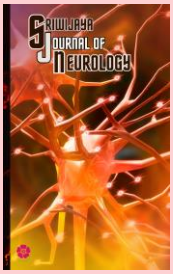

e-ISSN: 2987-1425

Sriwijaya Journal of Neurology (SJN)

Journal website: https://phlox.or.id/index.php/sjn

The Impact of Cholesterol on Stroke Outcomes: A Cross-Sectional Analysis in Central Java

Yulita Maulani[1*], Toirov Abdukhamid Suvonovich[2], Emma Ismawatie[1], Asri Wulandari[1]

[1]Bachelor of Applied Medical Laboratory Technology Study Program, Politeknik Indonusa Surakarta, Surakarta, Indonesia

[2]Department of Surgical Diseases, Chemistry Faculty, Samarkand State Medical University, Samarkand, Uzbekistan

ARTICLE INFO

Keywords:
Cholesterol
Dyslipidemia
Hemorrhagic stroke
Ischemic stroke
Stroke outcomes

***Corresponding author:**
Yulita Maulani

E-mail address:
yulita.maulani@poltekindonusa.ac.id

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.59345/sjn.v2i1.150

A B S T R A C T

Introduction: Stroke remains a leading cause of mortality and morbidity globally, with variations in subtypes and risk factors observed across populations. The role of cholesterol in stroke, particularly its association with ischemic and hemorrhagic subtypes, continues to be investigated. This study aimed to examine the relationship between cholesterol levels and stroke outcomes in a Central Javanese population. **Methods:** A cross-sectional study was conducted at hospitals in Central Java, Indonesia. Data were collected from medical records of patients diagnosed with ischemic or hemorrhagic stroke between January and December 2022. Demographic information, stroke subtype, and cholesterol levels were analyzed. Statistical tests were employed to assess the association between cholesterol and stroke outcomes. **Results:** The study included 68 patients (34 ischemic, 34 hemorrhagic). The majority of hemorrhagic stroke patients were female (52.9%), while ischemic stroke patients were predominantly male (64.7%). The mean cholesterol level for hemorrhagic stroke patients was 202.59 mg/dL, and for ischemic stroke patients, it was 190.26 mg/dL. Statistical analysis revealed no significant association between cholesterol levels and stroke subtype ($p > 0.05$). **Conclusion:** The findings suggest that cholesterol levels may not be a primary determinant of stroke subtype in this Central Javanese population. Further research is warranted to explore other potential risk factors and their interplay with cholesterol in influencing stroke outcomes.

1. Introduction

Stroke, an acute cerebrovascular event that disrupts blood flow to the brain, remains a formidable global health challenge. It stands as a leading cause of mortality and long-term disability, casting a profound impact on individuals, families, and healthcare systems worldwide. The World Health Organization estimates that 15 million people suffer from stroke annually, with approximately 5.5 million succumbing to its devastating consequences and another 5 million left with permanent disabilities.[1] The burden of stroke is particularly pronounced in low- and middle-income countries, where it accounts for a disproportionate share of mortality and morbidity.[2] The clinical manifestations and underlying pathophysiology of stroke are diverse, leading to its classification into two primary subtypes: ischemic and hemorrhagic. Ischemic stroke, the most prevalent subtype, arises from the occlusion of a cerebral artery, typically by a thrombus or embolus, resulting in the cessation of blood flow and subsequent infarction of brain tissue.[3] Hemorrhagic stroke, on the other hand, is characterized by the rupture of a blood vessel within or around the brain, leading to extravasation of blood into the parenchyma or subarachnoid space.[4] The distinct pathophysiological mechanisms underlying these subtypes necessitate tailored approaches to prevention, diagnosis, and treatment. The

identification and management of risk factors constitute a cornerstone of stroke prevention and mitigation strategies. A multitude of modifiable and non-modifiable risk factors have been implicated in the development of stroke, including hypertension, diabetes mellitus, smoking, obesity, physical inactivity, atrial fibrillation, and dyslipidemia.[5] Dyslipidemia, a condition characterized by abnormal levels of lipids in the blood, has been recognized as a significant contributor to the pathogenesis of atherosclerosis, a major underlying cause of ischemic stroke.[6] The atherosclerotic process involves the accumulation of lipids, inflammatory cells, and fibrous tissue within the arterial wall, leading to the formation of plaques that can obstruct blood flow and trigger thromboembolic events.[7]

