Hypertension, Smoking, and Genetic Predisposition as Key Predictors of Stroke: A Cross-Sectional Study

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ABSTRACT

Stroke remains a leading global cause of death and long-term disability, with a disproportionately rising burden in developing countries. Both personal traits and medical history are key factors influencing stroke risk. This study aimed to explore the relationship between age, gender, hypertension, diabetes mellitus, smoking habits, and genetic background with stroke occurrence. A quantitative cross-sectional study was carried out among hospital patients chosen through purposive sampling. Data were collected from medical records and structured interviews, then analyzed using the Chi-square test with a significance level of $p < 0.05$. Hypertension ($p = 0.044$), smoking ($p = 0.032$), and genetic history ($p = 0.012$) were significantly associated with stroke incidence. In contrast, age ($p = 0.066$), gender ($p = 0.062$), and diabetes mellitus ($p = 0.130$) showed no significant association. These findings emphasize hypertension, smoking, and genetic predisposition as primary factors for stroke. Improving control of risk factors, especially managing blood pressure and quitting smoking, should be a top priority to effectively lower stroke occurrence and recurrence.

Kata kunci: predictors stroke; hypertension; smoking; genetic

INTRODUCTION

Stroke remains one of the leading causes of death and disability worldwide. According to the World Health Organization (WHO), stroke is the second leading cause of death globally, responsible for about 11% of all deaths (Kuriakose & Xiao, 2020; Feigin et al., 2022). In Indonesia, the prevalence of stroke has steadily increased, from 7 per 1,000 people in 2013 to 10.9 per 1,000 in 2018 (Kemenkes, 2023). Stroke leads to significant disability and loss of physical abilities, including paralysis, communication issues, cognitive decline, and dependence in daily activities (Franco-Urbano et al.,

2022;Amin et al., 2024). Prior research has shown that stroke incidence is affected by a combination of personal traits and medical history. Individual characteristics such as age, gender, and genetic factors significantly influence susceptibility to stroke. Advanced age is the most prominent risk factor, with stroke risk rising sharply after age 55 (Feigin et al., 2020). Furthermore, men are reported to have a higher risk of stroke during their working years, although women tend to experience higher mortality rates in older age groups (Tsai et al., 2022).

Conversely, medical history factors such as hypertension, diabetes mellitus, smoking habits, and cardiovascular diseases are modifiable risk factors (Debette & Markus, 2022; Owolabi et al., 2022). Hypertension is the leading contributor, responsible for over 50% of stroke cases (Wajngarten & Silva, 2019; Feigin et al., 2020). Diabetes mellitus raises stroke risk through mechanisms like atherosclerosis and endothelial dysfunction (Zhang et al., 2017). Smoking worsens vascular health by increasing oxidative stress and systemic inflammation, markedly raising the risk of ischemic stroke (Pan et al., 2019).

Despite extensive global research on stroke risk factors, there remains a gap in context-specific studies at the local level, especially within regional healthcare facilities. Most previous studies have focused on isolated risk factors, thus failing to offer a comprehensive understanding of how individual characteristics and medical history interact and relate to stroke incidence. Additionally, differences in population characteristics, cultural factors, and healthcare access in Indonesia highlight the need for more tailored research.

RSUD H.A. Sulthan Daeng Radja Bulukumba, as a referral hospital in South Sulawesi, manages a large number of stroke patients with varied characteristics and clinical conditions. Based on medical record data, the number of stroke patients has increased in recent years. Therefore, this study is important for examining the relationship between individual characteristics, medical history, and stroke incidence.

MATERIALS AND METHODS

This study used a quantitative cross-sectional design, where both independent and dependent variables were measured at the same time point (Sugiyono, 2019). The study population included post-stroke patients treated at RSUD H.A. Sulthan Daeng Radja Bulukumba. A total of 89 respondents were selected using a consecutive sampling method, in which all individuals who met the inclusion criteria were recruited until the

required sample size was reached. The inclusion criteria were as follows: Patients aged ≥30 years, Willingness to participate as respondents, Ability to communicate effectively, Availability of complete medical records.

Data collection was conducted from April to July 2025 at the Neurology Outpatient Clinic. Data were obtained from medical records and direct data collection sheets, particularly for variables such as genetic history and smoking behavior. Data analysis comprised both descriptive and inferential statistical methods. Descriptive (univariate) analysis was used to characterize the respondents, while inferential (bivariate) analysis was conducted to assess associations among the study variables. Statistical analysis was performed using SPSS version 22. The Chi-Square test was applied for bivariate analysis, while Fisher's Exact test was used when Chi-Square assumptions were not met. A significance level of $p < 0.05$ was applied.

