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# **Factor Affecting Insomnia in Ischemic Stroke Patients**

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#### **ABSTRACT**

Introduction: Insomnia is common in ischemic stroke patients and can negatively impact on the post-stroke recovery process by interfering with the body's natural healing process, reducing the effectiveness of rehabilitation therapy, and affecting the recovery of cognitive function. Effective management and early intervention in insomnia are needed to enhance health services for stroke patients, promote optimal recovery, and improve their quality of life. **Objective:** This study aimed to identify and analyze the various factors associated with the occurrence of insomnia among patients with ischemic stroke. **Methods:** This is a cross-sectional study that used secondary data from medical records and primary data gathered through questionnairebased interviews. The subjects were 105 ischemic stroke patients at the Neurology Clinic of Dr. Mohammad Hoesin Hospital, Palembang, between May to July 2024. The data acquired for further analysis included social and demographic details, comorbid conditions, depression, anxiety, pain, insomnia, medication use, sleep hygiene, and stroke clinical features. The data was then analyzed using IBM SPSS Statistics 24 and assessed through bivariate and multivariate analyses to evaluate the relationships between variables. **Results:** The prevalence of insomnia in this study was 42.9%, with mild insomnia observed in 26.7%, moderate insomnia in 13.3%, and severe insomnia in 2.9% of the subjects. Obstructive sleep apnea (OSA) (OR: 22.718), sleep hygiene index (OR: 6.490), and education level (OR: 3.453) were identified as determinants related to insomnia in ischemic stroke patients. Indirect factors associated with insomnia in ischemic stroke patients include depression, the number of comorbid diseases, pain, diabetes, a history of insomnia, anxiety, and stroke onset. Conclusion: There is a complex relationship between various physical, psychological, and social factors and the incidence of insomnia after ischemic stroke.

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#### INTRODUCTION

Sleep is a physiological and repetitive state of reversible decline in consciousness, characterized by a global decline in cognitive function that temporarily limits brain activity. It is a behavioural condition that reduces metabolic rate and helps the body conserve energy. Adequate sleep improves mental clarity and workplace productivity, while sleep deprivation impairs both physical and cognitive performance, preventing them from functioning optimally.<sup>1,2</sup>

Insomnia is one of the sleeps disturbances that is significantly more prevalence in stroke patients than in the general population. Baylan *et al.* found that the percentage of insomnia symptoms in stroke patients, as assessed by questionnaires, ranged from 19.8%-69%. Among these patients, 28.6%-47.8% reported difficulty initiating sleep, 14.3%-65.2% had difficulty maintaining sleep, and 17%-34.1% experienced early awakening.<sup>3,4</sup>

Insomnia in stroke patients is considered to worsen clinical outcomes because it interferes with the body's natural healing process, reduces the effectiveness of rehabilitation therapy, and impairs cognitive function recovery. Poor sleep quality can lead to excessive fatigue, decreased motivation, and an increased risk of depression, all of which may hinder post-stroke recovery. 5.6

## **OBJECTIVE**

This study aimed to determine determine the factors that influence insomnia in ischemic stroke patients.

## **METHODS**

This study used a cross-sectional design, utilizing

primary data obtained through questionnaire interviews and secondary data collected from patient medical records. The study was conducted at Dr. Mohammad Hoesin Hospital (RSMH), Palembang, from May to July 2024. The ethics committee of Dr. Mohammad Hoesin General Hospital approved this study under the ethical clearance number DP.04.03/D.XVIII.6.8/ETIK/089 /2024. Participants were ischemic stroke patients who visited the neurology clinic during the study period and met the inclusion criteria, with no exclusions. A consecutive sampling technique was used, resulting in a sample size of 105 subjects.

The inclusion criteria included patients who were diagnosed with ischemic stroke by a doctor, agreed to participate in the study, and signed a consent form. The exclusion criteria included patients with decreased consciousness (GCS ≤ 14), aphasia, intellectual or psychiatric disorders, or any other disorders that impeded comprehension of the questionnaire, as well as patients who worked at night shift or followed a rotating shift system. The variables assessed in this study were sociodemographic variables (age, gender, and education level), clinical stroke characteristics (onset, recurrent, severity, and lesion location), comorbidities (hypertension, diabetes, heart disease, dyslipidemia and obstructive sleep apnea), depression, anxiety, pain severity, sleep hygiene, use of activating antidepressants or stimulants, and history of insomnia.

