

Prevalence of Cognitive Impairment in Obstructive Sleep Apnea and Its Association with the Severity of Obstructive Sleep Apnea: A Cross-sectional Study

Preethi Vasudev¹, Padmanabhan Arjun², Ameer K Azeez³, Sanjeev Nair⁴

ABSTRACT

Background: Cognitive impairment in obstructive sleep apnea (OSA) is a widely unrecognized entity. Earlier studies have shown variable results for the prevalence of this entity. Hence, this study was done to determine the prevalence of cognitive impairment in patients diagnosed to have OSA and its association with the severity of OSA.

Materials and methods: All in-patients and outpatients who were diagnosed to have OSA by polysomnography in a tertiary care hospital in Kerala, India, were included in this study. Cognitive function was assessed by Montreal cognitive assessment (MoCA) and their scores were calculated. Daytime sleepiness was assessed by the Epworth sleepiness scale (ESS).

Results: 96 OSA patients were included in the study. 19.8% of patients had mild OSA, 29.2% of patients had moderate OSA, and 51% of patients had severe OSA. The prevalence of cognitive impairment in OSA patients in this study was found to be 58.3% (95% confidence interval, 47.8–68.3%). There were 35 (62.5%) patients with cognitive impairment in the severe OSA group, while the moderate and mild OSA groups had 17 (30.4%) and 4 (7.1%) patients, respectively. There was a significant negative correlation between AHI and MoCA score, indicating that cognitive impairment is associated with the severity of OSA.

Conclusion: The prevalence of cognitive impairment in our study was 58.3%, which was found to be more in those with severe OSA. It was also found that cognitive impairment is associated with the severity of OSA.

Clinical implications: Cognitive impairment in OSA is associated with the severity of OSA and is a correctable condition that can improve the quality of life.

Keywords: Cognitive impairment, Montreal cognitive assessment score, Obstructive sleep apnea.

Indian Journal of Sleep Medicine (2020): 10.5005/jp-journals-10069-0059

INTRODUCTION

Obstructive sleep apnea (OSA) is a common disorder characterized by repetitive episodes of apnea during sleep and oxygen desaturation. OSA is a major public health problem, but the majority of physicians and the general public are unaware of this problem. Most of the time, OSA remains undiagnosed, which has serious health implications.

The development of OSA is associated with several factors like age, gender, anatomical variations, obesity, alcoholism, and drug intake.¹ There are many health implications of OSA. OSA has been associated with serious cardiovascular and metabolic comorbidities. Some of the conditions associated with OSA are hypertension, diabetes, cardiovascular disease, stroke, depression, endocrine abnormalities, neurocognitive impairment, and increased risk of automobile accidents.¹ It has also been found that undiagnosed or untreated OSA among workers in industry has adverse effects on their work performance as well as their safety in work place¹ by affecting their attention and vigilance.²

One of the major health impacts of OSA is in cognitive function.² Many studies have reported a range of cognitive impairment in OSA including selective and sustained attention, short-term memory, and executive functioning.^{3–7} Cognitive impairment can be due to the excessive daytime sleepiness in OSA patients and also due to other mechanisms affecting the brain due to poor sleep quality, sleep fragmentation, and hypoxia. Neuroinflammation, oxidative stress, and sympathetic overactivity have also been implicated in

^{1–3}Department of Respiratory Medicine, Kerala Institute of Medical Sciences, Thiruvananthapuram, Kerala, India

⁴Department of Respiratory Medicine, Government Medical College, Thiruvananthapuram, Kerala, India

Corresponding Author: Padmanabhan Arjun, Department of Respiratory Medicine, Kerala Institute of Medical Sciences, Thiruvananthapuram, Kerala, India, Phone: +91 471 3041322, Fax: +91 471 2446535, e-mail: dr.p.arjun@gmail.com

How to cite this article: Vasudev P, Arjun P, Azeez AK, *et al.* Prevalence of Cognitive Impairment in Obstructive Sleep Apnea and Its Association with the Severity of Obstructive Sleep Apnea: A Cross-sectional Study. *Indian J Sleep Med* 2020;15(4):55–59.

