

Study of Obstructive Sleep Apnea in Acute Ischemic Stroke Patients

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ABSTRACT

Context: The study was done to assess the impact of obstructive sleep apnea (OSA) on acute ischemic stroke.

Aims and objectives: To see the prevalence and severity of obstructive sleep apnea in patients with acute ischemic stroke in Rajasthan, to identify patients with acute ischemic stroke who should be screened for OSA, and to compare short-term neurological and functional outcomes in stroke patients with and without OSA.

Settings and design: This is a prospective analytical study of 50 patients with acute ischemic stroke.

Materials and methods: National Institute of Health Stroke Scale (NIHSS) and modified Rankin scale (mRS) scores were calculated at admission. After 10 days, all patients underwent minimum 4 hours of polysomnography. OSA was diagnosed when apneas hypopneas index (AHI) is more than 5 per hour. NIHSS scoring was done at discharge, and mRS scoring was done after 1 month.

Statistical analysis used: Categorical variables were compared using the χ^2 test and numerical variables using the *t*-test for independent samples. Statistical significance was set at 5%.

Results: The prevalence of OSA was 36%. Obesity and high Epworth sleepiness scale were predictors of OSA. The distribution of stroke topography was similar in OSA and non-OSA groups. NIHSS and mRS were comparable in OSA and non-OSA groups. Difference in recovery of NIHSS was significant between OSA and non-OSA groups (1.16 and 2, respectively, *p*-value: 0.0017). There was a statistically significant difference in mRS at 1 month between OSA and non-OSA groups (2.88 and 2.53, respectively, *p*-value: 0.02).

Conclusions: As poor neurological recovery during the hospital stay and poor functional recovery at 1 month in patients with acute ischemic stroke with OSA were found, our study highlights screening of OSA particularly for obese patients and patients with high Epworth sleepiness scale.

Keywords: Acute ischemic stroke, Modified Rankin scale, Obstructive sleep apnea.

Indian Journal of Sleep Medicine (2020): 10.5005/jp-journals-10069-0060

INTRODUCTION

Stroke is the third most common cause of death in the world after ischemic heart disease and all types of cancer combined. It is often a crippling disease, and it poses a major socioeconomic challenge in the occupational and neurorehabilitation programs of the "stroke survivors."

In India, the prevalence rates (or estimates) for completed strokes for different zones are 143/100,000 persons for North India (Kashmir), 245/100,000 for West India (Mumbai), 64/100,000 for South India (Vellore), and 270/100,000 for East India (Assam). Studies have shown that the incidence of stroke rises with advancing age, the maximum being in the age band of 41–70 years.¹

Identification and active modification of risk factors, as well as progress in acute stroke care, underlie the improvements in stroke statistics. Modifiable risk factors such as high blood pressure, hyperlipidemia, diabetes, smoking, physical inactivity, and unhealthy diet are responsible for 90% of the risk of stroke. However, stroke incidence has not dropped significantly in young adults and is still soaring in low- and middle-income countries. Insufficient modification of the established risk factors, or the ongoing effects of under-recognized risks, might explain the high global burden of stroke. Recently, the role of sleep pathology in the development of cardiovascular and metabolic diseases has been highlighted by experimental and observational studies.² It has been shown that obstructive sleep apnea (OSA) is a risk factor for stroke and an independent predictor of outcome in terms of functional recovery and mortality.³

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How to cite this article: Shah VS, Sardana V. Study of Obstructive Sleep Apnea in Acute Ischemic Stroke Patients. *Indian J Sleep Med* 2020;15(4):60–64.

Source of support: Nil

Conflict of interest: None

Obstructive sleep apnea, a common breathing disorder, is characterized by recurrent episodes of airway collapse, resulting in occlusion of airflow during sleep. These episodes of hypopnea and apnea can manifest as transient or prolonged hypoxemia, sleep arousals, and sympathetic nervous system activation, resulting in symptoms, such as snoring, headaches, daytime sleepiness, and impaired alertness.⁴ Several pathophysiologic changes occur in OSA that contribute to stroke, including repeated episodes of hypoxia, resulting in increased negative thoracic pressure with the remodeling of the atria and the development of abnormal electric conduction, presenting as atrial fibrillation. The oxidative stress of intermittent hypoxia activates the sympathetic nervous system and renin–angiotensin–aldosterone system, resulting in hypertension and increased plasma fibrinogen levels and platelet activity, creating a state of hypercoagulability. OSA also

induces inflammation, which contributes to atherosclerosis and hypertension commonly present in stroke. Hypertension and chronic bouts of hypoxia and hypercapnia associated with OSA may also remodel systemic and cerebral vasculature and impair cerebral autoregulation.⁵

Some studies have demonstrated that patients with stroke and OSA have an increased risk of poor functional outcome and mortality compared to patients with stroke without OSA. OSA is easily modifiable; the diagnosis is simple, and the treatment is straightforward.² A study of patients with acute ischemic stroke demonstrated that obstructive sleep apnea persisted despite a neurologic recovery, suggesting that the obstructive sleep apnea syndrome may have predated the development of stroke.⁶ These characteristics make OSA an ideal target for interventions aimed to reduce the cerebrovascular disease burden.

