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Impact of Obstructive Sleep Apnea on Neurological Recovery after Ischemic Stroke: A Prospective Study

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ABSTRACT

Objectives: In this investigation, the prevalence, clinical features, and impact of obstructive sleep apnea (OSA) on the prognosis of acute ischemic stroke patients were examined. **Study design:** Prospective Study. **Settings:** Department of Neurology, Shifa International Hospital, Islamabad. **Study Duration:** February 2025 to April 2025. **Methods:** Forty-nine patients with acute ischemic stroke were included. Lab findings, demographic data, and PSG features were collected. The modified Rankin Scale (mRS) was used to quantify the functional result, and the National Institutes of Health Stroke Scale (NIHSS) was utilized to gauge the extent of the initial neurologic loss. An poor prognosis was defined as an mRS ≥3 three months after the onset of acute ischemic stroke. Multivariate logistic regression was employed to assess the correlation between OSA severity and functional outcome. **Results:** OSA [apnea-hypopnea index (AHI)≥5/h] was present in 43 (87.8%) of the 49 patients who suffered an acute ischemic stroke. Of the patients, 13 (26.5%) had severe OSA, 16 (32.7%) had moderate OSA, and 14 (28.6%) had mild OSA. OSA-related factors, such as oxygen desaturation index (ODI) and AHI, were linked to poor clinical outcomes three months after stroke (mRS ≥3), according to univariate logistic regression. After controlling for age and initial NIHSS, multivariate logistic regression analysis showed that a rise in AHI and ODI was linked to a poor functional outcome three months following a stroke. **Conclusions:** Poor functional outcomes are linked to OSA in patients who have had an acute ischemic stroke.

INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep breathing disorder that affects 3–7% of general adult males and 2–5% of adult females. It is characterized by frequent awakenings and hypoxemia as a result of repetitive obstruction of the upper airway during sleep.[1] Untreated, it can interfere with regular sleep cycles and result in a number of symptoms during the day and night, such as snoring, sleep apnea, and excessive daytime drowsiness. It can also raise the risk of developing diabetes, high blood pressure, erectile dysfunction, depression, heart disease, stroke, and cognitive impairment.[2,3]

OSA and stroke are strongly associated, and a research by Hermann et al. found that the prevalence of sleep breathing difficulties in stroke patients is significantly higher than that of the general population, which is between 50 and 70 percent.[4] Prior large-scale prospective investigations have also shown that OSA plays a significant role in stroke development.[5,6] Atherosclerosis, vascular endothelial dysfunction, metabolic syndrome, obesity, low physical activity, high intracranial pressure, atherosclerosis, cardiac arrhythmias, embolism through open oval holes, inflammation, hypercoagulation, and low cerebral blood flow are some of the factors that have been linked to stroke in OSA patients.[7-10] It has also been demonstrated to negatively impact stroke prognosis when OSA is present, however this is primarily based on mortality.[11-13] The majority of studies examining how OSA affects functional recovery in stroke patients use on oximetry data or questionnaires, and there are issues with the precision of OSA diagnosis.[14,15] Polysomnography studies yield varying results. Although it is advised that stroke patients undergo sleep testing and treatment to identify OSA, active testing has not yet been carried out in real-world clinical settings.[16,17]

Thus, we want to employ polysomnography to detect OSA in stroke patients and look into how OSA impacts neurological and functional recovery. This will serve as proof that universal sleep testing is necessary going forward to detect OSA in stroke patients.

MATERIALS AND METHODS

Preliminary and prospective observational, this study was carried out at a single institution on patients with acute ischemic stroke who were admitted between February 2025 and April 2025 to the Department of Neurology at Shifa International Hospital in Islamabad. Acute patients

who arrived at the hospital within a week of the onset of neurological symptoms and were diagnosed with ischemic stroke using magnetic resonance imaging with diffusion-stressed imaging were included in the study. Situations in which follow-up observation was not conducted, patient data, including polysomnography, was inadequate, and formal informed consent was not obtained. The Institutional Review Board gave this study its approval (IRB).

