

Association Of Hypertension And Diabetes Mellitus With Recurrent Stroke In Post-Stroke Patients

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Abstract

Introduction: Stroke remains a global health problem with high mortality and morbidity rates worldwide. Post-stroke patients who do not manage risk factors well are at high risk of recurrent stroke. Recurrent stroke has a more fatal impact with higher mortality rates, the risk of more serious severity and worse neurological disorders that can affect the economic conditions and patient quality of life. This study aimed to analyze the association of hypertension and diabetes mellitus with the incidence of recurrent stroke in post-stroke patients.

Methods: This study was conducted at RSD dr. Soebandi Jember using a case-control design with 54 patients in the case group and 108 patients in the control group selected by simple random sampling. Data collection used hospital medical records and data analysis was performed univariate, bivariate and multivariate.

Results: The results of bivariate analysis showed a significant association between age and diabetes mellitus with recurrent stroke ($p\text{-value} < 0,05$). Multivariate analysis showed that age, hypertension, and diabetes mellitus had an effect on recurrent stroke, with diabetes mellitus as the main determinant of recurrent stroke.

Conclusion: Diabetes mellitus is the main determinan of recurrent stroke in post-stroke patients, followed by hypertension and age.

Keywords: Recurrent stroke, Risk factors, Post-stroke, Hypertension, Diabetes mellitus

Hubungan Hipertensi Dan Diabetes Melitus Dengan Kejadian Stroke Berulang Pada Pasien Pasca-Stroke

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Abstrak

Pendahuluan: Stroke masih menjadi masalah kesehatan global dengan angka mortalitas dan morbiditas yang tinggi di seluruh dunia. Pasien pasca-stroke yang tidak mengelola faktor risiko dengan baik berisiko tinggi mengalami stroke berulang. Stroke berulang memiliki dampak yang lebih fatal dengan tingkat kematian yang lebih tinggi, risiko keparahan yang lebih serius dan gangguan neurologis yang lebih buruk yang dapat berpengaruh terhadap kondisi ekonomi dan kualitas hidup pasien. Tujuan penelitian ini adalah untuk menganalisis hubungan hipertensi dan diabetes melitus dengan kejadian stroke berulang pada pasien pasca-stroke.

Metode: Penelitian ini dilakukan di RSD dr. Soebandi Jember menggunakan desain case-control dengan 54 pasien pada kelompok kasus dan 108 pasien pada kelompok kontrol yang dipilih menggunakan simple random sampling. Pengumpulan data menggunakan data rekam medis dan analisis data dilakukan secara univariat, bivariat dan multivariat.

Hasil: Hasil analisis bivariat menunjukkan terdapat hubungan yang signifikan antara usia dan diabetes melitus dengan kejadian stroke berulang ($p\text{-value} < 0,05$). Analisis multivariat menunjukkan bahwa usia, hipertensi, dan diabetes melitus berpengaruh terhadap kejadian stroke berulang, dengan diabetes melitus sebagai determinan utama stroke berulang.

Kesimpulan: Diabetes melitus merupakan determinan utama stroke berulang pada pasien pasca-stroke, diikuti dengan hipertensi dan usia.

Kata kunci: Stroke berulang, Faktor risiko, Pasca-stroke, Hipertensi, Diabetes melitus

Introduction

Stroke remains a global health problem with high mortality and morbidity rates worldwide. Data from World Stroke Organization (WSO) shows an increase in the Case Fatality Rate (CFR) due to stroke by 13,18%, from 40,42% in 2016 to 53,6% in 2019.^{1,2} Based on the Indonesian Health Survey (SKI) 2023, the prevalence of stroke cases based on a doctor's diagnosis in the population aged ≥ 15 years in Indonesia reached 8,3%, while in East Java Province showed a higher rate of 9,0%.³ This high prevalence rate indicates a significant burden of stroke disease and needs to be a concern not only related to the increase in the number of new cases, but also the risk of recurrence or what is known as recurrent stroke.