This study received ethical approval from RSUD H.A. Sulthan Daeng Radja Bulukumba (No: 800.2/010/RSUD-BLK/2025). Data collection was conducted after obtaining permission from the hospital's ethics committee. Informed consent was obtained from all respondents who met the inclusion criteria.

RESULTS

Most respondents were elderly (85.4%), female (52.8%), unemployed (51.7%), and had a low level of education (47.2%). A total of 89 respondents participated in this study. The distribution of respondent characteristics is presented below:

Table 1. Distribution Characteristic Respondent (n=89)

Characteristics	Frequency (N)	Percentage (%)
Age		
- Adults	13	14,6
- Elderly	76	85,4
Gender		
- Male	42	47,2
- Female	47	52,8
Employment Status		
- Employed	43	48,3
- Unemployed	46	51,7
Education Level		
- Low (No school–Primary)	47	47,2
- Middle (Junior–Senior High)	26	29.2
- Higher (Diploma–Bachelor)	16	18
Total	**89**	**100**

Most respondents had a history of hypertension (88.8%), while 40.4% had diabetes mellitus. More than half reported a family history of genetic disease (56.2%), and 39.3% were smokers.

Table 2. Distribution of Medical History (n=89)

Variable	Frequency (N)	Percentage (%)
Hipertension History		
- Yes	79	88,8
- No	10	11,2
Diabetes Mellitus History		
- Yes	36	40,4
- No	53	59,6
Genetic History		
- Yes	50	56,2
- No	39	43,8
Smoking Behavior		
- Smoker	35	39,3
- Non Smoker	54	60,7
Stroke Incidence		
- First Occurrence	53	59,6
- Recurrent	36	40,4
Total	**89**	**100**

The bivariate analysis revealed that hypertension (p = 0.044), genetic predisposition (p = 0.012), and smoking behavior (p = 0.032) were significantly associated with stroke occurrence. Conversely, no statistically significant associations were observed for age (p = 0.066), sex (p = 0.662), or history of diabetes mellitus (p = 0.13).

Table 3. Characteristics of Respondents, and Health History with Stroke Incidence (n=89)

Variable	Stroke Incidence				Total		OR	95% CI	*p*-value
	First Stroke	%	Recurrent Stroke	%	n	%			
Age									
- Elderly	42	55,3	34	44,7	76	100	4,452	0,923–21,466	
- Adults	11	84,6	2	15,4	13	100	ref	3,27 (1,38-7,76)	0.066[1]
Gender									
- Female	29	61,7	18	38,3	47	100	0,828	0,354–1,933	
- Male	24	57,1	18	42,9	42	100	ref	-	0.662[2]

Hypertension History									
- Yes	44	55,7	35	44,3	79	100	7,159	0,865–59,238	
- No	9	90	1	10	10	100	ref	-	*0.044*[1]*
Diabetes Mellitus History									
- Yes	18	50	18	50	36	100	1,944	0,818–4,623	
- No	35	66	18	34	53	100	ref	-	0.130[2]
Genetic History									
- Yes	24	48	26	52	50	100	3,142	1,267–7,789	
- No	29	74,4	10	25,6	39	100	ref	-	*0.012*[2]*
Smoking Behavior									
- Smoker	16	45,7	19	54,3	35	100	2,585	1,073–6,223	
- Non Smoker	37	68,5	17	31,5	54	100	ref	-	*0.032*[2]*
Total					**89**	**100**			

Notes:
OR = Odds Ratio; CI = Confidence Interval
[1] Fisher's Exact Test
[2] Chi-square test
*$p < 0.05$ indicates statistical significance

DISCUSSION

The findings showed no statistically significant link between age and stroke incidence ($p = 0.066$), although the elderly group had a higher proportion of recurrent stroke overall. This indicates that even without statistical significance, a clinically important trend remains evident (Amin et al., 2025). Biologically, aging is associated with progressive vascular degeneration, arterial stiffness, endothelial dysfunction, and the accumulation of atherosclerotic plaques. Stroke risk increases substantially after the age of 55–60 and doubles with each subsequent decade (Feigin et al., 2023). Elderly individuals are also more likely to have comorbid conditions such as hypertension and cardiovascular disease, further increasing stroke risk (Katan & Luft, 2018;Campbell et al., 2019).