Source of support: This research has not received any specific grant from any funding agency in the public, commercial or not-for-profit sectors

Conflict of interest: We, the authors declare that there are no competing interests present as far as this submission for publication is concerned

the mechanism of cognitive impairment in OSA. Studies suggest that severe OSA can increase the risk of dementia in the elderly.⁸ It is considered to be one of the potentially modifiable risk factors for dementia.

OSA is diagnosed by sleep study or polysomnography. Studies conducted previously measure cognitive impairment objectively with tests such as Mini Mental State Examination, Montreal

cognitive assessment, Wechsler test, etc. Excessive daytime sleepiness is measured by the Epworth Sleepiness Scale in studies of cognitive impairment. Recently neuroimaging is used to find the areas of the brain affected in patients with cognitive impairment.²

Cognitive impairment and sleepiness have been found to be improved with continuous positive airway pressure (CPAP) therapy for OSA. Therefore, early recognition and treatment of OSA are important.² Even though studies have demonstrated consistent improvement in cognition and performance, the exact magnitude of improvement has been found to be variable.

OSA typically shows a “tip of the iceberg” phenomenon, that is, very few cases are diagnosed even though the prevalence in populations, both Indian and Western, have been found to be high.⁹ It has been found that cognitive impairment due to OSA can lead to increased risk of automobile accidents and workplace-related accidents. Thus it becomes very important to assess the effect of OSA on cognitive functions in the population.

Studies conducted previously for assessing cognitive function in OSA have shown variable results.⁹ Some studies assess only particular neurocognitive domains and their impairment. Hence, more research is required in this field to assess the levels of neurocognitive impairment due to OSA and the benefit of treatment.

In this background, this study was done to determine the prevalence of cognitive impairment in patients diagnosed to have OSA and its association with the severity of OSA.

MATERIAL AND METHODS

Study Subjects

All outpatients and in-patients who were evaluated in the sleep lab of Kerala Institute of Medical Sciences (KIMS), Thiruvananthapuram, a tertiary care center, and diagnosed to have OSA by polysomnography were included in the study. There were a total of 96 patients who gave informed consent for the study. All those patients who did not give consent, those who had dementia or psychiatric illness, or those who were on antidepressants or sedatives were not included in the study. The study was done after obtaining Institutional Human Ethics Committee clearance for the protocol. Confidentiality of the participants was maintained.

Study Design

This is a cross-sectional study done from September 2017 to May 2018. The sample size calculated was 96 patients with OSA based on the prevalence in previous studies.

Objectives

The primary objective of the study was to determine the prevalence of cognitive impairment in patients with OSA diagnosed by polysomnography in a tertiary care center in South India and the secondary objective was to determine the association of cognitive impairment with the severity of OSA.

Methods

All in-patients and outpatients who were evaluated in the sleep lab of Kerala Institute of Medical Sciences and who were diagnosed to have OSA and who gave informed consent were included in this study. OSA was diagnosed by Level 1 Polysomnography. Cognitive function was assessed by Montreal cognitive assessment¹⁰ (English version) (MoCA) and their scores were calculated. This is a 30-point test covering eight cognitive domains: visuospatial and executive,

naming, memory, attention, language, abstraction, delayed recall, and orientation. Those patients who got scores < 26 were considered to have cognitive impairment. Daytime sleepiness was assessed by the Epworth Sleepiness Scale.¹¹ Epworth Sleepiness Scale score (ESS) is a measurement of excessive sleepiness during daytime in adults that requires the person to rate the probability of dozing off in eight different day- to day situations on a scale of 0–3. Thus, the sum of the score can vary from 0 to 24. A value of more than 10 indicates significant daytime sleepiness.

Study variables included in this study were age, sex, occupation, smoking status, symptoms, duration of symptoms, presence of comorbidities like diabetes, systemic hypertension, coronary artery disease, stroke, obesity, hypothyroidism, history of any road traffic accidents while driving, height, weight, body-mass index, apnea-hypopnea index (AHI), scores of cognitive assessment, and Epworth Sleepiness Scale.