Recurrent stroke is a condition where a person experiences a second or more stroke attacks that occur within a certain period of time after the first attack.⁴ Every year, almost 1 in 4 stroke patients experience recurrent stroke.⁵ Recurrent stroke can occur especially in patients who do not manage risk factors well.⁶ Recurrent stroke has a more fatal impact than the first stroke. A study by Mardiana et al. in 2021 states that patients with recurrent stroke have worse outcomes with moderate to severe stroke severity. The higher the frequency of stroke, the more the widespread brain damage will be, resulting in the onset of new and worse symptoms.⁷ Recurrent stroke also has a higher mortality rate, the risk of more serious severity and long-term disability that can affect the economic conditions and patients quality of life.⁸⁻¹⁰

A factor that contributes to the incidence of recurrent stroke is the presence of comorbidities, especially hypertension and diabetes mellitus. These two conditions are common modifiable risk factors, which if not managed properly can increase the occurrence of recurrent stroke in patients who have had a previous stroke. Hypertension is recognized as a major risk factor for stroke, both in first and recurrent attacks. High blood pressure can cause an increased load on the blood vessel wall, which exacerbates the process of atherosclerosis and increases the risk of rupture or blockage of cerebral blood vessels.¹¹⁻¹⁴ Previous studies have found that patients with uncontrolled hypertension have 2 to 3 times the risk of recurrent stroke compared to those with controlled hypertension.^{14,15} In addition, diabetes mellitus is also a significant risk factor contributing to the incidence of recurrent stroke in post-stroke patients. Diabetes mellitus causes chronic hyperglycemia which can damage blood vessels and accelerate the process of atherosclerosis which can then lead to an increased risk of recurrent stroke. Research by Uzuner & Uzuner showed stroke patients with diabetes mellitus had a 2,16 times higher risk of recurrent stroke compared to patients without diabetes mellitus.¹⁶ Therefore, controlling risk factors is important to prevent recurrent stroke and to minimize health, social and economic impact.

Soebandi Jember Regional Hospital (RSD) is a type B hospital that is a referral center in the eastern region of East Java. This hospital has a high rate of stroke cases in Jember Regency in 2023 and shows an increase of 23,27% from the previous year. In addition, the stroke mortality rate ≥ 48 hours in RSD dr. Soebandi Jember is still relatively high. The mortality rate in recurrent stroke patients reaches 28,4%, higher than that of first stroke patients who have a mortality rate of 13,7%. This condition indicates that patients with recurrent stroke have worse clinical outcomes and a high fatality rate. This study aimed to analyzing the association of hypertension and diabetes mellitus with the incidence of recurrent stroke at RSD dr. Soebandi Jember.

Method

This study was an observational analytic study with a case-control design. The case population in this study were all stroke patients who were recorded as having recurrent stroke at RSD dr. Soebandi Jember in 2023. The control population in this study were all stroke patients who were recorded

as having a first stroke at RSD dr. Soebandi Jember in 2023. The ratio used in this study was 1:2, with 54 case samples and 108 control samples. Sampling was conducted with simple random sampling using excel. Data collection used in this study used secondary data obtained through hospital medical record data. Data analysis was performed using univariate, bivariate and multivariate analysis. Bivariate analysis used the chi-square test to determine the relationship between the dependent variable (recurrent stroke) and the independent variables (gender, age, hypertension and diabetes mellitus). A significant relationship occurs if the p-value $< 0,05$ and then the magnitude of significance is supported by the OR and CI values listed. Variables in the bivariate analysis with p-value $< 0,25$ will be selected as candidate models for multivariate analysis conducted using logistic regression analysis. This study has obtained an ethical review certificate from the Health Research Ethics Commission of the Faculty of Public Health, University of Jember with No. 503/KEPK/FKM-UNEJ/V/2024.

Result

The distribution of stroke patient in the case group (recurrent stroke patients) as many as 54 patients and the control group (first stroke patients) as many as 108 patients based on age, gender, hypertension and diabetes mellitus is presented in Table 1.