Polysomnography

Under the supervision of a Level 3 sleep technologist, the polysomnography utilized in this study was conducted at night in the patient's bed using a mobile device called the Embletta MPR. The apparatus has sensors for posture, oxygen saturation, pulse, and airflow through the nose, chest, and abdominal girdle to gauge breathing exertion. To be eligible for the study, participants had to sleep for at least four hours, and screening had to be finished within 30 days of the stroke (median 7 days, range 2~30 days). An experienced sleep technician examined the items kept in the Embletta MPR.

Hypopnea was defined as a decrease in oxygen saturation of 3% or more and a decrease in the amplitude of breathing volume of more than 30% for more than 10 seconds. For more than ten seconds, a drop in breathing of more than 90% while maintaining respiratory effort was considered apnea. The number of apnea and hypopnea episodes per hour of sleep was found to be the apnea-hypopnea index (AHI). If the AHI, a gauge of the severity of the ailment, was 5 or higher, apnea was diagnosed. They were split into two groups: moderate OSA (15≤AHI<30/h), normal (AHI<5/h), mild OSA (5≤AHI<15/h), and depth OSA (AHI≥30/h). They were also split into two groups: deep OSA (AHI≥30/h) and control (AHI<30/h). The oxygen desaturation index (ODI) was defined as the frequency of drops in oxygen desaturation of greater than 3% per hour.

Demographic Characteristics, Stroke Severity and Prognosis Assessment

The gender, age, height, and weight of stroke patients were analyzed based on their medical records, and data on stroke risk factors, including DM, HTN, dyslipidemia, IHD, and smoking status, were gathered. In addition to the findings of blood tests such as hemoglobin, white blood cell count, the body mass index (BMI) was calculated using height and weight.

The severity of the stroke was assessed at admission using the National Institutes of Health Stroke Scale (NIHSS), and three months after the stroke started, the prognosis was assessed using the modified Rankin Scale (mRS). If the mRS was ≥3, the prognosis was considered poor.

Analytics

For all statistical studies, SPSS software version 22 was used. For categorical data, the representative value is shown as a number (fraction). For continuous variables, it is shown as the median (interquartile range). We used the Mann-Whitney test to look at continuous variables that don't follow the normal distribution. We used Fisher's exact test to look at the category data. We used binary logistic regression analysis to look at how the severity of OSA affects the prognosis of stroke. We looked at AHI and ODI as separate components that show how bad OSA is, and we characterized the dependent variables as having a bad prognosis (mRS ≥3) after three months. Furthermore, there was a strong correlation found between the prognosis of stroke and demographic parameters including age and gender, blood test results, NIHSS at the time of admission, and stroke risk factors such diabetes and hypertension. In order to ascertain whether AHI or ODI demonstrated an independent correlation with prognosis even after adjusting for other variables that might influence the prognosis of stroke, we first used univariate analysis to identify variables that had a significant correlation with poor prognosis after three months with $p<0.05$. Then, we included these variables in the multivariate analysis. Due to the substantial connection between AHI and ODI, which are both indicators of OSA severity ($rs=0.932$, b11>$p<0.001$, spearman correlation), multivariate analysis was conducted independently for both variables, and all variable input methods were used. Every analysis was deemed significant if the p value was less than 0.05.

RESULTS

Forty (81.6%) of the 49 patients who were targeted were male, nine (18.4%) were female, and forty-three (81.8%) were OSA (AHI≥5/h) patients. The subjects were classified as follows: 6 (12.2%) had normal OSA, 14 (28.6%) had mild OSA, 16 (32.7%) had moderate OSA, and 13 (26.5%) had profound OSA. The subjects' AHI was 19.6 (8.7~30.5) and their ODI was 16.0 (8.35~29.8). The frequency of mRS was considerably greater and the frequency of mRS ≥3 was higher after three months in deep OSA compared to the control group (Table 1). After three months, patients with profound OSA had a higher mRS ($p=0.002$) than those with normal, after post-hoc testing and the Bonferroni method was applied.

According to univariate analysis, a poor prognosis (mRS ≥3) at three months was strongly correlated with the severity of OSA. Additionally, mRS and early NIHSS and age [$p=0.027$] were significantly correlated. There was no significant correlation between sex, BMI, blood tests, or other stroke risk factors and a poor prognosis (mRS ≥3) (Table 2).