All the data were collected in a structured pro forma. The collected data were analyzed at the end of the study.

Analysis

All data collected were entered into MS Excel and analyzed using SPSS software version 20.0. Proportion and 95% confidence limits were determined for cognitive impairment in OSA. Linear regression was done for scores of cognitive impairment against AHI. R-squared was used to determine how well the model fit the data and the significance. All numerical variables were summarized with mean and standard deviation and categorical variables as percentages and 95% confidence limits. The difference between the different severities of OSA was determined for the variables using ANOVA to test significance in the difference in means and difference in proportions was tested using the Chi-square test.

Outcome

The primary outcome of the study is the prevalence of cognitive impairment in patients with OSA included in the study and the secondary outcome is the association of cognitive impairment with the severity of OSA as well as determining the relation between AHI and MoCA and between ESS and MoCA.

RESULTS

Characteristics of Study Participants

A total of 96 patients with OSA were included in this study (Table 1). Of these, 19 (19.8%) patients had mild OSA, 28 (29.2%) patients had moderate OSA, and 49 (51%) patients had severe OSA. The majority of OSA patients were males (75%). The number of males was more in the severe OSA group ($n = 40$, (55.6%)). The age of the patients ranged from 25 to 72 years with a mean age of 49.6 years (standard deviation of 10.8 years). The median age was 50 years. 31.25% of patients belonged to the age group of 51 to 60 years.

Symptoms and Comorbidities

The most common comorbidity observed in the study group was obesity (67.7%), followed by systemic hypertension (52.1%), and diabetes mellitus (39.6%). The number of patients with diabetes, hypertension, and obesity was more in the severe OSA group. There were only 25% of smokers in the study group. Snoring was the most common symptom, reported by all the 96 patients. History of automobile accidents could be obtained only in 4 patients (4.2%). The symptoms were found to be more in patients with severe OSA.

Table 1: General characteristics of the study group

Variable	Category	n (%)
Age	≥50	29 (30.2%)
	<50	67 (69.7%)
Sex	Male	72 (75%)
	Female	24 (25%)
Apnea-hypopnea index	Mild OSA	19 (19.8%)
	Moderate OSA	28 (29.2%)
	Severe OSA	49 (51%)
Comorbidities	Diabetes mellitus	38 (39.6%)
	Systemic hypertension	50 (52.1%)
	Coronary artery disease	12 (12.5%)
	Stroke	1 (1.04%)
	Obesity	65 (67.7%)
	Hypothyroidism	16 (16.7%)
Symptoms	None	10 (10.4%)
	Snoring	96 (100%)
	Witnessed apneas	56 (58.3%)
	Gasping during sleep	42 (43.8%)
	Unrefreshing sleep	70 (72.9%)
	Morning headache	42 (43.8%)
	Excessive day time sleepiness	83 (86.5%)
	History of automobile accidents	4 (4.2%)
Irritability/memory loss	54 (56.3%)	

AHI, apnea-hypopnea index; OSA, obstructive sleep apnea

Outcomes of the Study

The prevalence of cognitive impairment in OSA patients in this study was found to be 58.3% (95% confidence interval 47.8–68.3%) (Table 2). There were 4 (7.1%), 17 (30.4%), and 35 (62.5%) patients with cognitive impairment in the mild, moderate, and severe OSA groups, respectively. The proportion of patients with cognitive impairment was found to be highest in the severe OSA group. Linear regression analysis showed a significant but mild negative correlation between AHI and MoCA score (Fig. 1). Thus cognitive impairment was found to be associated with the severity of OSA.

Excessive Daytime Sleepiness and Severity of Obstructive Sleep Apnea

As many as 58.3% of patients in the total study group had excessive daytime sleepiness as indicated by an Epworth Sleepiness Scale score >10. There were more number of patients with excessive daytime sleepiness in the severe OSA group. It was also found that 38 (67.9%) of patients with excessive daytime sleepiness had cognitive impairment while only 18 (45%) of patients without excessive daytime sleepiness had cognitive impairment. However, the correlation between ESS and MoCA score was not found to be statistically significant (Fig. 2).

