Original Research Paper

Sleep quality and low-density lipoprotein cholesterol levels with the risk of ischemic stroke

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Abstract

Stroke is a multi-causal disease, and many factors can lead to stroke. There are also some unseen behavioral factors, such as poor diet. In recent years, poor sleep quality has been considered a potential trigger of stroke. If these factors are not well controlled, it can have an impact on the incidence of ischemic stroke. The aim of this research is to assess the correlation between sleep quality and low-density lipoprotein cholesterol levels with the incidence of ischemic stroke. This study used an analytic observational design with a cross-sectional approach using the PSQI (Pittsburgh Sleep Quality Index) questionnaire and secondary data. A total of 60 respondents were selected with a purposive sampling technique and met the inclusion and exclusion criteria. This research was conducted at Fatmawati Soekarno Hospital, Surakarta City. Statistical analysis showed that the Chi-Square test produced a significance value, with a p value of 0.007 for the correlation of sleep quality with the incidence of ischemic stroke, and a p value of 0.688 for the correlation of low-density lipoprotein cholesterol levels with the incidence of ischemic stroke. It can be concluded that there is a correlation between sleep quality and the incidence of ischemic stroke, but there is no relationship between low-density lipoprotein cholesterol levels and the incidence of ischemic stroke.

Keywords: ischemic stroke; low-density lipoprotein; sleep quality

1. Introduction

According to the World Health Organisation (WHO), stroke is a disease that appears quickly, characterised by neurological deficits both locally and in the whole body. Stroke can be progressive and in severe cases, can last more than 24 hours, even fatal. The occurrence of stroke is related to blockage or rupture of arteries in the brain, resulting in disruption of the blood supply of oxygen to certain areas of the brain, which can cause necrosis of cells or tissues. Based on the condition, stroke is divided into two types, namely ischemic stroke and hemorrhagic stroke. Ischemic stroke is caused by the formation of blood clots called embolus in the blood vessels of the brain (Haryati & Yunaningsi, 2020). Meanwhile, hemorrhagic stroke occurs due to rupture of an artery, which causes the appearance of an intracranial hematoma (Chugh, 2019).

Based on the Global Stroke Fact Sheet published in 2022, the lifelong risk of stroke has increased by 50% over the past 17 years and now 1 in 4 people are expected to experience a stroke during their lifetime. From 1990 to 2019, there was a 70% increase in stroke incidence, a 102% increase in stroke prevalence, and a 143% increase in Disability Adjusted Life Years (DALYs). The majority of global strokes, including 86% of stroke mortality and 89% of cases each year, occur in people with low economic standards of living. Projections for 2020 predict a significant increase of more than 20 million cases per year, with estimates for 2030 reaching more than 24 million cases per year (Ernaningrum et al., 2024).

Various factors influence the occurrence of stroke, involving modifiable and non-modifiable factors. Non-modifiable factors include age, gender, race-ethnicity, and genetic factors. In contrast, modifiable factors include lifestyle, active smoking, unhealthy diet, physical activity levels, hypercholesterolemia and even sleep duration. An unhealthy diet with characteristics of high sugar, salt and low fiber as well as less activity plays a role in increasing body mass index to obesity. This can be a risk factor for stroke (Kuriakose & Xiao, 2020; Ananta & Yuniartika, 2024; Devi et al., 2024).

Poor sleep quality is an independent modifiable factor in cardiovascular disease and ischemic stroke. The lower a person's sleep quality, the greater the likelihood of experiencing ischemic stroke. Conversely, good quality sleep can act as a protective factor against ischemic stroke. Research involving ischemic stroke patients showed a negative correlation between poor sleep quality and ischemic stroke incidence in those with insomnia scores above 5 (Brunetti et al., 2022) although there is debate in it. Based on previous studies, there is inconsistency in the findings regarding the relationship between sleep quality and stroke. A study by Zhang et al (2023) found no correlation between sleep quality and the severity of acute stroke, while a study by Gottlieb (2019) found sleep disturbance significantly increased the risk of ischemic stroke. Meanwhile, a recent study by Ramadhini et al. (2020) also indicated that poor sleep quality is associated with stroke incidence in ischemic stroke patients who experience insomnia (Zhang et al., 2023; Gottlieb et al., 2019; Ramadhini et al., 2020; Wang et al., 2019). The differences in the results of this study indicate a research gap in understanding more deeply how sleep quality affects the pathophysiological mechanisms of stroke. The inconsistency of previous findings suggests the need for further research to explore other factors that may play a role in the relationship between sleep quality and stroke, such as sleep duration, specific sleep disorders, or other clinical variables.

