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Association between Obstructive Sleep Apnea and Ischemic Stroke: A Case-Control Study

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ABSTRACT

Previous evidence has suggested an association between obstructive sleep apnea (OSA) and cardiovascular and cerebrovascular conditions. There is, however, little data examining the prevalence and severity of OSA among individuals with ischemic stroke, specifically within Pakistan. **Objectives:** To determine if the prevalence and severity of OSA were significantly higher in individuals with ischemic stroke compared to age and gender matched control participants without a stroke. **Methods:** A case-control study was conducted at Khyber Teaching Hospital. A total of 184 individuals were enrolled in the study. The study consisted of 92 individuals diagnosed with ischemic stroke supported by radiographic evidence and 92 individuals without cerebrovascular disease, all matched for age and sex. Clinical and demographic data were collected using a standard questionnaire. Participants who scored ≥ 3 on the STOP-BANG questionnaire were referred for Type III daytime portable polysomnography testing. **Results:** Participants with ischemic stroke had significantly higher rates of OSA ($AHI \geq 5$) than controls (80.4% in stroke vs 50.0% in controls, $p < 0.0001$). The incidence of severe OSA in stroke participants was 26.1% compared to only 6.5% of control participants. **Conclusions:** Many patients who experience an ischemic stroke also have OSA (Obstructive Sleep Apnea), and OSA increases the risk of having a stroke independent of the actual ischemic stroke. This evidence supports the use of OSA screening and treatment as part of their prevention strategies against future strokes.

INTRODUCTION

Obstructive Sleep Apnea (OSA) is recurrent, mostly under-identified, and very frequent, with an estimated incidence of 936 million adults aged 30 to 69 years worldwide, 425 million of whom have moderate to severe OSA [1]. Recurring episodes of upper airway obstruction occur during sleep in patients with OSA, often associated with intermittent hypoxia, decreased sleep efficiency, and the activation of the SNS [2]. Clinical signs and symptoms associated with OSA include excessive daytime fatigue, witnessed apneas, and the presence of snoring. There has

been increased attention to the relationship between OSA and cardiovascular and cerebral vascular diseases over the last few years [3]. Ischemic stroke constitutes a serious vascular effect of OSA and is typically caused by an obstruction of blood flow to the brain [4]. There are many people globally who suffer from ischemic stroke each year, and over 5 million people die due to ischemic stroke [5]. Stroke is currently ranked as the second leading cause of death globally today and the third leading cause of long-term disability worldwide [6]. In this case, over 87% of all



strokes are classified as ischemic strokes [7]. Understanding modifiable risk factors for ischemic strokes, particularly those due to sleep-disordered breathing or OSA, is essential to early identification, prevention, and intervention of such strokes. Numerous pathophysiological processes, such as systemic inflammation, oxidative stress, endothelial dysfunction, hypercoagulability, and hyperactivity of the sympathetic nervous system, are shared by OSA and ischemic stroke [4]. Reactive oxygen species and pro-inflammatory cytokines are produced in greater quantities when OSA patients experience nocturnal hypoxemia regularly [8]. This can harm the cerebral vasculature and encourage atherosclerosis. Additionally, OSA can exacerbate insulin resistance, hypertension, and atrial fibrillation, all of which are recognized risk factors for stroke [4]. These findings suggest that, concomitant with other traditional cardiovascular comorbidities, OSA can be a risk factor for ischemic stroke. There have been studies that investigated the relationship between OSA and stroke and therefore, people with moderate to severe OSA are at a risk of stroke two to three times higher [9, 10]. The severity of sleep apnoea was significantly correlated with the risk of incident stroke and especially in men, according to the Sleep Heart Health Study [11]. Stroke is one of the most common causes of death and disability in such countries as Pakistan, ischemic stroke being the major part of them [12]. At the same time, OSA is progressively becoming a diagnosis in adults of middle-aged and old age, especially with obesity and metabolic syndrome but is not frequently considered in the regular risk screening assessments of stroke. The overlap of the symptomatology and inaccessibility to a polysomnography can lead to OSA remaining undiagnosed in a considerable proportion of stroke patients, meaning that a second-time prevention may be overlooked. Assessment of the burden and the impact of OSA in populations with stroke is urgently needed based on well-designed and locally relevant research studies. The detection of OSA in patients with ischemic stroke may help in instituting timely interventions with the help of Continuous Positive Airway Pressure (CPAP) therapy, which has been established to reduce recurrent cardiovascular events as well as neurologic outcomes. Despite several international studies showing that there is a greater risk of ischemic stroke amongst patients with OSA, most of these studies have been done among Western populations with little representation of South Asian cohorts.

