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The Impact of Medication Adherence and Depression on Stroke Recurrence in Post-Stroke Patients at Taman Husada Regional General Hospital

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ABSTRACT

Patient compliance in adhering to stroke treatment recommendations becomes one of the factors influencing the occurrence of recurrent strokes. Depression in post-stroke patients inhibits functional brain recovery, increases the potential for recurrent strokes, lowers the quality of life, and raises the risk of death compared to patients without depression. The aim of this study is to analyze the relationship between drug therapy compliance and the level of depression on the occurrence of recurrent strokes in post-stroke patients. This cross-sectional study involved 60 patients aged between 30 and 85 years, all undergoing outpatient stroke treatment at a hospital in Indonesia. Recurrent stroke incidents were defined as experiencing a secondary stroke within 30 days after the initial stroke occurrence. Out of the total participants, 12 individuals had experienced recurrent strokes after their initial episode, while 48 patients had not experienced recurrent strokes up to the point of data collection. Medication adherence data were evaluated using the MMAS-8 (Morisky Medication Adherence Scale), and depression levels were measured using the PHQ-9 (Patient Health Questionnaire-9). The research results show that in the post-stroke patient group, the level of patient adherence is high at 41.7%, and in the recurrent stroke group, the level of patient adherence is moderate at 41.7%. Meanwhile, in the post-stroke patient group, the dominant depression level is low (50%), while in the recurrent stroke group, the dominant depression level is mild, followed by severe depression. The analysis indicates that medication adherence is not associated with stroke recurrence, while depression is related to stroke recurrence with an OR value of 2.060, p <0.05. Further research on more efficient monitoring methods and proper depression management is recommended to reduce the risk of stroke recurrence.

Keywords: Medication Adherence; Depression; Post-Stroke; Recurrent Stroke

INTRODUCTION

Stroke is a neurological dysfunction caused by disrupted blood flow to the brain. Hemorrhagic stroke patients require long-term care, incur high medical costs, and often face decreased productivity[1]. Globally, over 101 million people suffer from stroke, with 12.2 million new cases annually and 6.5 million deaths each year. In 2019, 63% of strokes occurred in individuals under 70 years[2]. In Indonesia, approximately 500,000 people suffer from strokes each year, with 2,5% experiencing some form of disability[3]. Data from Riskesdas (Indonesia Basic Health Research) 2018 reported that stroke prevalence increased from 7 per 1,000 in 2013 to 10.9 per 1,000 in 2018, with the highest prevalence in East Kalimantan, Yogyakarta, and North Sulawesi[4].

Taman Husada Regional General Hospital in Bontang, a type B referral hospital, has recorded a significant number of stroke cases. Although not listed in the top 10 diseases in the region's health department report, in 2022, there were 133 outpatient stroke visits, and in January–February 2023, 30 cases were recorded. These figures align with local statistics showing a high prevalence of stroke risk factors, namely hypertension and diabetes mellitus.

Patient adherence to stroke treatment recommendations is one of the factors that influence stroke recurrence. Medication adherence is key to secondary prevention in patients with stroke. Poor medication adherence can lead to recurrence, disability, or death in stroke patients[5]. Prevention of stroke recurrence requires effective medication accompanied by adherence to therapy as recommended. Poor medication adherence increases the risk of stroke recurrence and mortality in patients after the first stroke attack.[6] A meta-analysis of more than 8,000 patients showed that improved adherence to antihypertensives, statins, and antithrombotic agents reduced mortality by 13–15%. Conversely, poor adherence was associated with an increased risk of death and recurrent stroke events[7]. A controlled clinical trial demonstrated that one year of pharmaceutical care increased adherence to 86.5% and reduced the stroke recurrence rate from 10.6% to 2.2%[8].

Depression is one of the most common mental health disorders following a stroke, with an estimated prevalence of 18 to 33%.[9] Severe post-stroke depression (PSD) can reduce patients' confidence in therapy and recovery, thereby affecting the rehabilitation process, worsening the patient's condition, and increasing the risk of death[10,11]. Depression in post-stroke patients hinders functional brain recovery, increases the risk of stroke recurrence, reduces quality of life, and raises the risk of death compared to patients without depression.[12] A meta-analysis on depression in stroke patients showed a significant association between depression and mortality. The meta-analysis revealed a hazard ratio for death of 1.20 among individuals experiencing depression after stroke.[13] Another meta-analysis found a higher mortality rate among subjects with post-stroke depression compared to those without depression[14].

This research aims to examine the connection between medication adherence and depression levels with the occurrence of recurrent stroke in patients who have had a stroke, focusing on Bontang City, East Kalimantan. The study is significant because depression may reduce a patient's motivation to

follow treatment plans, potentially heightening the risk of stroke recurrence. The study aims to provide a deeper insight into the link between these two factors, while also filling the gap in data related to stroke in the region. The results are expected to inform the development of more effective interventions, such as combining depression management with medication adherence education, to enhance the quality of life for post-stroke patients.