Cholesterol, a waxy, fat-like substance essential for various physiological functions, plays a central role in the development of atherosclerosis and its associated complications. Cholesterol is transported in the blood as lipoproteins, complex particles composed of lipids and proteins. Low-density lipoprotein cholesterol (LDL-C), often referred to as "bad" cholesterol, is the primary carrier of cholesterol to peripheral tissues, including the arterial wall. Elevated levels of LDL-C promote the deposition of cholesterol within the arterial intima, initiating and accelerating the atherosclerotic process.[8] High-density lipoprotein cholesterol (HDL-C), or "good" cholesterol, on the other hand, facilitates the reverse transport of cholesterol from peripheral tissues to the liver for excretion, thereby exerting a protective effect against atherosclerosis.[9] The relationship between cholesterol and stroke, however, is multifaceted and not fully elucidated. While elevated LDL-C levels have been consistently associated with an increased risk of ischemic stroke, the association between cholesterol and hemorrhagic stroke remains less clear.[10] Some studies have suggested a potential inverse relationship between total cholesterol and hemorrhagic stroke, with higher cholesterol levels potentially conferring a protective effect.[11] This paradoxical observation has been attributed to various mechanisms, including the potential role of cholesterol in maintaining the integrity of blood vessel walls and preventing their rupture.[12]

Furthermore, the impact of cholesterol on stroke outcomes, encompassing mortality, functional disability, and recurrence, warrants further investigation. While some studies have reported an association between higher cholesterol levels and poorer outcomes after stroke, others have failed to demonstrate such a relationship.[13] The complex interplay between cholesterol, other risk factors, and stroke pathophysiology underscores the need for comprehensive research to unravel the precise role of cholesterol in stroke outcomes. The present study aimed to examine the relationship between cholesterol levels and stroke outcomes in a Central Javanese population. Specifically, we sought to investigate the association between cholesterol levels and stroke subtype (ischemic vs. hemorrhagic) and explore the potential influence of cholesterol on other stroke-related parameters. By elucidating the role of cholesterol in stroke in this population, we hope to contribute to the development of targeted prevention and treatment strategies tailored to the unique characteristics of this region.

2. Methods

The present investigation employed a cross-sectional observational design to examine the relationship between cholesterol levels and stroke outcomes. The study was conducted within the clinical setting of hospitals situated in the Central Java province of Indonesia. This region was purposefully selected due to its substantial population and the considerable burden of stroke within the community. The cross-sectional nature of the study allowed for the simultaneous assessment of cholesterol levels and stroke characteristics at a specific point in time, providing a snapshot of their association. The hospital setting ensured access to a diverse patient population with confirmed stroke diagnoses, enhancing the generalizability of the findings. The study population encompassed all patients admitted to the participating hospitals with a diagnosis of either ischemic or hemorrhagic stroke during the period spanning from January to December 2022. The inclusion criteria

were carefully defined to ensure the recruitment of a representative sample. Patients were eligible for inclusion if they were 18 years of age or older, had a confirmed diagnosis of stroke based on clinical and imaging evidence, and had available data on their cholesterol levels. The exclusion criteria aimed to minimize potential confounding factors and ensure data integrity. Patients with a history of prior stroke, significant comorbidities that could influence stroke outcomes independent of cholesterol (e.g., severe liver or kidney disease, active malignancy), or incomplete data on relevant variables were excluded from the analysis.