Additionally, a great deal of the previous research used self-reported sleep adversity or questionnaire-based screening without a confirmatory polysomnography or small non-comparative samples. Pakistan's evidence is

limited, especially that which has used a matched case-control study with standardized diagnostic assessment of OSA. Hence, the current study aimed at assessing the correlation between OSA and ischemic stroke in a matched case-control study (in a hospital environment) with STOP-BANG screening results subjected to objective confirmation of OSA by means of portable polysomnography and assessment of the level of its severity. The research question specifically seeks to identify whether the presence and the severity of OSA are significantly increased in ischemic stroke patients compared with age and sex matched controls who have never had a stroke. This study aims to determine the relationship between obstructive sleep apnea and ischemic stroke, and to additionally determine whether OSA severity is more common in stroke patients than in age- and sex-matched controls.

METHODS

The case-control study was a hospital-based study that was carried out in the Department of Medicine, Khyber Teaching Hospital, Peshawar, between 1st November 2024 and 31st October, 2025. Ethical approval was given by the Institutional Review Board (IRB) of Khyber Medical College, Peshawar, before the commencement of the study, and permission No: 660/DME/KMC. The minimum sample size used was calculated with Open Epi Version 3.01, 95% confidence level, and 80% power, where the frequency of OSA amongst ischemic stroke patients was estimated to be 70%, and the frequency of the expected frequency among the controls was estimated to be 40% [13]. This would give an expected odds ratio of 3.5. Based on these parameters, the size of the required sample was determined to be 92 per group (n=184), which will provide enough power to support a statistically significant correlation between OSA and ischemic stroke. The method used was non-probability sequential sampling. The reason for non-probability sequential sampling was that ischemic stroke patients who fulfilled the eligibility criteria arrived at the hospital at random and unpredictable times, and recruitment was limited to the study period and the availability of polysomnography tests. The design enabled sequential recruitment of all eligible and willing cases and controls, which reduced the investigator's discretion in selection and made it feasible in a hospital-based environment. The study included age- and sex-matched individuals without a 'history of stroke or transient ischemic attack' (TIA) who were recruited from general outpatient departments or accompanying attendants and patients aged 30 to 75 years who had been diagnosed with acute ischemic stroke and confirmed by neuroimaging (CT/MRI) within 7 days of symptom onset. Hemorrhagic stroke history, sleep disorders other than OSA that have

been previously diagnosed, use of sedatives, hypnotics, or alcohol abuse, neurological conditions that interfere with sleep assessment (e.g., dementia, Parkinson's), severe pulmonary diseases (e.g., COPD), and unwillingness or incomplete consent are among the exclusion criteria. Data for this study were collected through a standardized, pre-tested questionnaire along with a clinical assessment. The first step in a standardized data collection method followed by each participant was eligibility testing. A neurologist used neuroimaging techniques (CT or MRI) in the case group to confirm they had been diagnosed with an ischemic stroke. The control group was screened to ensure that all participants had no history of prior cerebrovascular events (i.e., stroke, transient ischemic events). Once participants were determined to be eligible, demographic and clinical data were recorded. Age and sex frequency matching were conducted so that the distribution of these factors was similar between cases and controls, and thus demographic confounding was reduced. The possible confounding factors to ischemic stroke, such as obesity, hypertension, diabetes mellitus, and smoking status, were well evaluated. BMI was calculated with weight and height measured, and obesity was considered to have a BMI at or above 30 kg/m². Hypertension was considered as having been previously diagnosed by a physician, taking antihypertensive medication, or having measured blood pressure 140/90mmHg twice. The definition of diabetes mellitus was a previous diagnosis, on glucose-lowering medication, or on a fasting plasma glucose level of 126mg/dl or higher. Smoking status was identified through a structured interview and was classified as current, former, or never smoker. Informed written consent had been taken before each participant was incorporated into the study, and they were also briefed on the nature, objective, and confidentiality of the research. All participants filled in the STOP-BANG questionnaire, a commonly utilized screening instrument in clinical and research practice to determine the risk of obstructive sleep apnea (OSA) [14]. The participants were all exposed to the STOP-BANG questionnaire, which is a commonly used screening tool in a clinical and research setting to determine the possible existence of OSA. To identify the likelihood of OSA all the participants were exposed to the STOP-BANG questionnaire that is one of the most prevalent screening instruments in clinical and research practice. The respondents who were categorized as STOP-BANG score of 3 and over underwent OSA overnight testing under the assistance of the ResMed ApneaLink Air Type III home sleep apnea testing device (ResMed, Sydney, Australia). It is a handheld device that can measure airflow, respiratory effort, oxygen saturation, pulse rate and snoring to calculate the apnea-hypopnea index. The ApneaLink Air