DISCUSSION

In this study, 58.3% of patients (out of the total of 96 OSA patients) were found to have cognitive impairment as indicated by a Montreal cognitive assessment (MoCA) score < 26. The prevalence of cognitive impairment in OSA in this study is 58.3%, which is the primary outcome of the study. It was also found that as the severity of OSA increases, the MoCA score decreases, indicating

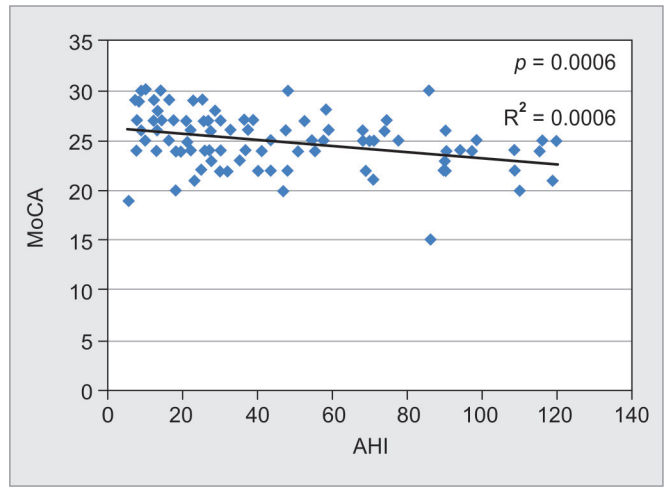


Fig. 1: Correlation between apnea-hypopnea index (AHI) and Montreal cognitive assessment (MoCA) score

Table 2: Characteristics of the different obstructive sleep apnea (OSA) groups

	Mild OSA (n = 19)	Moderate OSA (n = 28)	Severe OSA (n = 49)	p-value
Mean age (years)	49.8 ± 10.3	50.9 ± 11.3	48.7 ± 10.9	0.694
Mean duration of symptoms (years)	6.7 ± 5.1	8.5 ± 6.1	10 ± 8.2	0.238
Mean BMI (kg/m ²)	30.6 ± 6.2	33.1 ± 6.1	33.5 ± 5.6	0.192
Mean AHI values	10.6 ± 2.7	23.3 ± 4.4	69.2 ± 26.8	<0.001
Mean ESS score	8.3 ± 3.4	12.1 ± 3.8	12.7 ± 5.5	0.002
Mean MoCA score	27.1 ± 2.8	25 ± 2.4	24.2 ± 2.6	<0.001
Number of patients with cognitive impairment (n, %)	4 (7.1%)	17 (30.4%)	35 (62.5%)	0.001
Number of patients with excessive daytime sleepiness (n, %)	5 (8.9%)	18 (32.1%)	33 (58.9%)	0.007

AHI, apnea-hypopnea index; BMI, body mass index; ESS, Epworth sleepiness scale; MoCA, Montreal cognitive assessment; OSA, obstructive sleep apnea

an association between cognitive impairment and severity of OSA. The study could not find a significant association between ESS and MoCA score. This is the secondary outcome of the study.

This study had more patients with severe OSA, similar to the study by Chen et al.¹² This study was comparable to previous studies in terms of age and sex distribution and showed an increased prevalence of OSA with increasing age. There were more males than females in the study group. Obesity, systemic hypertension, and Type 2 diabetes mellitus were common in the study group and the number of patients with these comorbidities was more in the severe OSA group. The increased number of patients with obesity, systemic hypertension, and diabetes mellitus in this study could be due to the increased prevalence of these conditions among the general population in our part of the state.