The independent connection between each OSA characteristic and stroke prognosis was subsequently evaluated using multivariate analysis. AHI or ODI were used as independent variables in two multivariate analyses, and factors that demonstrated a significant correlation with mRS ($p<0.05$) were incorporated into the statistical model. An increase in AHI [adjusted OR (AOR), 1.079 (95% CI, 1.007 to 1.156), <b11>$p = 0.031$] or a higher ODI [AOR, 1.095 (95% CI, 1.020 to 1.174), $p = 0.011$] was substantially linked to a poor prognosis of stroke (mRS ≥ 3), even after controlling for age and early NIHSS. Although age was less significant in multivariate analysis, the initial NIHSS also revealed a significant correlation (Table 3).

Table 1
Distribution of variables

	No or non-severe OSA (n=36)	Severe OSA (n=13)	*p-value*
Demographics			
Age (years)	69 ± 6.76	71 ± 7.32	0.408
Male	31 (86.1%)	9 (69.2%)	0.220
BMI (kg/m^2)	24.95 ± 6.43	26.13 ± 5.76	0.321
HTN	18 (50.0%)	9 (69.2%)	0.333
DM	9 (25.0%)	4 (30.8%)	0.723
IHD	4 (11.1%)	1 (7.7%)	1.000
Smoking	17 (47.2%)	5 (38.5%)	0.748
Dyslipidemia	5 (13.9%)	3 (23.1%)	0.422
Laboratory findings			
White blood cell count, /mL	7410 ± 1324	8405 ± 1893	0.721
Hemoglobin, g/dL	14.2 ± 2.54	13.4 ± 2.91	0.372
Clinical findings			
NIHSS at admission	4 ± 2.43	6 ± 5.42	0.106
mRS at 3 months later	1 ± 0.76	3 ± 1.32	0.001
Unfavorable prognosis (mRS ≥3) at 3 months later (%)	7 (19.4%)	10 (76.9%)	<0.001

OSA: obstructive sleep apnea, NIHSS: National Institutes of Health Stroke Scale, mRS: modified Rankin Scale

Table 2
Three-month prognosis following stroke using a univariate logistic regression model (modified Ranking Scale ≥3)

	OR	95% CI		*P*
		Lower endpoint	Upper endpoint	
Demographics				
Age (years)	1.065	1.007	1.125	0.027
Male (%)	0.343	0.078	1.504	0.156
BMI (kg/m^2)	0.951	0.800	1.131	0.572
HTN	0.875	0.269	2.850	0.825
DM	1.250	0.336	4.655	0.739
IHD	0.438	0.045	4.259	0.476
Smoking	0.793	0.241	2.607	0.703
Dyslipidemia	2.154	0.464	9.988	0.327
Laboratory findings				
White blood cell count, /mL	1.000	1.000	1.000	0.333
Hemoglobin, g/dL	0.807	0.588	1.109	0.186
Clinical findings				
NIHSS at admission	1.249	1.095	1.426	0.001

Table 3
Three-month prognosis following stroke using a multivariable logistic regression model (modified Ranking Scale ≥3)

	AOR	95% CI		p
		Lower endpoint	Upper endpoint	
Age, years	1.068	0.990	1.152	0.090
NIHSS at admission	1.282	1.079	1.522	0.005
Oxygen desaturation index, /h	1.095	1.020	1.174	0.011
Age, years	1.085	0.999	1.179	0.053
NIHSS at admission	1.321	1.092	1.596	0.004

DISCUSSION

One significant risk factor for the onset of stroke is obstructive sleep apnea. The main goal of earlier research was to demonstrate that OSA is a comorbid disease that influences the course of a cerebrovascular event. Little is known about how it contributes to the emergence of possible problems after a stroke. The prevalence and clinical features of obstructive sleep apnea (OSA) in patients with acute ischemic stroke were examined in this study, as well as the impact of OSA on the prognosis of acute ischemic stroke. According to our findings, people with OSA and stroke have a marginally higher risk of post-stroke sequelae, but those who have severe stroke have a considerably higher risk. In these investigations, death, depression, and cognitive impairment were the most common results.