has been reported to have a sensitivity and specificity of 67 percent and 93 percent, respectively and has been demonstrated in a number of studies to be comparable when compared to in-laboratory polysomnography in terms of their ability to diagnose moderate-to-severe OSA (AHI ≥ 15). The ResMed ApneaLink Air is a level 3 sleep research device that consist of four channels: 1. Heart rate; 2. Oxygen saturation (all of which pulse oximeters can measure); 3. Airflow through a nasal canula pressure transducer; and 4. Respiratory effort through a chest band with a pneumatic sensor. The loan devices were made available to the lenders who could use them at home at night after the devices were demonstrated to them in a clinic. Desaturation index of oxygen (ODI) of sleep and AHI were the sleep measures that were required, and program analysis was done automatically. ODI is the mean of 3 percent of 3 oxygen desaturations above the baseline/baseline in every hour of sleep (in PSG) or recording time (in level 3 or 4 devices). Previous studies have found ApneaLink automatic scoring software, which may have the potential to offer good diagnostic accuracy, compared to concurrent PSG, in a group of a sleep center (AUC, 0.87; standard error, 0.06) [15]. AHI of five or more episodes of apnea-hypopnea in one hour of sleep became the diagnostic criterion of OSA. Based on the known clinical outcomes, OSA ratings included three categories: mild OSA (AHI 514), moderate OSA (AHI 1529), and severe OSA (AHI 30 and above). Data analysis was done with the help of SPSS 26.0. Descriptive statistics were used to calculate the baseline characteristics, which were presented as means and standard deviations (SD) when dealing with continuous data and frequencies and percentages when dealing with categorical data. Continuous variables (age, BMI, and neck circumference) were tested to test the normality of the data to apply the parametric tests using the Shapiro-Wilk test. Variables that have a normal distribution were summarized using means and standard deviations. The cases and controls were compared using an independent t-test of continuous variables and a chi-square test of categorical variables. The presence of multicollinearity among independent variables was checked by variance inflation factors (VIF); it was not detected (VIF less than 2). The stability of the model estimates was investigated by looking at the residuals and influential observations. As frequency matching was performed on age and sex, the two variables were used as covariates in the multivariate binary logistic regression model to remove residual confounding. Multivariate analysis candidate covariates were a priori chosen on the basis of clinical relevance and existing relationships with ischemic stroke and OSA, as published in previous literature. These were age, sex, BMI, high blood pressure,

diabetes mellitus, and smoking. The final adjusted model omitted dyslipidemia and neck circumference since they showed strong collinearity with BMI and hypertension during initial diagnostics (variance inflation factor >2 when added together), and were thus omitted to cause over-adjustment and model instability. The first variable that was analyzed was BMI, which was characterized as a continuous variable. In the main regression model, the BMI was dichotomized based on the level of 30kg/m², which is the WHO-defined obesity level, to ensure consistency with previous OSA-stroke studies. In order to minimize the loss of information and to make it stronger, sensitivity analysis was performed, whereby BMI was received as a continuous variable. Odds ratios (ORs) with their respective 95% confidence intervals (CIs) of the logistic regression models were presented. A p-value of under 0.05 was taken to be statistically significant in all two-tailed statistical tests.

RESULTS

Several significant differences were observed between cases of an ischemic stroke and controls in this research, particularly regarding known vascular risk factors. The results showed that the body mass index (BMI) and the neck circumference of stroke patients are significantly elevated and statistically significant, which suggests that obstructive sleep apnea is likely to be present. The comorbidities of cardiovascular disorders, including diabetes mellitus and hypertension, were also found to be substantially high in cases of stroke, which supports their presence in the cerebrovascular pathology. Also, a higher percentage of stroke patients smoked and were dyslipidemic than the control group, which suggests that the modifiable risk factors are clustering in this population (Table 1).