In this study, the number of patients with excessive daytime sleepiness, as indicated by an Epworth Sleepiness Score of > 10

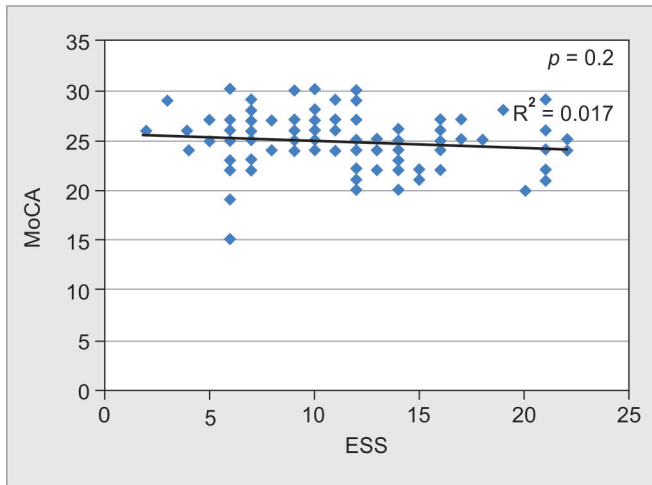


Fig. 2: Correlation between Epworth sleepiness scale (ESS) and Montreal cognitive assessment (MoCA) score

was 56. The number of patients with excessive daytime sleepiness was more in the severe OSA group. This was similar in the study by Chen et al.¹²

Studies conducted previously to assess cognitive impairment in OSA have shown variable results for the prevalence of cognitive impairment. In the case-controlled neuro electrophysiological study by Wen et al.,¹³ the prevalence rates of cognitive impairment using mismatch negativity and Montreal Cognitive Assessment scores were 73.99 and 76.54%, respectively. A total of 127 out of 348 obstructive sleep apnea-hypopnea syndrome (OSAHS) (36.5%) patients were found to have cognitive impairment in the study by Chen et al.¹² In a prospective sleep and cognition study conducted on 298 elder women without dementia, with a mean age of 82.3 years, it was found that 44.8% of women with sleep-disordered breathing developed mild cognitive impairment or dementia after a five year follow up.¹⁴ Kales et al.¹⁵ have found a prevalence of 76% for cognitive impairment in a study on 50 patients with OSA. In a cross-sectional study by Yusop et al.,¹⁶ in moderate and severe OSA patients, using Mini Mental State Examination to assess cognitive impairment, only 5 patients with severe OSA among the total 38 patients in the study had cognitive impairment (prevalence: 13.2%). The prevalence rate of cognitive impairment obtained from our study (58.3%) was intermediate between that obtained from other studies that were conducted previously. Both the studies by Chen et al.¹² and Wen et al.¹³ assessed and analyzed the various MoCA subdomain scores. But this was not done in our study. Similar to other studies, the mean MoCA score of the severe OSA group in our study was indicative of cognitive impairment.

The number of patients with cognitive impairment was found to be the highest in the severe OSA group. This may be due to the fact that mean AHI scores and mean ESS scores were higher in the severe OSA group, indicating the severity of OSA and also increased daytime sleepiness both of which can contribute to the cognitive impairment. It is also important to note that out of 4 patients who reported a history of automobile accidents, 3 were in the severe OSA group. Though studies by Chen et al.¹² and Yusop et al.¹⁶ showed that patients with increased severity of OSA had cognitive impairment, a statistical correlation was not obtained in these studies between severity of OSA and cognitive impairment.

Strength of the Study

- Very few similar studies assessing the prevalence of cognitive impairment in OSA are available.
- Montreal Cognitive Assessment is an easy-to-use tool and less time consuming to assess cognitive impairment.

Limitations of the Study

- Follow-up of the patients and reassessment of their cognitive function after a period of CPAP use was not done, which would have been helpful in assessing the improvement with CPAP use.
- Assessment of various subdomains of cognitive function, as done in many previous studies, was not done.

CONCLUSION

OSA is an important health condition but early recognition and treatment of this problem seldom happen. One of the important health implications of OSA is the impairment of cognitive function. It becomes very important for the early detection and treatment of OSA and assessment of cognitive impairment in patients suspected of having OSA. The prevalence of cognitive impairment in our study is 58.3%, and it was found to be associated with the severity of OSA. It is recommended that cognitive impairment should be assessed in patients with moderate to severe OSA and in those with significant excessive daytime sleepiness.

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