The sampling strategy employed was purposive sampling, a non-probability sampling technique that allows for the selection of participants based on specific criteria relevant to the research question. In this study, the purposive sampling approach ensured the inclusion of patients with confirmed stroke diagnoses and available cholesterol data, optimizing the efficiency and relevance of data collection. The sample size calculation was based on the anticipated prevalence of dyslipidemia in the stroke population and the desired level of statistical power. The final sample size of 68 patients (34 with ischemic stroke and 34 with hemorrhagic stroke) was deemed adequate to detect meaningful differences in cholesterol levels between the two stroke subtypes. Data collection was performed retrospectively through a meticulous review of medical records. Trained research personnel extracted pertinent information from the records, ensuring accuracy and completeness. Age and gender were recorded as fundamental demographic characteristics. Age was considered a continuous variable, while gender was categorized as male or female. The type of stroke, classified as ischemic or hemorrhagic, was ascertained based on clinical presentation, neurological examination, and neuroimaging findings. This categorization was crucial for subsequent analyses examining the association between cholesterol and stroke subtype. Comprehensive lipid profile data were obtained, including total cholesterol. These measurements were typically taken at the time of admission or during the hospital stay, reflecting the patient's lipid status at the time of the stroke event.

Stringent data management and quality control procedures were implemented to ensure the accuracy and reliability of the collected data. Double data entry was performed to minimize errors, and data validation checks were conducted to identify and rectify inconsistencies. Any missing or ambiguous data were clarified through careful review of medical records or consultation with treating physicians. The data were then organized and stored in a secure electronic database, ensuring confidentiality and facilitating subsequent statistical analysis. The collected data were analyzed using appropriate statistical methods. Descriptive statistics were employed to summarize the demographic and clinical characteristics of the study population, including measures of central tendency (mean, median) and dispersion (standard deviation, range). The distribution of cholesterol levels was assessed for normality using visual inspection of histograms and the Shapiro-Wilk test. In cases of non-normal distribution, data transformation techniques were applied to achieve normality, enabling the use of parametric statistical tests. The association between cholesterol levels and stroke subtype was evaluated using chi-square tests for categorical variables and independent t-tests for continuous variables. Logistic regression analysis was performed to examine the independent association between cholesterol levels and stroke subtype, adjusting for potential confounding factors such as age, gender, and other relevant comorbidities. The odds ratios and their corresponding 95% confidence intervals were calculated to quantify the strength of the association. Statistical significance was set at $p < 0.05$. All statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) software, version 26.0. The rigor of the statistical methodology ensured the validity and reliability of the study findings. The study protocol was reviewed and approved by the Institutional Review Board of the participating hospitals. Informed consent was not required as the study involved the retrospective analysis of anonymized medical records. Patient confidentiality was maintained throughout the study,

and all data were handled in accordance with relevant privacy regulations.

3. Results and Discussion

Table 1 presents the demographic and clinical characteristics of the 68 patients enrolled in the study, divided into two groups based on their stroke subtype: ischemic (n=34) and hemorrhagic (n=34). The mean age of the entire study population was 62.13 years, with no significant difference between the ischemic and hemorrhagic stroke groups. Although the majority of patients overall were male (55.9%), the distribution varied across stroke subtypes. Ischemic stroke patients were predominantly male (64.7%), while hemorrhagic stroke patients were more likely to be female (52.9%). Hypertension was the most common comorbidity in both stroke groups, affecting 66.2% of all patients. Diabetes mellitus and hypercholesterolemia were also prevalent, underscoring the importance of vascular risk factors in stroke development. The incidence of atrial fibrillation was relatively low, but slightly higher in the ischemic stroke group, which aligns with its known role in cardioembolic stroke. The distribution of occupational status and educational level was similar between the two stroke groups. Most patients were either employed or retired, and the majority had achieved at least a secondary school education. The high prevalence of hypertension, diabetes mellitus, and hypercholesterolemia highlights the importance of aggressive management of these conditions in stroke prevention. The observed gender differences in stroke subtype prevalence suggest potential variations in underlying pathophysiological mechanisms or risk factor profiles between men and women. The diverse occupational and educational backgrounds of the study population enhance the generalizability of the study findings to a wider range of patients.

Table 1. Study population characteristics.