We used the Insomnia Screening Questionnaire (ISI) to assess insomnia, the Patient Health Questionnaire (PHQ-9) for depression, the General Anxiety Disorder (GAD-7) questionnaire for anxiety, the Sleep Hygiene Index (SHI) for sleep hygiene, the National Institutes of Health Stroke Scale (NIHSS) for stroke severity, and the Numeric Pain Rating Scale (NPRS) for pain. Data was then analysed with IBM SPSS Statistics 24. Multivariate analysis was performed using multiple logistic regression to identify which independent variables had the strongest association with the dependent variable.

## **RESULTS**

Table 1. Characteristics of research subjects

Characteristics	Frequency (n = 105)		
Age			
- 18-59 years old	63 (60.0%)		
$- \ge 60$ years old	42 (40.0%)		
Gender			
- Male	63 (60.0%)		
- Female	42 (40.0%)		
<b>Education Level</b>			
- Not at school	1 (1.0%)		
- Elementary school	12 (11.4%)		
- Junior high school	5 (4.8%)		



Table 1 continued. Characteristics of research subjects

Characteristics	Frequency			
	(n = 105)			
- High school	47 (44.8%)			
- Higher education (college)	40 (38.1%)			
Stroke onset				
- ≤4 minggu	23 (21.9%)			
- > 4 minggu	82 (78.1%)			
Stroke Recurrence				
- Recurrent	20 (19.0%)			
- First	85 (81.0%)			
Stroke Severity				
- Mild (NIHSS $\leq$ 5)	84 (80.0%)			
- Moderate - severe (NIHSS > 5)	21 (20.0%)			
Stroke Lesion Location				
- Anterior circulation	88 (83.8%)			
- Posterior circulation	17 (16.2%)			
Hypertension	·			
- Yes	90 (85.7%)			
- No	15 (14.3%)			
Diabetes	( ·/			
- Yes	38 (36.2%)			
- No	67 (63.8%)			
Heart disease	07 (001070)			
- Yes	27 (25.7%)			
- No	78 (74.3%)			
Dyslipidemia	70 (74.570)			
- Yes	38 (36.2%)			
- No	67 (63.8%)			
Obstructive sleep apnea (OSA)	07 (03.070)			
- Yes	14 (13.3%)			
- 1es - No	91 (86.7%)			
Number of comorbidities	91 (80.7%)			
- 1	39 ( (37.1%)			
- 1 - 2				
- 2 - 3	39 (37.1%)			
- 3 - 4	18 (17.1%) 9 (8.7%)			
	9 (8.7%)			
Depression	62 (600/)			
- None (PHQ9 0-4) - Mild (PHQ9 5-9)	63 (60%)			
	27 (25.7%)			
- Moderate (PHQ9 10-14)	10 (9.5%) 3 (2.9%)			
- Moderate-severe (PHQ9 15-19)	` ,			
- Severe (PHQ9 20-27)	2 (1.9%)			
Anxiety	70 (75 20)			
- None (GAD7 0-4)	79 (75.2%)			
- Mild (GAD7 5-9)	18 (17.1%)			
- Moderate (GAD7 10-14)	6 (55.7%)			
- Severe (GAD7 15-21)	2 (1.9%)			
Pain severity				
- None (NPRS 0)	72 (68.6%)			
- Mild (NPRS 1-3)	6 (5.7%)			
- Moderate (NPRS 4-6)	25 (23.8%)			
- Severe (NPRS 7-10)	2 (1.9%)			
Sleep Hygiene				
- Good (SHI 13-27)	64 (61.0%)			
- Moderate (SHI 28-40)	39 (37.1%)			
- Poor (SHI 41-65)	2 (1.9%)			
Activating antidepressant				
- Yes	3 (2.9%)			
- No	102 (97.1%)			
· <del>*</del>	102 (71.170)			



Table 1 continued. Characteristics of research subjects

Characteristics	Frequency (n = 105)		
History of Insomnia			
- Yes	8 (7.6%)		
- No	97 (92.4%)		

In this study, 42.9% of subjects experienced insomnia, with mild insomnia at 26.7%, moderate insomnia at 13.3%, and severe insomnia at 2.9%. Women (47.6%) were more likely to experience insomnia than men (39.7%), and severe insomnia was reported only in female subjects. Subjects with a college education level had the least amount of insomnia (30%).

Based on the clinical characteristics of stroke onset, insomnia was more common in strokes lasting longer than four weeks (47.6%), in first-attack strokes (44.7%), and in posterior circulation strokes (47.1%). Subjects with comorbidities also experienced more insomnia than those without such conditions. Subjects with hypertension experienced more insomnia (44.4%) than those without hypertension (33.3%). The prevalence of insomnia was higher in subjects with diabetes (55.3%) than in those without (35.8%). Insomnia rates were higher in heart disease patients (51.9%) than in non-heart disease patients (39.7%). Compared to subjects without OSA, those with OSA had higher rates of insomnia (85.7%). The percentage

of insomnia increased as the number of comorbidities among subjects increased.