We conducted this study to see the prevalence and severity of obstructive sleep apnea in patients with acute ischemic stroke in Rajasthan, to identify patients with acute ischemic stroke who should be screened for OSA, and to compare short-term neurological and functional outcomes in stroke patients with and without OSA.

MATERIALS AND METHODS

This was a prospective analytical study conducted for a period of 1 year from April 2019 to March 2020 after getting ethical committee clearance.

The study population was 50 patients with acute ischemic stroke with age between 20 years and 85 years admitted to the hospital. Patients with serious psychiatric diseases, a known preexisting sleep disorder (patients who were under treatment or had a diagnosis of a sleep disorder, at the time of admission), increased psychomotor agitation, history of chronic respiratory disease, and New York Heart Association (NYHA) class III–IV congestive cardiac failure were excluded from the study. Comatose patients were also not included in the study. On admission, patients were assessed by physical examination and neurological examination. Diagnosis of ischemic stroke was made based on a history of sudden onset of weakness after ruling out hypoglycemia. Hemorrhagic stroke was ruled out by CT brain imaging. Ischemic stroke severity was decided by National Institute of Health Stroke Scale (NIHSS) scoring at admission. NIHSS was further graded as mild (NIHSS ≤ 5), moderate (NIHSS 6–15), and severe (NIHSS 16–25). Patients with very severe stroke with NIHSS ≥ 25 were excluded from the study. Functional status was decided by modified Rankin scale (mRS) scoring at admission. Admission sugar levels were taken and considered high if >180 mg/dL. MRI imaging with MR/CT angiogram was done for all patients and accordingly classified as per the TOAST classification. The patients were also classified according to the stroke topography into the following groups: cortical stroke, subcortical stroke, brainstem stroke, cerebellar stroke, or multiple sites involved. Data were collected from all patients on demographic, clinical (age, sex, sleep history, and Epworth sleepiness scale self-reports of their status before the acute stroke), anthropometric (body mass index in kg/m^2), and other risk factors, including arterial hypertension, hypercholesterolemia, diabetes mellitus, smoking status (Yes/No), and alcohol consumption (Yes/No).

After 10 days of hospital stay, patients were assessed again. Patients who developed sepsis required oxygen supplementation and/or ventilatory support during the hospital stay, persistent deranged creatinine >1.2 after 10 days, and who remained in

altered sensorium after 10 days of hospital stay were excluded from the study. Those patients who pass the acute phase of the neurological event and fulfill all exclusion criteria underwent polysomnography (PSG) after 10 days of hospital stay. According to a review of sleep-related breathing and sleep–wake disturbances in ischemic stroke, breathing abnormalities are exacerbated by an acute ischemic stroke, which recovers in the subacute stroke phase; hence, a PSG done during acute stage may not reflect the preexisting sleep disorder nor the sleep disorder prevalent in the long term. Minimum 4 hours of polysomnography was considered as adequate. Polysomnography was done using two channels each for electroencephalography (EEG); electromyography (EMG); and electrooculography (EOG); airflow recording through the nose by thermistor; thoracic and abdominal efforts by plethysmography; and oxygen saturation through pulse oximetry. OSA was diagnosed when apneas hypopneas index (AHI) is more than 5 per hour. OSA was further classified as mild, moderate, or severe based on AHI corresponding to 5–15/h, 15–30/h, and >30 /h, respectively. The diagnosis was based on the criteria laid down in the AASM Manual for the Scoring of Sleep and Associated Events.⁷

NIHSS scaling was done at discharge. Patients were called for follow-up after 1 month when short-term disability was assessed by mRS. According to mRS, patients were further categorized into dependent (mRS ≥ 3) and independent (mRS ≤ 2).

All the data obtained were recorded systematically and analyzed using standardized statistical methods. Categorical variables were compared using the χ^2 test and numerical variables using the *t*-test for independent samples. Statistical significance was set at 5% (corresponding to *p*-value less than 0.05).