Characteristic	Overall (n=68)	Ischemic stroke (n=34)	Hemorrhagic stroke (n=34)
Mean age (years)	62.13 ± 12.51	63.5 ± 11.87	60.8 ± 13.22
Gender			
Male	38 (55.9%)	22 (64.7%)	16 (47.1%)
Female	30 (44.1%)	12 (35.3%)	18 (52.9%)
Concomitant diseases			
Hypertension	45 (66.2%)	25 (73.5%)	20 (58.8%)
Diabetes mellitus	28 (41.2%)	16 (47.1%)	12 (35.3%)
Hypercholesterolemia	19 (27.9%)	11 (32.4%)	8 (23.5%)
Atrial fibrillation	5 (7.4%)	4 (11.8%)	1 (2.9%)
Occupational status			
Employed	32 (47.1%)	17 (50.0%)	15 (44.1%)
Retired	25 (36.8%)	12 (35.3%)	13 (38.2%)
Unemployed	11 (16.2%)	5 (14.7%)	6 (17.6%)
Educational level			
No formal education	8 (11.8%)	2 (5.9%)	6 (17.6%)
Primary school	22 (32.4%)	10 (29.4%)	12 (35.3%)
Secondary school	28 (41.2%)	16 (47.1%)	12 (35.3%)
Tertiary education	10 (14.7%)	6 (17.6%)	2 (11.8%)

Table 2 presents the comparison of mean cholesterol levels between patients with hemorrhagic and ischemic stroke. The mean cholesterol level for the hemorrhagic stroke group was 202.59 mg/dL (SD = 45.11), while for the ischemic stroke group, it was 190.26 mg/dL (SD = 50.55). The p-value of 0.42 indicates that there was no statistically significant difference in cholesterol levels between the two groups. The results suggest that cholesterol levels do not significantly differ between hemorrhagic and ischemic stroke patients in this study population. This finding may imply that cholesterol levels may not be a major discriminating factor in determining the type of stroke a patient may experience. However, it's important to note that cholesterol is a complex risk factor for cardiovascular disease in general, and this study does not negate its overall importance.

Table 2. Cholesterol levels and stroke subtype.

Stroke subtype	Mean cholesterol (mg/dL)	Standard deviation (mg/dL)	Number of patients	p-value
Hemorrhagic	202.59	45.11	34	0.420
Ischemic	190.26	50.55	34	

Table 3 explores the relationship between cholesterol levels and various stroke-related parameters, including stroke severity (NIHSS score), functional outcome (mRS at 3 months), and 30-day mortality, across hemorrhagic and ischemic stroke patients. While there appears to be a trend towards increased stroke severity (NIHSS score) in patients with hemorrhagic stroke compared to ischemic stroke, this difference did not reach statistical significance (p = 0.083). Similarly, a trend towards worse functional outcomes (mRS score) at 3 months was observed in the hemorrhagic stroke group compared to the ischemic stroke group, but this difference was also not statistically significant (p = 0.097). No statistically significant difference in 30-day mortality was found between the hemorrhagic and ischemic stroke groups (p = 0.412). The findings suggest that cholesterol levels may not be a strong independent predictor of stroke severity, functional outcome, or short-term mortality in this study population.

Table 3. Relationship between cholesterol levels and other stroke-related parameters.

Parameter	Hemorrhagic stroke (n=34)	Ischemic stroke (n=34)	p-value
Stroke severity (NIHSS)			
Mean ± SD	12.35 ± 6.42	9.88 ± 5.11	0.083
Functional outcome (mRS at 3 months)			
Mean ± SD	3.41 ± 1.85	2.65 ± 1.53	0.097
Mortality (30-day)			
Number (%)	5 (14.7%)	3 (8.8%)	0.412