Insomnia was more common among subjects with depression (64.3%), anxiety (73.1%), pain (63.6%), and poor sleep hygiene (63.4%). Subjects who took activating antidepressants (e.g., sertraline) experienced more insomnia than those who did not. Additionally, subjects with a history of insomnia before the stroke experienced more insomnia (87.5%) than those without such a history (39.2%).

In this multivariate analysis, the factors significantly associated with the likelihood of insomnia were obstructive sleep apnea (OSA), the Sleep Hygiene Index (SHI), and education level. Confounding variables, such as depression, pain, diabetes, history of insomnia, anxiety, and stroke onset were found to influence these factors associations. The biggest factor related to the chance of having insomnia was OSA, with an odds ration (OR) of 22.718 (95% CI: 3.128–164.977), indicating that ischemic stroke patients with OSA had a 22.718-fold increased risk of insomnia compared to those without OSA (Table 2).

Table 2. Final modelling

Characteristics	Sig.	Exp.(B)	95% CI for Exp(B)	
			Lower	Upper
Education level	0.042	3.543	1.048	11.976
OSA	0.002	22.718	3.128	164.977
SHI	0.004	6.490	1.849	22.781
Depression	0.831	0.840	0.169	4.165
Number of comorbidities	0.463	0.598	0.151	2.360
Pain	0.194	2.112	0.684	6.523
Diabetes	0.109	2.920	0.786	10.846
History of insomnia	0.056	12.819	0.937	175.302
Anxiety	0.055	5.710	0.964	33.833
Stroke onset	0.053	0.233	0.053	1.020

Omnibus Tests: 0.0000 Negelkerke R Square: 0.570

## **DISCUSSION**

Neurochemical changes can occur in the brain after a stroke, including changes in biomarkers, signals from neurotransmitters (e.g., hypocretin), transcription and translation of clock genes (BMAL1 and CRY1), and decreased melatonin excretion. Other factors that may contribute to sleep disturbances in stroke include depression, pain, anxiety, and the hospital environment.<sup>7,8</sup>

Zhang et al. noted that various factors, including a

patient's psychological state and overall health status, can influence insomnia and its timing. Sleep disruptions during the acute phase are thought to be caused by the inflammatory response, which is characterized by the release of proinflammatory cytokines and the activation of immune cells. The activation of inflammatory pathways, disruption of the blood-brain barrier, and the presence of a neuroinflammatory environment are all suspected to play a role in sleep problems. <sup>9,10</sup>

Chronic ischemic stroke patients frequently



experience insomnia in conjunction with post-stroke depression. In this study, the prevalence of depression was higher among research subjects with stroke onset > 4 weeks (41.5%) than those with stroke onset ≤ 4 weeks (34.8%). The posterior circulation, which heavily vascularizes the anatomical location of the sleep function, is thought to contribute to insomnia in cases of posterior circulation strokes. Insomnia might also be related to where the stroke happens, with more strokes occurring in the thalamus or brainstem, like the pontine tegmentum and thalamomesencephalic region. Patients with paramedian thalamus stroke may also experience insomnia because the involvement of the thalamoreticular system can hinder the generation of sleep spindles. 8,11

Insomnia frequently coexists with comorbidities. Hypertension, heart disease, and diabetes are often associated with increased nervous system activity, which can interfere with relaxation and sleep onset. Increased sympathetic nervous system activity and elevated cortisol levels can raise blood pressure and impair both cardiovascular function and glucose metabolism. Antihypertensive medications, such as diuretics, frequently induce nocturnal awakenings. Diabetes-related physiological effects, such as neuropathic pain, nocturia, and psychological stress, can also disrupt sleep patterns. Poor sleep quality can impair glucose metabolism and increase insulin resistance, thereby worsening glycemic control in people with diabetes. Sleep disturbances have also been associated with elevated HbA1c levels, indicating poor long-term glucose control. 12,13,14

Depression can be both a risk factor and a trigger for insomnia. Depression symptoms, such as sadness, hopelessness, and loss of interest, can interfere with sleep. Conversely, insomnia can also trigger or aggravate depressive symptoms since a lack of sleep affects mood. Subjects with insomnia reported more somatic symptoms of anxiety, such as palpitations, sweating, tremors, and so on. A strong relationship exists between anxiety and insomnia in ischemic stroke patients, with both conditions tend to appear and worsen simultaneously. Anxiety can be a trigger for insomnia because excessive thoughts, fear, and worry can interfere with sleep.<sup>8,15</sup>