RESULTS

The prevalence of OSA was 36%. Out of 50 patients, 18 patients were found to have OSA. Baseline characteristics of patients with and without OSA were compared. The mean age of patients with and without OSA was 60.5 ± 8.1 years and 65.7 ± 6.97 years, respectively. The mean body mass index (BMI) was 26.7 ± 2.5 and 30.6 ± 2.69 , and the mean Epworth sleepiness scale was 2.28 ± 0.943 and 5 ± 1.45 , respectively, in OSA and non-OSA groups. In the non-OSA group, 68.8% were males and 31.2% were females, 65.6% had hypertension, 37.5% had diabetes mellitus, 46.9% smoker, 25% alcoholics, 50% tobacco chewer, 28.1% had dyslipidemia, and 31.2% had ischemic heart disease. Similarly, in the OSA group, 83.3% were males and 16.7% were females, 77.8% had hypertension, 50% had diabetes mellitus, 50% smoker, 16.7% alcoholics, 55.6% tobacco chewer, 44.4% had dyslipidemia, and 33.3% had ischemic heart disease. Differences in age, BMI, and Epworth sleepiness scale were found to be statistically significant (*p*-value < 0.05). All the risk factors were found to be nonsignificant (*p*-value > 0.05) (Table 1).

The distribution of stroke topography was similar in both groups. Majority of the patients had cortical stroke (33.3% in OSA and 37.5% in non-OSA), followed by subcortical stroke (27.7% in OSA and 28.1% in non-OSA), brainstem stroke (16.7% in non-OSA and 18.7% in OSA), multiple sites (11.1% in OSA and 9.3% in non-OSA), and cerebellar stroke (5.5% in OSA and 6.25% in non-OSA) (Table 2). The presence of OSA had no relation to stroke topography (*p*-value > 0.05). Similarly, there was a statistically nonsignificant difference in stroke subtype in both OSA and non-OSA patients as per the TOAST classification. In both OSA and non-OSA patients,

Table 1: Comparison of baseline characteristics of stroke patients with and without OSA

	Non-OSA (N = 32)	OSA (N = 18)	p-value
Age	60.5 ± 8.1	65.7 ± 6.97	0.0267
BMI	26.7 ± 2.5	30.6 ± 2.69	0.0001
Epworth sleepiness scale	2.28 ± 0.943	5 ± 1.45	0.0001
Gender			
Male	22 (68.8%)	15 (83.3%)	0.2540
Female	10 (31.2%)	4 (16.7%)	0.2482
Risk factors of stroke			
Hypertension	21 (65.6%)	14 (77.8%)	0.2819
DM	12 (37.5%)	9 (50%)	0.3033
Smoking	15 (46.9%)	9 (50%)	0.9222
Alcohol	8 (25%)	4 (16.7%)	0.505
Tobacco	16 (50%)	10 (55.6%)	0.8743
Dyslipidemia	9 (28.1%)	8 (44.4%)	0.3933
IHD	10 (31.2%)	6 (33.3%)	0.9913

BMI, body mass index; DM, diabetes mellitus; IHD, ischemic heart disease; OSA, obstructive sleep apnea

Table 2: Obstructive sleep apnea (OSA) and stroke topography

Topography	Non-OSA	OSA	p-value
Brainstem	6 (18.7%)	4 (16.7%)	0.7655
Cerebellar	2 (6.25%)	1 (5.5%)	0.9843
Cortical	12 (37.5%)	6 (33.3%)	0.7786
Multiple sites	3 (9.3%)	2 (11.11%)	0.7590
Subcortical	9 (28.1%)	5 (27.7%)	0.9011

small vessel disease (44.4%; 31.2%), followed by large artery atherosclerosis (33.33%; 31.2%), was a common type of stroke. The severity of OSA also had no relation to the topography or subtype of stroke.

Patients were almost equally distributed in mild, moderate, and severe NIHSS groups in both OSA and non-OSA groups (mild NIHSS—18.66 and 18.75%, respectively, moderate NIHSS—72.22 and 71.88%, respectively, and severe NIHSS—11.11 and 9.38%, respectively). There was no statistical difference in mean NIHSS at admission between OSA and non-OSA groups (9.77 and 9.25, respectively, *p*-value: 0.62). Similarly, the difference in mean NIHSS at discharge was also nonsignificant between OSA and non-OSA groups (8.61 and 7.25, respectively, *p*-value: 0.14). However, difference in recovery of NIHSS was significant between OSA and non-OSA groups (1.16 and 2, respectively, *p*-value: 0.0017). Neurological recovery during hospital stay was significantly better in the non-OSA group compared to the OSA group. While comparing NIHSS recovery between the severity of OSA and non-OSA groups, we found that difference was statistically significant between mild OSA group and non-OSA groups, and moderate OSA group and non-OSA groups, but the difference was nonsignificant between severe OSA and non-OSA groups (Fig. 1).

