

## Review Article

# Depression Prevalence in Obstructive Sleep Apnea

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### Abstract

The prevalence of Depressive Disorder (DD) is higher in Obstructive Sleep Apnea (OSA) than non OSA patients and depression can be a presenting complaint in women with untreated OSA. It is important for clinicians to recognize the existence of co morbid OSA in DD patients because pharmacotherapy for depression, such as antidepressants, could exacerbate the OSA leading to worsening of the underlying OSA symptoms and an adverse effect on their functional ability and quality of life. Symptoms of suspected OSA, such as loud snoring, daytime sleepiness, and difficulty in breathing at night that occur in patients with DD, especially those with residual depressive symptoms despite receiving antidepressant therapies, should be evaluated for sleep apnea by polysomnography and, if present, treated with appropriate treatment, such as CPAP.

**Keywords:** Continuous positive air pressure; Depression; OSA

### Abbreviations

OSA: Obstructive Sleep Apnea

PAP: Positive Airway Pressure

CPAP: Continuous Positive Air Pressure

BDI: Becks Depression Index

DD: Depressive Disorder

MDD: Major Depressive Disorder

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**Citation:** Riaz U, Thorpy M, Riaz SA (2020) Depression Prevalence in Obstructive Sleep Apnea. J Psychiatry Depress Anxiety 7: 038.

**Received:** February 17, 2021; **Accepted:** February 19, 2021; **Published:** February 26, 2021

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### Introduction

Obstructive sleep apnea, the most common form of a sleep related breathing disorder is characterized by decreases (hypopneas) or pauses (apneas) in respiration during sleep [1]. The prevalence of OSA increases with age and is higher among males than females. Among the population between 30 to 65 years of age, 24% of men and 9% of women have been shown to suffer from OSA [2].

Depression is prevalent in people with OSA, ranging from 5% to 63% in clinical and community studies [3]. A significantly higher prevalence of depression was identified in people with OSA (21.8%) compared to those without OSA (9.43%) [4]. While this higher prevalence of depression among OSA points toward an underlying association, some OSA and depressive symptoms such as, fatigue, tiredness, loss of interest, and poor concentration may overlap [5], thus making it more difficult to recognize underlying OSA. Although prior studies have addressed the link between OSA and depression, results in the literature are mixed. Some studies, including two large-scale studies [6,7], have reported no association between the disorders, while one longitudinal study reported an increased risk of consequent depression that exhibited a dose response relationship with OSA severity [8]. Two retrospective studies also observed OSA to be linked with depression [9,10].

Inconsistencies in previous findings may be attributable to inadequate control of confounders (e.g. obesity, hypertension, diabetes, alcohol consumption), biases (e.g. self-reported data) and other measurement issues (e.g. different study populations, questionnaires, and scales) [11]. Based upon the heterogeneity of these data and numerous confounding factors, follow-up studies of patient populations have been suggested to better address the link between OSA and depression [1]. In addition, while males are more frequently diagnosed with OSA [2], higher rates of depression have been found in female patients with OSA [12]. Studies have rarely examined the modifying effects of gender, due to insufficient numbers to report sex-stratified risks of consequent depression.

It has been speculated that the fatigue and sleepiness of OSA can be misinterpreted as symptoms of depression, or that adverse effects of OSA might affect the expression of clinical depression. Although the specific mechanism of the association of symptoms of depression with OSA remains undefined, these symptoms might be amenable to treatment with Continuous Positive Airway Pressure (CPAP). The effect of CPAP therapy produces a statistically significant improvement in those symptoms of depression, as defined by the BDI 4 to 6 weeks after initiation of CPAP therapy. Whether the improvement is sustained with ongoing treatment is unknown. A long-term follow-up study, one year or more after initiation of CPAP indicated that results persisted long term [13].

## Pathophysiology

The underlying mechanisms explaining the association between OSA and DD are not clearly delineated. Yet, a biological plausibility exists. First, sleep fragmentation or oxygen desaturation during sleep in OSA patients may have an effect on mood symptoms, although the results regarding this possibility are mixed. OSA and the subsequent sleep fragmentation might cause neurochemical alterations in the brain that result in depression.

In a randomized controlled trial, hypoxia in OSA was shown to associate with depression, as a significant reduction of depressive symptoms was observed for patients with OSA receiving oxygen therapy [14]. Recent preliminary imaging data also suggested that hypoxemia linked with OSA might play a part in affecting mood [1]. Sleep fragmentation, contributing to excessive daytime sleepiness in OSA, could add to the depressive symptomatology of OSA [15]. Nevertheless, however, depression was not found to be associated with either sleep fragmentation or hypoxia in OSA in one study [16]. Studies utilizing larger sample sizes and the appropriate consideration of confounders (e.g. body mass index, hypertension) will help to clarify this association.

It is possible that there is a shared signaling pathway involving pro inflammatory markers, neurotransmitters, or undisclosed underlying factors between the two conditions. While OSA was associated with increased levels of IL-6 and tumor necrosis factor [17], an immune response implicating pro inflammatory cytokines IL-1, IL-6, and interferon- $\gamma$  was observed among patients with DD [18]. Excitatory and inhibitory neurotransmitters, such as serotonin, nor epinephrine and  $\gamma$ -amino butyric acid (GABA), are also be involved in both the sleep/wake cycle and mood regulation. Shared common risk factors such as, obesity, cardiovascular disease, and metabolic syndrome are other potential contributing factors. Finally, as depression is more common in patients with chronic medical diseases [19], OSA by decreasing quality of life, may further lead to depression [9].