Table 1: Baseline Characteristics of Study Participants (n=184)

Variables	Cases (n = 92)	Controls (n = 92)	p-value
Age (Years), Mean ± SD	58.4 ± 9.7	56.9 ± 10.1	0.248
Male Gender, n (%)	60 (65.2%)	58 (63.0%)	0.751
BMI (kg/m ²), Mean ± SD	29.3 ± 4.6	27.1 ± 3.9	0.001**
Neck Circumference (cm)	41.2 ± 3.5	38.6 ± 2.9	<0.001**
Hypertension, n (%)	65 (70.7%)	39 (42.4%)	<0.001**
Diabetes Mellitus, n (%)	50 (54.3%)	31 (33.7%)	0.005**
Smoking History, n (%)	34 (37.0%)	21 (22.8%)	0.037*
Dyslipidemia, n (%)	45 (48.9%)	28 (30.4%)	0.011*

The STOP-BANG score distribution showed a distinct statistically significant difference between the ischemic stroke and control groups in the risk categories of OSA. The proportion of the low-risk group in stroke patients (15.2%) was significantly lower than in controls (41.3%), with the proportion of the high-risk category in stroke patients (50.0%) being significantly greater than in controls (26.1%), and the p-value was 0.0001. The percentage of

respondents in the intermediate-risk group was the same in both groups (Table 2).

Table 2: STOP-BANG Score and Risk Category of OSA

STOP-BANG Risk Category	Cases (n = 92)	Controls (n = 92)	p-value
Low Risk (Score 0-2)	14 (15.2%)	38 (41.3%)	0.001
Intermediate (Score 3-4)	32 (34.8%)	30 (32.6%)	
High Risk (Score ≥5)	46 (50.0%)	24 (26.1%)	

Only 19.6% of stroke cases had no OSA (AHI <5), whereas 50.0% of controls fell into this category, indicating a significant disparity (p<0.0001). While the proportion of mild OSA cases was similar between the two groups, moderate and severe OSA were markedly more common among stroke patients. Specifically, 30.4% of stroke patients had moderate OSA compared to 17.4% of controls, and 26.1% had severe OSA compared to just 6.5% of controls (Table 3).

Table 3: Frequency and Severity of OSA (Based on Polysomnography)

OSA Severity	Cases (n = 92)	Controls (n = 92)	p-value
No OSA (AHI <5)	18 (19.6%)	46 (50.0%)	<0.001
Mild OSA (AHI 5-14)	22 (23.9%)	24 (26.1%)	
Moderate OSA (AHI 15-29)	28 (30.4%)	16 (17.4%)	
Severe OSA (AHI ≥30)	24 (26.1%)	6 (6.5%)	

In the multivariable logistic regression study, patients with more than three times the odds of ischemic stroke were compared to those without OSA, and it was discovered that OSA was the strongest independent predictor of ischemic stroke. Obesity, hypertension, and diabetes mellitus were also identified as other metabolic and cardiovascular risk factors, which were significantly correlated with stroke, but smoking was not found to be significant after adjustment. Age and male gender as covariates to control the frequency matching were not significantly related to stroke, which means that the observed associations of OSA and other comorbidities with ischemic stroke were not much dependent on age and male gender (Table 4).

Table 4: Multivariate Logistic Regression Analysis of Factors Associated with Ischemic Stroke

Variables	Adjusted OR	95% CI	p-value
Age	1.02	0.99 – 1.05	0.184
Male gender	1.28	0.72 – 2.26	0.402
Presence of OSA	3.4	1.8 – 6.5	0.002 **
BMI ≥30 kg/m ²	2.2	1.1 – 4.3	0.023*
Hypertension	2.8	1.4 – 5.6	0.004 **
Diabetes Mellitus	1.9	1.0 – 3.6	0.046*
Smoking	1.6	0.8 – 3.2	0.173