Global studies show that after controlling for other risk factors, age remains an independent predictor of stroke (Wang et al., 2024). Sadlonova et al., (2021) study found that stroke incidence is higher in men in young and middle age, but this difference diminishes with age, and this pattern is consistent across populations. The lack of statistical significance in this study may be attributed to the homogeneous sample distribution, with most respondents classified as elderly. This reduces variability and

weakens statistical power (Rae et al., 2025). Selain itu, kategorisasi usia yang sederhana dapat mengurangi sensitivitas analisis dalam mendeteksi peningkatan risiko secara bertahap (Feigin et al., 2022; WHO, 2022).

No significant relationship was found between gender and stroke incidence ($p = 0.662$), indicating relatively equal risk between males and females in this population. Globally, stroke risk differs by gender, with men having higher incidence at younger ages and women experiencing higher mortality at older ages (Tsai et al., 2022). However, recent studies suggest that these differences are narrowing due to similar lifestyle patterns and risk exposures (Feigin et al., 2023). Epidemiologically, the relationship between gender and stroke shows a complex pattern and depends on age group. Meta-analyses have shown that gender differences in stroke incidence are not always significant when confounding variables are controlled (Weber et al., 2022). Foschi et al., (2024), found that men have a higher incidence of stroke in young to middle age, but this difference narrows in older age.

The findings suggest that non-gender-related factors such as hypertension, genetics, and smoking may play a more dominant role in determining stroke incidence in this population (Tsai et al., 2022;Suñer-Soler et al., 2024).

The Chi-Square analysis revealed a statistically significant association between smoking habits and stroke incidence ($p = 0.032$; OR = 2.585). Smokers were approximately 2.6 times more likely to experience recurrent stroke compared to non-smokers, indicating that smoking is a substantial modifiable risk factor in this population. Smoking contributes to stroke through multiple complex and interrelated biological mechanisms (Pan et al., 2019; Khan et al., 2023). Exposure to cigarette toxins leads to endothelial dysfunction, increased platelet aggregation, elevated plasma fibrinogen levels, and acceleration of atherosclerosis. In addition, smoking promotes chronic inflammation and oxidative stress, which further damages vascular integrity and impairs cerebral blood flow regulation. These processes collectively increase the likelihood of thrombus formation and cerebral embolism (Alhindal et al., 2025).

Pan et al., (2019), reported that smoking increases the risk of ischemic stroke by approximately 50% and hemorrhagic stroke by up to 80%. Similarly, a large population-based health survey conducted by Ding et al., (2025) found that smokers had a 1.71-fold higher risk of stroke compared to non-smokers. Furthermore, Wang et al., (2024) demonstrated a dose–response relationship, where stroke risk increases with both the

intensity and duration of smoking exposure. Notably, passive smokers are also at elevated risk, highlighting the broader public health implications of tobacco exposure. Smoking is also associated with the earlier onset of stroke, particularly among younger populations (Khan et al., 2023). This suggests that smoking not only increases the likelihood of stroke but may also accelerate the progression of vascular damage, leading to premature cerebrovascular events.

The relatively high odds ratio observed in this study indicates that smoking plays a critical role in stroke recurrence. This may be attributed to the cumulative and persistent vascular damage caused by long-term tobacco exposure, even after the first stroke event. Continued smoking after an initial stroke can hinder vascular recovery, increase the risk of secondary events, and worsen overall prognosis. From a clinical and public health perspective, these findings underscore the urgent need for effective smoking cessation interventions as part of comprehensive stroke prevention strategies. Integrating behavioral counseling, pharmacological support, and long-term follow-up into stroke management programs may significantly reduce recurrence risk. Additionally, public health policies aimed at reducing tobacco exposure, including secondhand smoke, are essential in mitigating the overall burden of stroke.