## Discussion

The incidence of DD was about twice as high among patients with OSA than as those without OSA. Patients with OSA are also independently associated with a 2.18 times increased risk of consequent DD, after taking confounders into consideration, including monthly income, geographic region, hypertension, diabetes, CHD, hyperlipidemia, obesity, and alcohol abuse/alcohol dependency syndrome. A higher risk of consequent DD is observed among female patients with OSA than their male counterparts. While increased risks of subsequent DD were observed for patients younger than 40 and 40-64 years old with OSA, no significant relationship between DD and OSA was observed among those with OSA older than 64 years [20]. Many previous studies exploring the link between OSA and DD have been cross-sectional or retrospective. For example, Aloia et al. conducted a retrospective study and recruited 93 patients from sleep clinics and found apnea severity (percent of sleep time < 90% oxygen saturation) to contribute to depressive symptomatology in OSA [9]. Another study conducted on this association was a population-based prospective study with 1,408 community participants designed to assess OSA as a longitudinal predictor of depression. Compared to those without OSA, the odds of developing depression during a 4-year interval increased by 1.6, 2.0 and 2.6 fold for participants with minimal, mild and moderate or worse OSA, respectively [8].

Nevertheless, a null association between OSA and DD was observed in two retrospective studies [21]. Methodological variation (e.g. different populations, study designs, disease definitions, and assessment instruments) or limitations (e.g. inappropriate consideration of confounding effects) may render comparison between investigations difficult. After considering confounding factors, it has been confirmed a prospective link between OSA and subsequent DD within the first year following OSA diagnosis in the nationwide population-based study. Regarding the modifying effects of gender, Enright et al. examined 5,201 community adults' aged 65 years and older and observed apneas to be associated with depression in women but not in men [22].

Consistent with previous findings [23], a large-scale study identified women as having higher risks of subsequent DD within the first year following OSA diagnosis. This might reflect a more general finding that depression is more prevalent in women than in men [24]. Co morbid DD was found to exacerbate OSA and to have a negative impact on self-management and treatment adherence of chronic medical illness such as OSA [25]. It is therefore possible that prompt detection and appropriate treatment of DD can aid in the management of OSA which suggests that clinicians should be more aware of the frequently observed link between OSA and DD. Since patients with OSA might not voluntarily voice mood symptoms in the context of a sleep evaluation, regular screening and monitoring of psychiatric conditions among patients with OSA is needed, especially among women. Proper and timely referral for assessment and treatment of mood symptoms, not just the treatment of OSA itself, might assist in promoting patient well-being and reducing the subsequent detrimental health consequences [8].

The presenting symptoms of both syndromes (OSA and depression) are similar enough to result in the potential for the clinic and to misdiagnose one with the other, and each disorder might increase the likelihood of the other occurring. Patients with OSA frequently report feeling tired, fatigued, sleepy, and poorly motivated which may affect work performance and affect the psycho social relationship with their family, ultimately limiting their quality of life [26-29].

Patients with OSAS can have difficulty concentrating, remembering factual data, become irritable or withdrawn, and may find themselves losing interest in, or deriving little pleasure from activities that should be an integral part of their lives [30]. These symptoms bear striking similarity to some of those ascribed to depression and may potentially fulfill the criteria for a major depressive episode using Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria [31]. Previous studies have documented improvement in some symptoms of depression in patients with OSA after institution of CPAP therapy. However, most of these reports have been limited to relatively short-term follow-up (4-12 weeks). One study provides a distinct data base in which a group of individuals with a well-defined syndrome, documented reversibility, and affirmed use of CPAP, have been followed and reassessed with a quantifiable measure of some symptoms of depression. The data support the potential for CPAP use to be associated with an improvement in some measured symptoms of depression both in the short term (4-6 weeks) and long term (one year and longer) [6].

Why the use of CPAP is associated with the changes in depressive symptoms is incompletely understood. Relief of the obstructive respiratory events with CPAP might ameliorate the symptoms

by improving sleep continuity, by reducing the adverse effects of various neurotransmitters (catecholamine's or cortisol-related peptides) [28], by alleviating the adverse effects of hypoxemia [14], or by a mechanism as yet unknown. However, the data from the studies suggests that successful CPAP therapy is associated with a statistically significant improvement in some symptoms of depression as delineated in the BDI, and that the improvement is sustained long term.

The symptoms of depression be acknowledged as a part of OSAS and not only should patients suspected of having OSAS be quired about the symptoms of depression, but patients presenting primarily with symptoms of depression should be quired regarding the possible presence of OSAS. An analysis of these parameters may subsequently affect the treatment of patients.

### Conclusion

The findings of multiple studies strongly suggest that the symptoms of depression interact in a bidirectional way with OSA; so not only should patients suspected of having OSA be queried with regard to the symptoms of depression, but patients presenting with depression should be queried with regard to the presence of the OSAS. The recognition of OSA in a patient with depression, or the recognition of depression in the OSA patient will lead to effective treatment that will not only improve both disorders but lead to greatly improved quality of life for the patient.

### Acknowledgement

None.

### Role of the Funding Source

Author's state that this study was not financed.

### Contributors

All authors contributed equally to this manuscript.

### Conflict of Interest

Authors have no conflict of interest.

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