The difference in mean mRS at admission between OSA and the non-OSA groups was nonsignificant (3.22 and 3.06, respectively, *p*-value: 0.58), but there was a statistically significant difference in mRS at 1 month between OSA and non-OSA groups (2.88 and 2.53, respectively, *p*-value: 0.02). While comparing mRS at 1 month

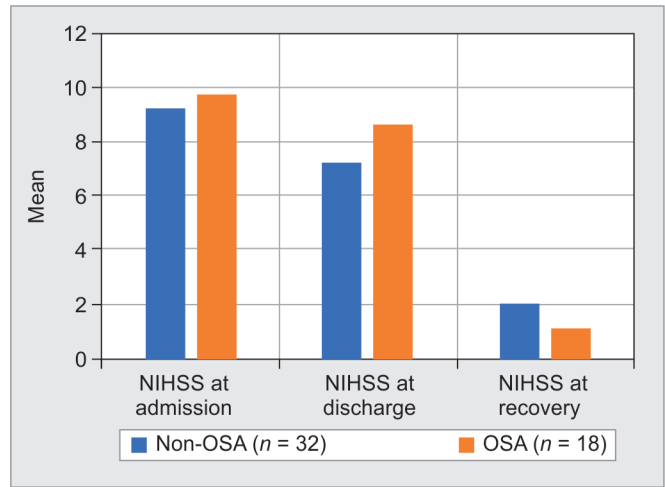


Fig. 1: Comparison of stroke severity between obstructive sleep apnea (OSA) and non-OSA patients. NIHSS, National Institute of Health Stroke Scale

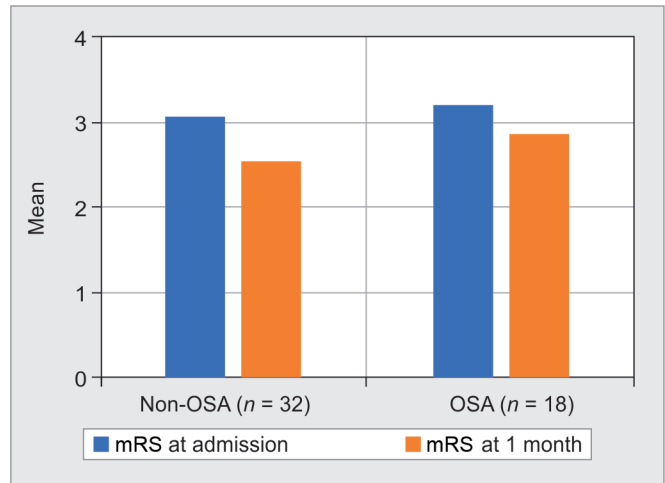


Fig. 2: Comparison of stroke disability between obstructive sleep apnea (OSA) and non-OSA patients. mRS, modified Rankin scale

between the severity of OSA and non-OSA groups, we found that difference was statistically significant between severe OSA and non-OSA groups (*p*-value: 0.01) (Fig. 2). We found that chances of developing dependency for the activity of daily living at 1 month (mRS ≥ 3) after stroke were 2.72 times higher in OSA patients compared to non-OSA patients; however, this difference was statistically not significant in this study; hence, OSA was not found to be an independent predictor of dependency at 1 month after acute ischemic stroke.

DISCUSSION

The prevalence of OSA in the stroke population is variable, ranging from 30% to as high as 80% in various studies, whereas in the general population, sleep-disordered breathing including OSA ranges from 8 to 57% in men and 9 to 35% in women.³ However, in our study, the prevalence of OSA was found to be 36% in stroke patients. A good correlation was noted between the Epworth

sleepiness scale and subsequent diagnosis of OSA, which signifies preexistent undiagnosed OSA rather than stroke contributing to OSA. We also found that advancing age and BMI were predictors of OSA. McKee and Auckley reviewed that obesity is one of the strongest risk factors, with increasing BMI associated with increased OSA prevalence.⁸

In our study, we found that the prevalence of OSA was high in males (83.3%) as compared to females (16.7%). Koo et al.² also reviewed that prevalence of moderate-to-severe OSA in the adult general population was 9 to 14% in men and 4 to 7% in women, increasing with age and even higher in a recent study (49.7% in men and 23.4% in women) by Heinzer et al.⁹ Yaranov et al.¹⁰ also found that percentage of men was higher among patients with OSA compared with those without OSA (73.1 and 59.2%, respectively).