Seven studies found that cognitive impairment was the most common thing that happened to those with obstructive sleep apnea after a stroke. Sleep apnea is a major cause of hypoxia-induced effects, even though other things like heart problems, insomnia, and genetic predisposition can make these neuropsychiatric effects more complicated, especially in stroke patients.[18,19] Zhu et al. employed the apnea–hypopnea index (AHI) to quantify OSA and found that higher AHI scores were strongly linked to cognitive deterioration. This was also linked to the lower oxygen saturation (SpO2) levels found in those with OSA compared to those without it.[12]

Previous studies have shown that episodes of apnea-hypopnea induce a state of persistent intermittent hypoxia, which causes oxidative stress and neuroinflammation in the body, which in turn leads to cognitive decline.[20,21] Bubu et al. also showed that obstructive sleep apnea makes tau and amyloid beta peptide (Aβ) build up faster in a roundabout way. When you think about the long-term repercussions of having had obstructive sleep apnea before a stroke, you should keep this in mind.[22] Kang et al. did a hospital-based study that showed that the presence of Aβ deposits started the process of cognitive impairment after a stroke. After a year, they observed that having Aβ positive meant that cognitive decline after a stroke was worse.[23] Our study's results demonstrate that early OSA screening is important so that patients can start receiving continuous positive airway pressure (CPAP) therapy, which has been found to improve symptoms, reduce severity, and improve neurocognition in CVA patients.[24,25]

Li et al. looked into the relationship between OSA and post-stroke depression (PSD) in a hospital-based study. The AHI and oxygen desaturation index (ODI) were used to measure the severity of OSA, and the Chinese Structured Clinical Interview and the Hamilton Depression Scale (HAMD) were used to assess the association between OSA and post-stroke depression. They found that the development of PSD was correlated with the severity of OSA.[8]

Our study during the literature review showed that there were very few studies that looked at this association. Earlier research examined a number of processes that contribute to the development of depression after a stroke.[26,27] There are always changes in the speed of blood flow to the brain during each apnea–hypopnea episode in OSA. Chronic hypoperfusion speeds up the development of cerebral small-vessel disease. This is because it causes hypoxemic–ischemic injury, damages the endothelium, stops the production of vasodilators like nitric oxide (NO), and damages the blood–brain barrier and causes neuroinflammation.[26,27] When other stroke-related health

problems are present, these biological and pathophysiological processes may work together to make neuropsychiatric difficulties more likely.

Zhang et al.'s study looked at how OSA and sleep disturbances affected cerebral function and overall mortality following a stroke. According to the results, those with OSA are more likely to die from all causes, particularly if they have severe OSA.[10] Prior research has demonstrated that OSA is independently associated with the development of a number of cardiovascular complications, such as hypertension, atrial fibrillation, coronary heart disease, heart failure, etc., as well as all-cause mortality from a variety of pathophysiological processes, the most notable of which are oxidative stress and autonomic dysregulation.[28-30] These results show that more research is needed to fully understand the links and mechanisms involved. They also show that more evidence is needed to support a better understanding of the link between OSA and problems that happen after a stroke, even though there isn't much data to back up the study's conclusions.

The study's limitations include the use of level 3 mobile polysomnography equipment rather than level 1 conventional polysomnography and the potential reduction in statistical power resulting from the small sample size for this early investigation. Furthermore, the probability of a selection mistake cannot be ruled out because only a portion of stroke patients who consented to polysomnography could be evaluated in this trial, and patients who did not follow up were excluded. Furthermore, it is challenging to conclude that all polysomnograms were carried out during the acute phase since, while they are typically performed seven days after hospitalization, the test period might range from two to thirty days, depending on the patient's state. However, it is anticipated that the results would be more lucid in the future when it is carried out with enough participants, since a prospective study was carried out on patients with acute ischemic stroke and a substantial association was verified despite the small sample size.

CONCLUSION

Particularly in individuals with severe stroke, OSA is a significant comorbidity that can raise the risk of death, cognitive decline, depression, and poor functional outcomes in the post-stroke period. These observational findings require additional research employing large-scale experimental study designs with varied populations, even though the precise processes behind the relationships remain unclear. According to available data, early OSA screening combined with the required interventions will help lower the burden of post-stroke disease, guide future interventions, and enhance recovery and management results.

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