This study has the novelty of examining the simultaneous relationship between sleep quality and LDL cholesterol levels on the incidence of ischemic stroke, which has not been widely explored in previous studies. Although poor sleep quality and hypercholesterolemia have been identified as risk factors for stroke, previous studies have shown inconsistent results regarding the relationship between LDL levels and ischemic stroke (Li et al., 2021). Therefore, this study attempts to fill the research gap by examining how sleep quality and LDL cholesterol levels jointly contribute to the risk of ischemic stroke.

This study will investigate two main variables, namely sleep quality and LDL cholesterol levels, in relation to the incidence of ischemic stroke. Using a correlational analysis method, this study will assess the sleep quality of ischemic stroke patients, using appropriate instruments such as the Pittsburgh Sleep Quality Index (PSQI) or polysomnography if possible. The analysis of the patient's LDL cholesterol levels is based on laboratory examinations. The study correlates these two variables with the incidence of ischemic stroke, in order to understand whether sleep quality and LDL cholesterol levels independently or simultaneously contribute to the incidence of stroke.

This study is expected to provide scientific evidence regarding the importance of sleep quality and cholesterol level management in preventing ischemic stroke, as well as become the basis for more comprehensive clinical interventions that can provide new perspectives on the potential pathophysiological mechanisms of ischemic stroke related to sleep disorders and dyslipidemia, and provide clinical implications for stroke prevention strategies based on sleep and cholesterol level management.

2. Research Methods

This research discusses epidemiological studies related to disease relationships. This research applies a cross-sectional approach with an observational approach and uses a purposive sampling method. The samples were selected based on the inclusion criteria, namely patients who had been

diagnosed with ischemic stroke, patients who were not diagnosed with ischemic stroke, willing to participate in the study, had LDL lipid profile laboratory results, did not experience cognitive impairment and for exclusion criteria, namely smokers, patients with diabetes mellitus, not equipped with lipid profile examination results. The sampling used was purposive sampling, in which the sample selection was based on inclusion criteria and exclusion criteria. This study was conducted at Fatmawati Soekarno Regional General Hospital, Surakarta City, in the October to November 2023 period, with a total sample of 60 participants. The research instrument was a questionnaire PSQI (Pittsburgh Sleep Quality Index) to measure sleep quality and medical records of patient laboratory results. PSQI score $\leq$ 5 showed good sleep quality, while score > 5 showed poor sleep quality. The analysis of data was conducted utilizing the bivariate chi-square test. This study has been approved by the health research ethics commission of Dr. Moewardi Hospital No. 1.857/X/HREC/2023.

3. Results and Discussions
3.1.Univariate Analysis Based on Sample Characteristics

Through the results of the chi-square bivariate test analysis, it was concluded that there was a significant correlation between sleep quality and the incidence of ischemic stroke, with a p-value of 0.007. There were 12 samples of ischemic stroke patients who had good sleep quality and 18 samples of patients who had poor sleep quality.

Table 1. Respondent Characteristics

Characteristics	Ischemic Stroke	Characteristics	Ischemic Stroke
Age			
Elderly	16 (53.3%)	11 (36.7%)	0.194
Pre-elderly	14 (47.7%)	19 (66.3%)	
Sex			
Male	20 (66.7%)	10 (33.3%)	0.010
Female	10 (33.3%)	20 (66.7%)	
Marital status			
Married	20 (66.7%)	10 (33.7%)	0.640
Not married	19 (33.3%)	20 (66.7%)	
Sleep quality			
Bad	18 (60%)	27 (87.5%)	0.007
Good	12 (40%)	3 (12.5%)	
LDL Cholesterol			
Abnormal	26 (60%)	27 (87.5%)	0.688
Normal	4 (40%)	3 (12.5%)	
Total cholesterol			
Abnormal	11 (36.7%)	6 (20%)	0.152
Normal	19 (63.3%)	24 (80%)	
Triglycerides			
Abnormal	2 (6.73%)	4 (13.3%)	0.389
Normal	28 (93.3%)	26 (83.7%)	
Uric acid			
Abnormal	5 (16.7%)	5 (16.7%)	1,000
Normal	25 (83.2%)	25 (83.3%)	