Table 1. Distribution of Patient Based on Age, Gender, Hypertension and Diabetes Mellitus

Variable	Cases		Control	
	n	%	n	%
Age				
≥ 60 years	30	55,6	41	38,0
< 60 years	24	44,4	67	62,0
Gender				
Male	26	48,1	59	54,6
Female	28	51,9	49	45,4
Hypertension				
Uncontrolled hypertension	45	83,3	76	70,4
Controlled hypertension	9	16,7	32	29,6
Diabetes Mellitus				
DM	24	44,4	29	26,9
Not DM	30	55,6	79	73,1

Based on Table 1. most of the recurrent stroke patients at RSD dr. Soebandi Jember were aged ≥ 60 years as many as 30 patients (55,6%), were female as many as 28 patients (51,9%), had uncontrolled hypertension as many as 45 patients (83,3%), and had diabetes mellitus as many as 24 patients (44,4%).

interval of 1,301 – 5,611 meaning that stroke patients with diabetes mellitus have a 2,702 fold risk of recurrent stroke compared to patients without diabetes mellitus.

Table 2. Relationship Between Age, Gender, Hypertension and Diabetes Mellitus with the Incidence of Recurrent Stroke at RSD dr. Soebandi Jember

Variable	Cases		Control		p-value	OR	95% CI		
	n	%	n	%			Lower	Upper	
Age									
≥ 60 years	30	55,6	41	38,0	0,050	2,043	1,053	3,963	
< 60 years	24	44,4	67	62,0					
Gender									
Male	26	48,1	59	54,6	0,519	0,771	0,401	1,484	
Female	28	51,9	49	45,4					
Hypertension									
Uncontrolled hypertension	45	83,3	76	70,4	0,110	2,105	0,921	4,810	
Controlled hypertension	9	16,7	32	29,6					
Diabetes Mellitus									
DM	24	44,4	29	26,9	0,038	2,179	1,099	4,323	
Not DM	30	55,6	79	73,1					

Based on Table 2. bivariate analysis in this study showed that the variables of age ($p=0,05$) and diabetes mellitus ($p=0,038$) had a significant association with the incidence of recurrent stroke because it had a p -value $< 0,05$. However, the variables of gender ($p=0,519$) and hypertension ($p=0,110$) had not significant relationship with the incidence of recurrent stroke because it has a p -value $> 0,05$.

Table 3. Final Model of Multivariate Analysis

Variable	p-value	OR	95% CI
Age	0,018	2,321	1,157 - 4,658
Hypertension	0,034	2,597	1,077 - 6,265
Diabetes Mellitus	0,008	2,702	1,301 - 5,611

Based on Table 3. multivariate analysis, the factors that significantly determine the incidence of recurrent stroke are age, hypertension, and diabetes mellitus with diabetes mellitus as the main determinant of recurrent stroke in post-stroke patients. The OR value of diabetes mellitus is 2,702 with a confidence

Discussion

The results showed a association between age and the incidence of recurrent stroke at RSD dr. Soebandi Jember. The results of this study are in line with previous research which states that there is a significant relationship between age and the incidence of recurrent stroke.⁹ This increase in age can cause vascular degeneration processes such as increased vascular stiffness, decreased elasticity, and endothelial dysfunction that can lead to inflammation and atherosclerosis. Atherosclerosis can continue to progress with age and in post-stroke patients can exacerbate previous damage. As a result, blood vessels become narrower and can lead to recurrent stroke.^{17,18} In hemorrhagic stroke, the aging process causes structural changes that can weaken the blood vessel wall. This makes the blood vessels more prone to rupture and bleeding in the brain as blood pressure changes.¹⁹ In addition, the aging process also reduces the body's ability to regenerate brain cells. In patients with advanced age, the regeneration of brain cells and tissues is slower. As a result, brain tissue that has been damaged by a previous stroke cannot fully recover, making