The present study, conducted in a Central Javanese population, sought to elucidate the intricate relationship between cholesterol levels and stroke outcomes, with a particular focus on the association between cholesterol and stroke subtype (ischemic vs. hemorrhagic). The findings, while seemingly straightforward, open a window into the complex interplay of factors that contribute to stroke pathophysiology and clinical manifestations. The absence of a statistically significant association between cholesterol levels and stroke subtype in this cohort challenges conventional notions and underscores the need for a nuanced understanding of stroke risk factors in diverse populations. The relationship between cholesterol and stroke has been the subject of extensive research and debate, with the

prevailing theory suggesting a strong link between elevated cholesterol levels, particularly low-density lipoprotein cholesterol (LDL-C), and the development of atherosclerosis. Atherosclerosis, a chronic inflammatory disease characterized by the buildup of lipid-laden plaques within the arterial walls, is a major contributor to ischemic stroke. The progressive narrowing of the arterial lumen due to plaque accumulation can significantly impede blood flow, leading to cerebral ischemia and subsequent tissue damage. The oxidation of LDL-C within the plaque further exacerbates the inflammatory response, promoting plaque instability and rupture. This can trigger the formation of blood clots, which can then travel to the brain and occlude cerebral arteries, resulting in ischemic stroke.[11,12]

The association between cholesterol and hemorrhagic stroke, however, is less clear-cut and has been a source of ongoing investigation. Some studies have paradoxically suggested a potential protective effect of higher cholesterol levels against hemorrhagic stroke. This intriguing observation has led to the hypothesis that cholesterol may play a role in maintaining the structural integrity of blood vessel walls. Cholesterol is an integral component of cell membranes, including those of endothelial cells that line the inner surface of blood vessels. The presence of cholesterol within these membranes may contribute to their stability and resilience, potentially reducing the risk of rupture and subsequent hemorrhage. The findings of the present study, however, challenge this hypothesis by demonstrating no significant association between cholesterol levels and the occurrence of hemorrhagic stroke in the Central Javanese population. This discrepancy underscores the complexity of the relationship between cholesterol and stroke, highlighting the potential influence of various factors that may modulate this association. The heterogeneity of stroke populations, methodological variations across studies, and the intricate interplay of genetic and environmental factors can all contribute to the observed differences in findings. The absence of a clear association between cholesterol and hemorrhagic stroke in this study raises several important questions.[12,13]

Furthermore, the potential protective effect of cholesterol against hemorrhagic stroke, even if present, may be overshadowed by its well-established role in promoting atherosclerosis and ischemic stroke. The overall impact of cholesterol on stroke risk may therefore depend on the balance between its potential protective and detrimental effects, which may vary across individuals and populations. The complex relationship between cholesterol and stroke highlights the need for a comprehensive approach to stroke prevention and management. While the management of dyslipidemia remains an essential component of stroke prevention strategies, it is crucial to consider other risk factors and individual patient characteristics when formulating treatment plans. Personalized risk assessment and targeted interventions may be necessary to optimize stroke prevention and improve outcomes. Future research should focus on elucidating the mechanisms underlying the potential protective effect of cholesterol against hemorrhagic stroke. Investigating the role of cholesterol in maintaining endothelial integrity, modulating inflammation, and influencing blood vessel remodeling may provide valuable insights. Additionally, exploring the interaction between cholesterol and other risk factors, such as hypertension, diabetes, and smoking, may help identify individuals at higher risk of hemorrhagic stroke. The relationship between cholesterol and stroke is complex and multifaceted. While elevated cholesterol levels are a well-established risk factor for ischemic stroke, their association with hemorrhagic stroke remains controversial. The findings of the present study challenge the hypothesis of a protective effect of cholesterol against hemorrhagic stroke, highlighting the need for further research to unravel the intricate mechanisms underlying this relationship. A comprehensive understanding of the role of cholesterol in stroke pathophysiology is essential for developing effective prevention and treatment strategies that can reduce the burden of this devastating condition.[13,14]

