establish the nature of the relationship[36].

Gender appears to moderate the relationships between apnoea severity, depression and anxiety. Men only showed an insignificant association with depression. On the other hand, Women only showed a relationship with depression, independent of apnoea severity. However, in our study, gender-specific relation was found

with anxiety rather than depression.

These findings suggest that men and women with apnoea manifest depressive symptoms differently. Pillar *et al*.[9] found that women with OSAS scored higher on depression and anxiety scales than did men with OSAS. They attributed these findings in part to basic gender differences in personality, suggesting that women tend to focus more on their symptoms than do men[37,38].

Given these findings, the gender-specific manifestation of depression and the mechanisms underlying these relationships deserves closer attention.

Noting that early studies showing links between depressive symptoms and sleep fragmentation or hypoxia in OSA had small numbers of patients and did not control for likely confounders, Bardwell *et al*.[39] with *n*=72 showed no relationship between depression and either sleep fragmentation or hypoxia when BMI and hypertension were controlled. Bardwell *et al*. later compared the effects of Continuous Positive Airway Pressure CPAP and oxygen therapy on depressive symptoms in a controlled randomised trial in 38 people with OSA. While other arms showed no significant effect, the oxygen therapy arm showed significant reduction in psychological symptoms. Authors concluded that in patients with OSA, hypoxaemia may play a stronger role than sleep disruption in depression. In contrast, a case–control study[40] showed psychological symptoms to be correlated with sleep fragmentation but not with oxygen desaturation. Thus, the actual relationship between depression, anxiety and sleep is not clear. In our study also we could not establish any such causal relation.

Our study has several limitations. First, based on the nature of our correlational analyses, causation cannot be inferred. Second, there was no significant correlation between severity of OSA and anxiety, may be due to a smaller population of study as compared with that of the population with depression.

Conclusions

Patients with OSA are more likely to have depressive and anxiety symptoms compared to controls (37% versus12% and 19.18% versus6.9%) regardless of their sex. OSA disease severity (measured by the RDI) is a predictor of PHQ-9 scores but not that of anxiety score predictor (GAD-7). Sex-related prevalence shows an increase with female sex but there is no correlation with severity of depression but there is a positive correlation with anxiety scores. However, we could not establish whether the relation between depression, anxiety and OSA is causal or not, further studies are required to establish that. Thus, any patient presenting with depression and anxiety should be evaluated for OSA and vice versa.

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