it more susceptible to subsequent strokes.^{18,20}

This study showed that there was no significant association between gender and the incidence of recurrent stroke at RSD dr. Soebandi Jember. The no significant difference between gender and the incidence of recurrent stroke indicates that both have the same risk of experiencing recurrent stroke. The results of this study are supported by the research of Firuza et.al. which states that both men and women have almost the same risk of recurrent stroke.²¹ Men generally experience stroke at an earlier age than women. This risk is influenced by men's tendency towards risk behaviors such as smoking and alcohol consumption which can accelerate the process of atherosclerosis and increase blood pressure.^{17,18} In addition, high testosterone and low estrogen levels may exacerbate inflammation and vascular damage, further contributing to the increased risk of recurrent stroke in both types of stroke.²² However, other studies have found that women are also at risk of recurrent stroke, especially after entering menopause due to a decrease in estrogen.²³

Hypertension variable in bivariate analysis showed no significant association with the incidence of recurrent stroke at RSD dr. Soebandi Jember. Although hypertension is a risk factor for stroke in general, its impact can also vary depending on duration, management, treatment compliance, and the persistence of other risk factors. Recurrent stroke is a multifactorial disease, so it is possible that there is an impact of other factors that are more dominant or more complex that affect the risk of recurrent stroke. However, multivariate analysis showed that hypertension had a significant correlation with recurrent stroke after controlling for age and diabetes mellitus. This finding is in line with previous studies which state that hypertension is a risk factor for recurrent stroke, because high blood pressure can cause stress on blood vessels and accelerate damage to cerebral blood vessels which can increase the risk of re-occlusion or re-hemorrhage.^{11,13,24} Previous studies have also stated that patients with uncontrolled hypertension are more at risk of recurrent stroke compared to patients who have normal or controlled blood pressure.¹²

This study found a significant association between diabetes mellitus and the incidence of recurrent stroke at RSD dr. Soebandi Jember. The results of this study are in line with previous research that states diabetes mellitus is a significant risk factor contributing to the incidence of recurrent stroke in

post-stroke patients.^{14,16} Chronic hyperglycemia causes endothelial damage to blood vessels through the process of increasing the production of free radicals such as Reactive Oxygen Species (ROS) which can cause oxidative stress that can lead to increased atherosclerotic plaque formation. This process then causes cerebral blood vessels to become more susceptible to blockage and increases the risk of recurrent stroke in post-stroke patients. Uzuner & Uzuner's study showed stroke patients with diabetes mellitus had a 2,16 times higher risk of recurrent stroke compared to patients without diabetes mellitus.¹⁶ Chronic hyperglycemia can also increase blood pressure, which if not managed properly can cause blood vessel walls to become weaker, so the risk of re-rupture also increases compared to patients without diabetes mellitus.^{25,26}

Multivariate analysis also showed that diabetes mellitus was the main determinant for recurrent stroke, with the highest OR value of 2,702. This indicates that patients with diabetes mellitus have a 2,7 fold risk of recurrent stroke compared to patient without diabetes mellitus after controlling for age and hypertension. The results of this study are similar to previous studies which state that diabetes mellitus is a major independent risk factor for recurrent stroke.²⁷ Diabetes mellitus affects blood vessels directly and has a more extensive impact on blood vessel damage and the complications it causes. Diabetes mellitus is known as the "mother of disease" because it can be the main cause of many chronic diseases. Diabetes mellitus can contribute as a trigger for various other cardiovascular and cerebrovascular disease such as hypertension, dyslipidemia, kidney failure and heart diseases which if not managed properly can lead to an increased risk of recurrent stroke.^{26,27}

Conclusion

Based on the results of the research conducted, it can be summarized that there is a significant relationship between age and diabetes mellitus with the incidence of recurrent stroke, while the variables of gender and hypertension are not significantly associated with the incidence of recurrent stroke at RSD dr. Soebandi Jember. Diabetes mellitus is the main factor in the incidence of recurrent stroke, followed by hypertension and age. The recommendation for stroke patients, especially those aged ≥ 60 years, are to check blood pressure and blood sugar regularly 2-3 times a week and/or at least 1 month at the nearest

health care facility.

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