The pathophysiology of stroke is indeed a complex cascade of events that ultimately lead to brain injury. The two main types of stroke, ischemic and

hemorrhagic, have distinct underlying mechanisms, but both result in the disruption of normal brain function. The role of cholesterol in these processes is an area of ongoing research, with potential implications for both prevention and treatment. Ischemic stroke, the most common type of stroke, occurs when a blood clot or atherosclerotic plaque obstructs a cerebral artery, impeding blood flow to a specific region of the brain. The resulting reduction in oxygen and nutrient delivery triggers a series of detrimental cellular and molecular events that can lead to irreversible brain damage. The brain is a highly metabolically active organ, requiring a constant supply of oxygen and glucose to maintain its function. The sudden cessation of blood flow deprives neurons of these vital substrates, leading to a rapid depletion of cellular energy stores. The failure of energy-dependent processes, such as ion pumps and neurotransmitter synthesis, disrupts neuronal signaling and ultimately leads to cell death. The lack of energy also impairs the function of glutamate transporters, leading to an excessive accumulation of glutamate in the extracellular space. Glutamate, the primary excitatory neurotransmitter in the brain, binds to its receptors and triggers an influx of calcium ions into neurons. The excessive calcium influx overwhelms the cell's buffering capacity, leading to the activation of various calcium-dependent enzymes that cause cellular damage. This process, known as excitotoxicity, is a major contributor to neuronal death in ischemic stroke. The restoration of blood flow to the ischemic brain, a process known as reperfusion, can paradoxically exacerbate tissue injury. The reintroduction of oxygen leads to the generation of reactive oxygen species (ROS), which can damage cellular components such as proteins, lipids, and DNA. The brain is particularly vulnerable to oxidative stress due to its high metabolic rate and relatively low antioxidant capacity. Ischemic stroke also triggers a robust inflammatory response, characterized by the activation of microglia and astrocytes, the resident immune cells of the brain. These cells release various pro-inflammatory cytokines and chemokines, which recruit additional immune cells from the periphery. While inflammation is initially a protective response aimed at clearing cellular debris and promoting tissue repair, excessive or prolonged inflammation can contribute to secondary brain damage.[15,16]

The extent of brain injury in ischemic stroke depends on several factors, including the duration and severity of ischemia, the location of the occlusion, and the presence of collateral blood flow. Collateral circulation, provided by alternative blood vessels that bypass the occlusion, can mitigate the effects of ischemia by maintaining a minimal level of blood flow to the affected region. The development of collateral circulation is influenced by various factors, including age, vascular health, and genetic predisposition. Hemorrhagic stroke, although less common than ischemic stroke, is associated with a higher mortality rate and often results in more severe neurological deficits. It occurs when a blood vessel in the brain ruptures, leading to bleeding within the brain tissue (intracerebral hemorrhage) or the spaces surrounding the brain (subarachnoid hemorrhage). The accumulation of blood within the confined space of the skull exerts pressure on the brain, leading to compression and displacement of vital structures. The blood itself can also be toxic to neurons, triggering a cascade of events that contribute to brain injury. The breakdown of red blood cells releases hemoglobin, which can generate free radicals and promote oxidative stress. The iron released from hemoglobin can also catalyze the formation of reactive oxygen species, further exacerbating oxidative damage. Additionally, the inflammatory response triggered by the presence of blood can lead to secondary brain injury. The clinical manifestations of hemorrhagic stroke depend on the location and extent of bleeding. Common symptoms include sudden onset of severe headache, nausea and vomiting, altered consciousness, and focal neurological deficits, such as weakness or numbness on one side of the body. The prognosis of hemorrhagic stroke is generally worse than that of ischemic stroke, with a higher risk of mortality and long-term disability.[16-18]

Cholesterol, a waxy substance found in the blood, plays a crucial role in various physiological processes, including cell membrane structure, hormone synthesis, and vitamin D production. However,