Source: Primary and Secondary data, 2023

Based on the respondent characteristics in Table 1, there are several important findings that can be discussed related to factors of the incidence of ischemic stroke. The majority of ischemic stroke patients

are elderly (53.3%), while in the non-ischemic stroke group there are more pre-elderly (63.3%). Although the p-value of 0.194 shows no statistically significant relationship, age remains a major risk factor for stroke because it is related to the degenerative process of blood vessels. Ischemic stroke occurs more often in men (66.7%) than women (33.3%), with a p-value of 0.010 indicating a significant relationship. This is in accordance with previous studies showing that men have a higher risk of stroke than women, possibly due to hormonal factors, smoking habits, and unhealthy diets. There was no significant relationship between marital status and the incidence of ischemic stroke (p = 0.640). However, marriage can affect lifestyle and stress levels, which contribute to general cardiovascular health. Patients with poor sleep quality were more common in the non-ischemic stroke group (87.5%) compared to ischemic stroke (60%), with a p-value of 0.007. These results indicate a significant relationship, which could mean that poor sleep quality may play a role in stroke. Disturbed sleep can increase blood pressure and inflammation, which contribute to stroke. The majority of ischemic stroke patients had abnormal LDL cholesterol levels (60%), but this difference was not statistically significant (p = 0.688). Meanwhile, abnormal total cholesterol levels were also more common in the ischemic stroke group (36.7%) compared to non-stroke (20%), but a p-value of 0.152 indicated no significant relationship. Most ischemic stroke patients had normal triglyceride levels (93.3%), while only 6.7% were abnormal. This difference was not significant (p = 0.389). There was no significant difference between uric acid levels in ischemic and non-ischemic stroke patients (p = 1.000), indicating that this factor may not have a direct relationship in this study sample.

Based on the results of this study, factors that have a significant relationship with the incidence of ischemic stroke are gender (males are at higher risk) and poor sleep quality. Although age, blood lipid levels, and uric acid do not show a significant relationship in this study, these factors remain a concern in stroke prevention.

The results of the study in Table 1 showed several factors that have a significant relationship with the incidence of ischemic stroke, such as gender (p = 0.010) and sleep quality (p = 0.007). Meanwhile, other factors such as age, marital status, cholesterol, triglycerides, and uric acid do not show a significant relationship. Similar findings have been reported in several other studies on gender and ischemic stroke. Research by Theofilis et al. (2021) shows that men have a higher risk of stroke than women at young to middle age, but this risk reverses in old age. Other studies have shown that sleep disorders, especially sleep apnea, increase the risk of ischemic stroke (Theofilis et al., 2021; Biose et al., 2024). A meta-analysis study found that sleep duration that is too short (<6 hours) or too long (>8 hours) is associated with an increased risk of stroke (Ji et al., 2020). Previous studies have also confirmed that dyslipidemia is one of the main risk factors for stroke (Mc Carthy et al., 2023).

3.2. Bivariate Test

Table 2. Bivariate Analysis Of Sleep Quality and Ischemic Stroke

| | | Stroke | | | | |
		Ischemic Stroke	Non-ischemic Stroke	Total	P Value	OR Value
Sleep quality	Bad	18	27	45	0.007	0.167
		40%	60%	100%		
	Good	12	3	15		
		80%	20%	100%		
	Total	30	30	60		
		100%	100%	100%		

Source: Primary data 2023

The results of the bivariate analysis using the Chi-Square test showed a p-value of 0.007 and an OR value of 0.167. Therefore, the research hypothesis (H1) can be approved and it can be concluded that

there are 54 significant correlations between sleep quality and the incidence of ischemic stroke. The results of this study are in line with and supported by the findings of Ji et al. (2020) research regarding the relationship between sleep quality and the incidence of ischemic stroke with a p-value of 0.010. This study used a questionnaire (Pittsburgh Sleep Quality Index) to assess how good and bad the sleep quality was in the sample (Ji et al., 2020).

The results of this study state that subjective sleep disturbances are associated with an increased risk of stroke in the adult population in China. There is an additive interaction between short sleep duration and poor sleep quality, which together affect the level of stroke risk. This finding is also in line with Chattu's research (2018) which shows a significant relationship between sleep disturbances and the risk of acute stroke with a p value (0.001). The occurrence of acute stroke increases in individuals with short sleep duration, especially when the duration of sleep at night is less than 6 hours, making it a potential risk factor for stroke. Other findings can be taken from the study conducted by Harianja et al. (2023) with the title of *Kualitas Tidur dan Keparahan Stroke Iskemik* (The Relationship Between Sleep Quality and the Severity of Ischemic Stroke). Using the chi-square test analysis with a p value of 0.000, a significant correlation was found between sleep quality and the incidence of ischemic stroke (Chattu et al., 2018; Harianja et al., 2023).

According to Zhang et al. (2023) it is considered that poorer sleep quality is experienced by individuals with poor quality of life and education, which is associated with cognitive levels, life stress, health literacy, stress resistance, and psychological factors. In addition, people who are physically inactive are also associated with poorer sleep quality. Therefore, aerobic exercise or intensive exercise can help people who have poor sleep quality. One of the possible risk factors that occurs due to increased activity of the sympathetic nervous system is decreased sleep quality or poor sleep quality. Lack of sleep increases various inflammatory markers and weakens the immune system, which encourages the development of various diseases. Sleep disorders are associated with various chronic diseases, including hypertension, diabetes, dyslipidemia, cardiovascular and so on, all of which are risk factors for stroke (Zhang et al., 2023).