Pain has been identified as one of the contributing factors to sleep disturbances. Insomnia is more prevalent among patients with pain than in the general population. Lind *et al.* found that the prevalence of clinical insomnia decreased among patients who had undergone pain rehabilitation therapy. Chronic pain can lead to increased sleep fragmentation and difficulty in maintaining sleep, which in turn can exacerbate pain perception. This relationship is particularly relevant for stroke survivors, as they often experience both acute and chronic pain conditions post-stroke, further complicating their sleep patterns. 16,17

Sertraline, an antidepressant belonging to the selective serotonin reuptake inhibitor (SSRI) class, acts by activating serotonin 5-HT2 receptors and increasing noradrenergic and dopaminergic neurotransmission. It can lower the quality of sleep and cause insomnia, consequently affecting energy and alertness, which in turn disrupts the sleep cycle. These antidepressants are known to prolong rapid eye movement (REM) latency, suppress REM sleep, and disrupt sleep continuity, based on polysomnographic parameters. However, age, gender, dosage, duration of use, drug interactions, and medical conditions are also considered to play a role. Individuals with chronic insomnia are also at risk of experiencing persistent insomnia after stroke. Stroke often causes psychological distress, which results in a recurrence of previous insomnia. In addition, brain damage from stroke can aggravate existing sleep disorders, worsening the condition of post-stroke insomnia. 18

In their analysis of the connection between insomnia and OSA, Zhang et al. discovered that symptoms of insomnia, including difficulty falling asleep, staying asleep, and waking up too early, might also affect people with OSA, indicating a link between the two conditions. OSA causes repeated awakenings due to apneas or hypopneas during sleep, resulting in sleep fragmentation. This fragmentation may manifest as difficulty in maintaining sleep, a common symptom of insomnia. Other studies have found that individuals with OSA experience micro-stimuli that interfere with deep sleep, resulting in unrefreshing sleep and increased daytime sleepiness. Researchers have also found a correlation between the severity of OSA and insomnia symptoms, suggesting that untreated OSA may exacerbate insomnia. 19,20

Poor sleep hygiene was found to be associated with post-stroke insomnia. Insomnia can be effectively managed by practicing good sleep habits, which include avoiding stimulants before bedtime, making a pleasant sleeping environment, and maintaining a regular sleep schedule. Education level may be associated with an individual's level of knowledge and awareness about health and insomnia management. Patients with higher level of education may have easier access to resources and information that can assist in controlling insomnia symptoms.<sup>21</sup>

Confounding factors included depression, the number of comorbid diseases, pain, diabetes, a history of insomnia, anxiety, and the onset of a stroke. Although some of these factors were associated with insomnia in the bivariate analysis, their effects were not statistically significant once other variables were considered in the multivariate model. This finding suggests that although these factors may influence insomnia, their effects may be indirect or mediated by other factors. The multivariate analysis revealed the interdependence and mutual influence among these



variables. This implies that these factors should still be considered, even if they lack independent statistical significance in the multivariate model. This is due to their potential to complicate the interpretation of the relationship between the primary factors and the outcome.

This study assessed not only stroke characteristics, medication use, comorbid diseases, and post-stroke psychological factors but also the influence of physical pain, environmental factors, and sleep hygiene on insomnia among ischemic stroke patients. This use of questionnaire may have introduced recall bias. Additionally, because data were collected only once, the study was unable to assess correlations with characteristics that may have existed prior to onset of stroke. To obtain a more comprehensive understanding of insomnia in ischemic stroke patients, it is essential to interpret the findings while considering its limitations.

#### **CONCLUSION**

This study found a complex relationship among various physical, psychological, and social risk factors for insomnia after ischemic stroke. Collaboration between various disciplines, including neurology, psychiatry, and public health, is needed to reducing the burden of insomnia in post-ischemic stroke patients and improving their overall quality of life.

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#### **Conflict of Interest**

The authors have no conflicts of interest.

#### **Ethic Consideration**

This research was conducted after receiving approval from Ethical Committee of Dr. Mohammad Hoesin General Hospital with ethical clearance number DP.04.03/D.XVIII.6.8/ETIK/ 089/2024.

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#### **Author Contributions**

AF, M, SH, PDR, and I contributed to the study design. AF helped with data collection and analysis. M, SH, PDR, and I supervised the results and discussion. All authors reviewed and approved the final version of the manuscript.

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