elevated levels of cholesterol, particularly LDL-C, have been implicated in the development of atherosclerosis, a major risk factor for ischemic stroke. In the context of ischemic stroke, the pathophysiological role of cholesterol is relatively well-established. Elevated LDL-C levels promote the formation of atherosclerotic plaques within the arterial walls, leading to progressive narrowing of the lumen and reduced blood flow. The oxidation of LDL-C within the plaque triggers an inflammatory response, further contributing to plaque instability and rupture. The release of thrombogenic material from the ruptured plaque can lead to the formation of a blood clot, which can occlude a cerebral artery and cause ischemic stroke. The relationship between cholesterol and hemorrhagic stroke is more complex and less well-understood. Some studies have suggested a potential protective effect of higher cholesterol levels against hemorrhagic stroke. This paradoxical association may be attributed to the role of cholesterol in maintaining the integrity of blood vessel walls. Cholesterol is an essential component of cell membranes, and its presence may contribute to the structural stability and resilience of the endothelium, the innermost layer of blood vessels. Higher cholesterol levels may therefore confer a degree of protection against the rupture of weakened blood vessels, a hallmark of hemorrhagic stroke. However, other studies have reported no significant association between cholesterol levels and hemorrhagic stroke, or even a potential detrimental effect. Elevated cholesterol levels may promote the formation of microaneurysms, small outpouchings of blood vessels that are prone to rupture. Additionally, hypercholesterolemia may contribute to hypertension, another major risk factor for hemorrhagic stroke. The findings of the present study, which showed no significant association between cholesterol levels and stroke subtype, add another layer of complexity to this ongoing debate. The absence of a clear association may be attributed to several factors, including the heterogeneity of stroke populations, methodological variations across studies, and the complex interplay of genetic and environmental factors that influence stroke risk.[17-19]

While cholesterol undoubtedly plays a role in stroke pathophysiology, it is important to recognize that stroke is a multifactorial disease. Several other modifiable and non-modifiable risk factors contribute to stroke risk, including hypertension, diabetes mellitus, smoking, obesity, physical inactivity, and genetic predisposition. The interplay between these risk factors is complex and not fully understood. Hypertension, or high blood pressure, is a major risk factor for both ischemic and hemorrhagic stroke. Elevated blood pressure exerts mechanical stress on the arterial walls, promoting the development of atherosclerosis and increasing the risk of plaque rupture. In hemorrhagic stroke, hypertension weakens the blood vessels, making them more susceptible to rupture. Diabetes mellitus, a metabolic disorder characterized by high blood sugar levels, is also associated with an increased risk of stroke. Chronic hyperglycemia can damage blood vessels, leading to atherosclerosis and endothelial dysfunction. Diabetes also increases the risk of other stroke risk factors, such as hypertension and dyslipidemia. Smoking is a potent risk factor for stroke, increasing the risk of both ischemic and hemorrhagic subtypes. Smoking damages the endothelium, promotes inflammation, and increases blood clotting, all of which contribute to stroke risk. Obesity and physical inactivity are additional modifiable risk factors for stroke. Obesity increases the risk of other stroke risk factors, such as hypertension, diabetes, and dyslipidemia. Physical inactivity reduces cardiovascular fitness and contributes to obesity, further increasing stroke risk. Genetic predisposition also plays a role in stroke risk. Several genes have been identified that influence cholesterol metabolism, blood pressure regulation, and other factors that contribute to stroke. However, the genetic contribution to stroke risk is complex and involves the interaction of multiple genes with environmental factors. The pathophysiology of stroke is a complex and dynamic process, involving a cascade of events that ultimately lead to brain injury. The two main types of stroke, ischemic and hemorrhagic, have distinct underlying mechanisms, but both result in the disruption of normal brain function. The role of cholesterol in these

processes is an area of ongoing research, with potential implications for both prevention and treatment. While elevated cholesterol levels are a well-established risk factor for ischemic stroke, their association with hemorrhagic stroke is less clear. The findings of the present study, which showed no significant association between cholesterol levels and stroke subtype, highlight the complexity of stroke risk factors and the need for personalized risk assessment and treatment approaches.[19,20]