We found that the prevalence of risk factors for stroke in patients with OSA was higher as compared to patients without OSA but none of the risk factors had a statistically significant impact.

We found that there was a statistically nonsignificant difference in stroke subtype and stroke topography between OSA and Non-OSA patients, and even, OSA severity had no relation with stroke subtype. Brown et al.¹¹ also found no association with the TOAST subtype of strokes and OSA grades. A second study¹² on 90 subjects suggested that the large artery atherosclerosis subtype was more common in subjects with an AHI ≥ 30 than in those with an AHI < 10 . Menon et al. found no relation between the presence of OSA with stroke subtype or infarct location and vice versa. Given that OSA has multiple potential mechanisms by which it can increase the stroke risk, it is not surprising that there is no differential impact of the presence of OSA favoring specific stroke subtypes.¹³

In our study, patients were equally distributed between mild, moderate, and severe NIHSS groups in both OSA and non-OSA groups. The difference in mean NIHSS at admission between both groups was nonsignificant. Hence, we can say that OSA had no impact on stroke severity, but this result should be considered with caution as patients with NIHSS > 25 were excluded from the study. We did not find any difference in mean NIHSS at discharge between OSA and non-OSA groups, but the difference was significant in the recovery of mean NIHSS score between OSA and non-OSA groups, particularly for mild and moderate OSA patients. Hence, in this study, we found that OSA delays short-term neurological recovery during the hospital stay. However, we did not measure NIHSS at 1-month follow-up, which would have given us more information on the neurological recovery trend between both groups. The insignificant difference in NIHSS score recovery between non-OSA and severe OSA groups can be due to a smaller number of patients (N=4) of severe OSA. Similarly, Menon et al.¹³ also found a significant difference in the recovery of NIHSS score during hospital stay between OSA and non-OSA groups.

The difference in admission mRS was not significant between OSA and non-OSA groups, which can be interpreted as OSA does not affect the functional status at the onset of acute ischemic stroke. However, a statistically significant difference in mean mRS at 1 month among OSA and non-OSA patients signifies the impact of OSA on functional status at 1 month after acute ischemic stroke. Mean mRS was significantly high in the severe OSA group compared to the non-OSA group at 1 month. In conclusion, severe OSA patients had a significantly lesser amount of short-term functional recovery at 1 month compared to those

without OSA. Menon et al.¹³ also found similar results, and results were significant even with ranks of mRS. However, in our study, when the test was repeated with ranks of mRS score at 1 month, the number of OSA patients with severe stroke disability (mRS 4) was high in number compared to non-OSA patients, but the difference was statistically nonsignificant (p -value: 0.09). These findings can be explained by a relatively smaller number of patients in our study.

In our study, we found dependency at 1 month in patients having OSA was 2.72 times more compared to non-OSA patients (odds ratio of 2.7222). After multivariate analysis, we found that none of the risk factors was an independent predictor of dependency status at 1 month. However, risk factors with high odds ratio were BMI (OR = 1.207), hypertension (OR = 1.2215), diabetes mellitus (OR = 1.9141), smoking (OR = 1.7046), alcohol (OR = 1.3384), tobacco (OR = 2.6757), dyslipidemia (OR = 2.9712), IHD (OR = 1.2286), and hyperglycemia at admission (OR = 1.04501) predicting the high likelihood of dependency at 1 month. Menon et al. found that advancing age, absence of hyperlipidemia, AF, stroke subtype (cardioembolic), and presence of OSA were found to have a probable association with outcome.¹³

In conclusion, we found the prevalence of obstructive sleep apnea of 36% in patients with acute ischemic stroke. BMI and Epworth sleepiness scale were found to be good predictors of OSA. This study highlights the poor neurological recovery during the hospital stay and poor functional recovery at 1 month in patients with acute ischemic stroke with obstructive sleep apnea. Considering OSA, a modifiable risk factor of acute ischemic stroke, with high prevalence and its strong impact on recovery found in our study, highlights the importance of screening for OSA. The subset of acute ischemic stroke patients with moderate-to-severe obesity and high Epworth sleepiness scale should definitely be screened for OSA, and OSA should be included in primary risk factors of stroke along with hypertension, diabetes mellitus, obesity, smoking, etc.

The sample size was the main limitation in our study as many of the patients after stroke were not tolerating overnight polysomnography. Another limitation was the absence of long-term follow-up at 3 months. Long-term follow-up would have given us a clearer picture of post-stroke disability in patients with and without OSA.

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