Table 3. Bivariate analysis of LDL and ischemic stroke

| | | Stroke | | | | |
		Non-Ischemic Stroke	Ischemic Stroke	Total	P Value	OR Value
LDL Cholesterol	Abnormal	27	26	53		
		50.9%	49.1%	100%	0.688	
	Normal	3	4	7		0.722
		42.9%	57.1%	100%		
	Total	30	30	60		
		100%	100%	100%		

Source: Secondary data, 2023

The results of the bivariate analysis using the Chi-Square Test obtained a p value of 0.688 and an OR value of 0.722. This means that the null hypothesis (H0) in this study can be accepted, so it can be concluded that there is no correlation between LDL cholesterol levels and the incidence of ischemic stroke.

Factors that affect LDL to have no relationship with the occurrence of ischemic stroke are that LDL is not the only risk factor for the occurrence of ischemic stroke. Several other factors that affect the formation of atherosclerosis such as total cholesterol, HDL, GDS, and triglycerides (Omelchenko et al., 2021). Low HDL levels can also cause necrosis of the arterial cell membrane. The necrosis that occurs causes endothelial disorders and results in the appearance of micro-sized blood vessel swelling or

microaneurysms. Microaneurysms that occur can cause blood vessel rupture, resulting in intracerebral hemorrhage (Omelchenko et al., 2021).

Increased total cholesterol levels in the blood will cause lipoprotein accumulation in the tunica intima. The lipoproteins that accumulate are mainly LDL and VLDL. LDL and VLDL deposits will be oxidized because the blood vessels are damaged, then oxidative stress occurs. Oxidative stress will cause an inflammatory reaction. Inflammatory cells produce Monocyte Chemotactic Factor (MCF) so that monocytes will enter the base of the tunica intima and then turn into macrophages. Macrophages migrate and phagocytose the accumulated LDL and foam cells are formed. In addition to macrophage migration, Smooth Muscle Cells (SMCs) migrate from the tunica media vasa to the tunica intima which causes accumulation of extracellular matrix (hyaline fibers, collagen, elastin, and fibrous) produced by SMCs. The accumulation of extracellular matrix causes calcification and fibrosis of atheromatous plaques so that the elasticity and diameter of blood vessels are reduced. Fat deposits (atheroma) or plaque will damage the artery walls, causing narrowing and hardening which causes reduced function in the tissue supplied by the arteries and affects the risk of ischemic stroke.

The findings of this study are also supported by Valdes-Marquez et al. (2019) who stated that 1 mmol/l higher genetically determined LDL is related to 50% risk of coronary heart disease, in contrast, the effect of LDL causality is much lower for ischemic stroke. This finding is also consistent with Djohar (2019) who found that there was no statistically significant correlation between the LDL cholesterol and the duration of hospitalization in acute phase ischemic stroke patients, whereas total cholesterol significantly influenced the duration of hospitalization in stroke patients (Valdes-Marquez et al., 2019; Djohar, 2019).

This study is inconsistent with the study conducted by Yuan et al. (2021) which states that there is an association between LDL cholesterol and the distribution of platelets in acute ischemic stroke with a p value of 0,00 which states that an increase in the LDL-C level is correlated with an increase in oxidized LDL, which encourages an oxidative stress response and the release of inflammatory cytokines (such as functional tissue factor, monocyte chemotactic protein 1, interleukin 10, interleukin 6, and tumor necrosis factor α) in the peripheral circulation which affects the incidence of ischemic stroke. The results of other studies that are not in line with this study were conducted by Hansen. et al. (2024) which states that there is an association between non-HDL cholesterol and the risk of residual cardiovascular cases in patients with ischemic heart disease and controlled LDL cholesterol with cohort studies (Yuan et al., 2021; Hansen et al., 2024).

4. Conclusion

Based on the results of the study, it can be concluded that there is a significant relationship between poor sleep quality and ischemic stroke. However, there is no significant relationship between low-density lipoprotein cholesterol levels and ischemic stroke. Poor sleep quality is a modifiable factor but is at risk of causing ischemic stroke. Further research needs to measure all components of the lipid profile more comprehensively, using objective methods for sleep and lipids, and including other variables that play a role in the occurrence of ischemic stroke. Stronger study designs and evidence-based health interventions may help in the prevention of ischemic stroke more effectively.

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