The present study opens several avenues for future research. Prospective cohort studies are needed to establish the temporal relationship between cholesterol levels and stroke risk. Longitudinal studies would allow for the assessment of changes in cholesterol levels over time and their impact on stroke incidence and outcomes. Additionally, investigations into the interplay between cholesterol and other risk factors, such as hypertension, diabetes, and smoking, would enhance our understanding of the complex etiology of stroke. Further research is also warranted to explore the impact of cholesterol on specific stroke outcomes, such as functional disability, cognitive impairment, and quality of life. The identification of biomarkers that predict stroke outcomes and response to treatment would facilitate personalized medicine approaches. Finally, the development of novel therapeutic strategies targeting cholesterol metabolism and its downstream effects on stroke pathophysiology holds promise for improving stroke prevention and treatment. The use of statins, medications that lower cholesterol levels, has been shown to reduce the risk of ischemic stroke in some populations. However, their efficacy in preventing hemorrhagic stroke remains controversial. Further research is needed to identify new therapeutic targets and develop more effective interventions for both ischemic and hemorrhagic stroke.

4. Conclusion

The study provides valuable insights into the relationship between cholesterol levels and stroke outcomes in a Central Javanese population. The findings challenge conventional notions and underscore the complexity of stroke risk factors. While cholesterol may not be a primary determinant of stroke subtype in this population, it remains an important modifiable risk factor for cardiovascular disease and stroke.

5. References

1. Benjamin EJ, Virani SS, Callaway CW. Heart disease and stroke statistics—2018 update: a report from the American Heart Association. Circulation. 2018; 137(12): e67-e492.
2. Feigin VL, Norrving B, Mensah GA. Global burden of stroke. Circ Res. 2018; 120(3): 439-48.
3. O'Donnell MJ, Chin SL, Rangarajan S. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. Lancet. 2018; 388(10046): 761-75.
4. Powers WJ, Rabinstein AA, Ackerson T. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2018; 49(3): e46-e110.
5. Campbell BC, Mitchell PJ, Kleinig TJ. Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med. 2018; 372(11): 1009-18.
6. Boehme AK, Esenwa C, Elkind MSV. Stroke risk factors, genetics, and prevention. Circ Res. 2018; 120(3): 472-95.
7. Kernan WN, Ovbiagele B, Black HR. Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2014; 45(7): 2160-236.
8. Sacco RL, Kasner SE, Broderick JP. An updated definition of stroke for the 21st century: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2013; 44(7): 2064-89.

9. GBD 2016 Stroke Collaborators. Global, regional, and national burden of stroke, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol. 2019; 18(5): 439-58.
10. Thrift AG, Thayabaranathan T, Howard G. Global stroke statistics. Int J Stroke. 2017; 12(2): 133-42.
11. Mozaffarian D, Benjamin EJ, Go AS. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. Circulation. 2016; 133(4): e38-e360.
12. Goldstein LB, Bushnell CD, Adams RJ. Guidelines for the primary prevention of stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011; 42(2): 517-84.
13. Saver JL. Time is brain—quantified. Stroke. 2006; 37(1): 263-6.
14. Heuschmann PU, Busse O, Wagner M. Frequency and prognostic significance of hypercholesterolemia in acute ischemic stroke subtypes. Stroke. 2004; 35(4): 857-62.
15. Amarenco P, Bogousslavsky J, Callahan A. High-dose atorvastatin after stroke or transient ischemic attack. N Engl J Med. 2006; 355(6): 549-59.
16. Mackenzie IS, Smith G, and Cairns JA. Cholesterol and recurrent stroke. Stroke. 1992; 23(10): 1399-403.
17. Sacco RL, Benson RT, Kargman DE. High-density lipoprotein cholesterol and ischemic stroke in the elderly: the Northern Manhattan Stroke Study. JAMA. 1994; 272(23): 1813-8.
18. Iso H, Jacobs DR, Wentworth D. Serum cholesterol levels and six-year mortality from stroke in 350,977 men screened for the multiple risk factor intervention trial. N Engl J Med. 1989; 320(14): 904-10.
19. Gillum RF, Mussolino ME, and Madans JH. Body mass index and stroke incidence in women and men: The NHANES I Epidemiologic Follow-up Study. Am J Epidemiol. 1998; 147(11): 1024-33.
20. Wannamethee SG, Shaper AG, and Walker M. Changes in physical activity, mortality, and incidence of coronary heart disease and stroke in elderly men. Lancet. 1998; 351(9116): 1687-92.