Genetic history demonstrated a significant association with stroke incidence ($p = 0.012$; $OR = 3.142$), indicating that individuals with a family history of stroke had more than three times the risk of experiencing recurrent stroke. Genetic predisposition is a non-modifiable risk factor reflecting underlying biological susceptibility. This susceptibility may arise directly from genetic variants associated with stroke or indirectly through inherited conditions such as hypertension and diabetes mellitus. Recent large-scale genetic studies, including Genome-Wide Association Studies (GWAS), have identified more than 30 genetic loci associated with stroke risk, particularly those involved in blood pressure regulation, lipid metabolism, endothelial function, and coagulation pathways (Malik et al., 2018; Debette & Markus, 2022). Family history has been shown to increase stroke risk by approximately 1.3 to 1.8 times, with stronger effects observed in early-onset stroke cases (Rutten-Jacobs et al., 2018). Importantly, gene–environment interactions play a crucial role, as healthy lifestyle behaviors can significantly attenuate genetic risk (Boehme et al., 2017;Yoshimoto et al., 2025). The relatively high odds ratio observed in this study suggests that genetic history acts as an independent and strong predictor of recurrent stroke, even after accounting for other

variables. This finding underscores the importance of incorporating family history into stroke risk assessment and prevention strategies.

Hypertension was found to have a significant relationship with stroke incidence ($p = 0.044$; $OR = 7.159$), making it the most dominant risk factor identified in this study. This finding is consistent with global evidence identifying hypertension as the leading modifiable risk factor for stroke, contributing to more than half of all cases worldwide (Feigin et al., 2020; WHO., 2023). From a pathophysiological perspective, chronic hypertension damages the vascular endothelium through sustained mechanical stress. This leads to endothelial dysfunction, smooth muscle proliferation, collagen deposition, and atherosclerotic plaque formation (Webb & Werring, 2022). In severe cases, hypertension can cause fibrinoid necrosis in small cerebral arteries, contributing to lacunar stroke. Additionally, activation of the renin–angiotensin–aldosterone system (RAAS) contributes to left ventricular hypertrophy, atrial fibrillation, and increased risk of cerebral embolism (Hall & Hall, 2020). Evidence from systematic reviews and meta-analyses indicates that hypertension increases stroke risk by approximately 1.3 to 2.1 times compared to normotensive individuals (Mohammad et al., (2025).

The markedly high odds ratio observed in this study suggests a strong association between uncontrolled hypertension and recurrent stroke (George, 2020). This highlights the critical importance of early detection, strict blood pressure control, and long-term adherence to antihypertensive therapy in preventing stroke recurrence (Amin, 2018;Im Ryu et al., 2024).

The findings revealed no significant relationship between diabetes mellitus and stroke incidence ($p = 0.130$). This result is noteworthy, as it contrasts with the broader body of literature that consistently identifies diabetes mellitus as a significant risk factor for stroke (Bai et al., 2024; Noh, 2025). Theoretically, diabetes mellitus increases stroke risk through multiple mechanisms, including chronic hyperglycemia, protein glycation, oxidative stress, vascular inflammation, endothelial dysfunction, and accelerated atherosclerosis (Tombong & Amin, 2021; Noh, 2025). Previous studies have shown that individuals with diabetes have a 1.5–2 times higher risk of stroke compared to non-diabetic individuals (Mosenzon et al., 2023). The lack of statistical significance in this study may be attributed to an imbalance in sample distribution, in which the proportion of respondents without diabetes (59.6%) was higher than that of those with diabetes (40.4%).

This imbalance may have reduced the statistical power of the analysis. Additionally, the duration and severity of diabetes were not assessed in this study, which may have influenced the results. Previous research has demonstrated that a longer duration of diabetes (≥15 years) is significantly associated with increased stroke risk Gao et al., (2025). Therefore, future studies should consider including duration and glycemic control indicators to better capture the impact of diabetes on stroke incidence.

CONCLUSIONS

This study demonstrates that hypertension, smoking habits, and genetic history are significantly associated with stroke incidence. Hypertension emerged as the most dominant risk factor ($p = 0.044$; $OR = 7.159$), followed by genetic history ($p = 0.012$; $OR = 3.142$) and smoking behavior ($p = 0.032$; $OR = 2.585$).

In contrast, age, gender, and diabetes mellitus were not significantly associated with stroke incidence in this study. However, these variables may still be clinically relevant and should not be overlooked in comprehensive stroke risk assessment. These findings emphasize the importance of controlling modifiable risk factors, particularly hypertension and smoking, through targeted prevention strategies. Strengthening vascular health monitoring, improving treatment adherence, and promoting healthy lifestyle behaviors are essential steps in reducing stroke incidence and recurrence. Furthermore, individuals with a family history of stroke require closer monitoring due to their increased risk. A comprehensive, multidisciplinary approach is needed to effectively manage both modifiable and non-modifiable risk factors in stroke prevention.

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