DISCUSSION

Obstructive sleep apnea (OSA) was found to be significantly more prevalent in ischemic stroke patients (80.4%) than in age- and sex-matched controls (50%) in the current case-control investigation. OSA was also found to be independently linked to a more than threefold increased risk of ischemic stroke. A Korean study of acute ischemic stroke patients reported an OSA frequency of 91.2%, with around 70% exhibiting moderate-to-severe OSA, and patients aged ≥ 65 had a threefold risk of more severe OSA, findings that resonate with our observed high frequency and OSA severity among stroke cases [10]. Similarly, a meta-analysis published in 2024 in the *Journal of Clinical Sleep Medicine* found that sleep-disordered breathing was present in up to 72% of stroke and TIA patients, consistent with our case frequency of 80% [16]. These studies reinforce the notion that OSA is exceedingly common in stroke populations and highlight the importance of systematic sleep assessment. Comparatively, a tertiary-care hospital study in India found a 76% frequency of OSA among stroke survivors, with increasing BMI independently associated with moderate-to-severe OSA, a finding consistent with our observation that elevated BMI was significantly higher among cases and independently predictive of stroke risk in the multivariate model ($p=0.0235$) [17]. Present result that moderate-to-severe OSA was more prevalent in cases (30.4% moderate, 26.1% severe) than controls (17.4% and 6.5%, respectively) support prior cohort and meta-analysis evidence showing that moderate and severe OSA, rather than mild, are the primary drivers of vascular risk. A study showed that moderate and severe OSA was associated with a significantly increased risk of stroke and vascular events ($RR = 2.15$ for stroke) compared to mild or no OSA [18, 19]. Furthermore, our logistic regression identified hypertension ($OR\ 2.8$) and diabetes mellitus ($OR\ 1.9$) as independent stroke predictors, consistent with known pathways linking OSA to cerebrovascular risk via sympathetic overactivity, endothelial dysfunction, and metabolic dysregulation. However, unlike our finding where smoking did not remain significant in multivariate analysis, other global studies often report smoking as a contributory, albeit less dominant, risk factor, indicating possible differences in population-level smoking patterns or interactions between risk factors. Current international consensus guidelines now recommend routine clinical screening for OSA in patients with ischemic stroke or TIA, given the high burden and emerging evidence that early diagnosis and treatment may reduce recurrent stroke and mortality. Yet randomized interventional trials on CPAP post-stroke have been limited by poor compliance, though some data suggest reduced cardiovascular risk with adherence. A recent systematic meta-analysis in the

Journal of Clinical Medicine evaluated post-stroke complications and found only a modest increase in risk among stroke survivors with OSA, particularly among those with more severe strokes ($RR = 1.06$ for high-severity survivors). Although our study did not assess post-stroke complications, our findings support the rationale to explore whether early OSA detection post-stroke could mitigate poorer neurological or functional outcomes [20]. Additionally, a 2024 systematic review of clinical prediction models for OSA in stroke patients highlighted the value of tools like STOP-BANG for early identification in acute settings, mirroring our practice of pre-screening with STOP-BANG before confirmation via polysomnography [21]. To conclude, our data are a part of the accumulating evidence that OSA is a prevalent independent risk factor of ischemic stroke, particularly among those with high BMI and cardiovascular comorbidities. These trends are universal among various populations, not only in Taiwan but also in India, and larger meta-analyses highlighting the applicability of sleep apnea in cerebrovascular disease are worldwide in scope. Future studies must focus on longitudinal studies to determine whether OSA (e.g., CPAP) treatment in stroke populations can decrease recurrence and enhance recovery, and in areas where this problem is under-acknowledged. Despite results indicating that OSA is very common among stroke patients and positively related to stroke risks, the idea of routine OSA is hindered, in part because of low adherence rates and inconsistent severity of stroke. Thus, although early detection of OSA can perhaps be useful, only large randomized controlled trials can answer the question whether CPAP or other interventions can be used to meaningfully decrease the risk of recurrent stroke or enhance long-term neurological outcomes.

The study had several limitations. Though our investigation detected a considerable independent association of OSA and ischemic stroke, the case-control design by itself does not provide the chance to prove temporality or causality. There is no way to analyze whether OSA was a previous condition or a side effect of the stroke. Prospective longitudinal and randomized interventional studies are needed to determine whether early diagnosis and treatment of OSA (e.g., CPAP therapy) can reduce stroke recurrence and improve long-term neurological outcomes.

CONCLUSIONS

Obstructive sleep apnea and ischemic stroke have a statistically significant relationship. Controlling for the frequency of obesity, diabetes, and hypertension, OSA was an independent predictor of stroke, and was very common and more severe among stroke patients than controls. Following these findings, routine OSA monitoring is necessary in stroke cohorts, and prompt diagnosis and

treatment of sleep-disordered breathing can be regarded as a significant opportunity to lower the incidence of stroke and enhance better neurological outcomes in the long run.

Authors' Contribution

Conceptualization: LH

Methodology: UI, AI, IS, SH

Formal analysis: RG, AI

Writing and Drafting: UI, LH, IS

Review and Editing: UI, LH, RG, AI, IS, SH

All authors approved the final manuscript and take responsibility for the integrity of the work.

Conflicts of Interest

All the authors declare no conflict of interest.

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