METHOD

This study used a cross-sectional design conducted at RSUD Taman Husada Bontang, East Kalimantan, from December 2023 to January 2024. Data were collected through patient questionnaire responses. The research was approved by the Ethics Committee of the Directorate of Research and Community Service, Yogyakarta State University, under approval number T/31/UN34.9/KP.06.07/2023. Sixty patients aged 30-85 years were enrolled in this study. The subjects of the study were stroke patients undergoing outpatient care. The sampling method used was purposive sampling, with a total sample of 60 patients, divided into 12 patients who experienced recurrent strokes after the first stroke, and 48 patients who did not experience a recurrent stroke until data collection. Inclusion criteria included patients aged 20–90 years undergoing neurological outpatient care with a confirmed stroke diagnosis (ICD I64) and at least one month of post-stroke therapy. Patients were classified as cases if they experienced a recurrent stroke at least one year after the initial event, and as controls if no recurrence occurred within one year. Exclusion criteria included patients who had died, were non-adherent to medication, or were newly diagnosed with stroke in December 2023 or January 2024. A total of 43 patients met the exclusion criteria.

Before participating, patients were informed about the study and signed informed consent; for elderly patients, this was completed by a caregiver. The MMAS-8 instrument was used to assess medication adherence in post-stroke patients. The questionnaire consists of 8 questions, where questions 1 to 7 scored 1 for "yes" and 0 for "no." Question 5 scored 0 for "yes" and 1 for "no." Question 8 scored 0 for answer "A" and 1 for answers "B-E." Scoring criteria: The results of the questionnaire were then summed and grouped. A score >2 indicates low adherence, a score of 1 or 2 indicates moderate adherence, and a score of 0 indicates high adherence. Depression levels in stroke patients were measured using the PHQ-9 (Patient Health Questionnaire) instrument. This questionnaire consists of 9 questions, with each answer scored from 1 to 4. The results of the Patient Health Questionnaire (PHQ-9) are as follows: minimal depression (score 0-4), mild depression (score 5-9), moderate depression (score 10-14), moderate-to-severe depression (score 15-19), and severe depression (score 20-27). Primary data were obtained from questionnaires, while secondary data such as birth date, insurance type, blood pressure, and comorbidities were collected from medical records. Data were analyzed using SPSS version 23, with a p-value <0.05 considered statistically significant. Chi-square tests were used to calculate the Odds Ratio (OR) based on medication adherence and depression levels, where an OR >1 indicates increased risk of stroke recurrence.

RESULTS

Based on the general characteristics of the respondents depicted in Table 1, it can be seen that the majority of respondents in both the stroke and recurrent stroke groups were under 40 years old (68.8% vs 50%), had BPJS health insurance (97.9% vs 100%), had a history of physiotherapy (68.8% vs 58.3%), underwent physiotherapy 1-2 times a week (35.4% vs 58.3%), and had comorbid hypertension (50% vs 83.3%). Male gender was more prevalent in the stroke group compared to the recurrent stroke group (54.2% vs 41.7%).

Table 1. Post-Stroke Patient Characteristics

Variable	Stroke n=48	%	Recurrent Stroke n= 12	%
Gender				
Male	26	54.2	5	41.7
Female	22	45.8	7	58.3
Age				
<40 years	33	68.8	6	50.0
>40 years	15	31.3	6	50.0
Health Insurance				
BPJS	47	97.9	12	100.0
Private/General Insurance	1	2.1	0	0.0
Physiotherapy				
Yes	33	68.8	7	58.3
No	15	31.3	5	41.7
Physiotherapy Frequency				
None	17	35.4	4	33.3
1-2 times a week	17	35.4	7	58.3
More than 2 times a week	14	29.2	1	8.3
Comorbidities				
Hypertension	24	50.0	10	83.3
Diabetes	11	22.9	3	25.0
Cholesterol	16	33.3	7	58.3

Table 2 shows the proportion of medication adherence and depression levels in stroke patients found in this study. Most patients in the stroke group exhibited minimal depressive symptoms (50%), while the recurrent stroke group predominantly experienced mild and severe depression (33.33%; 25%). Regarding medication adherence, the stroke group tended to have a high medication adherence (41.7%), whereas only 25% of the recurrent stroke group had high medication adherence.

Table 3 shows the results of the chi-square analysis performed to examine the relationship between medication adherence and depression levels with the recurrence of strokes in post-stroke patients. It was found that the significance value (p) for the depression variable was $p<0.05$, indicating a relationship between depression and recurrent stroke. However, medication adherence was not related to recurrent stroke, as the p-value was >0.05.

Table 2. Proportion of Medication Adherence and Depression in Stroke and Recurrent Stroke Patients

Variable	Stroke n=48	%	Recurrent Stroke n= 12	%
Medication Adherence				
Low	13	27.1	4	33.3
Moderate	15	31.3	5	41.7
High	20	41.7	3	25.0
Depression				
Low Depression	24	50	2	16.7
Mild Depression	15	31.3	4	33.3
Moderate Depression	6	12.5	2	16.7
Moderate-Severe Depression	3	6.2	1	8.3
Severe Depression	0	0	3	25.0

The data analysis from Table 3 shows that the Odds Ratio for the medication adherence variable is 0.429 ($p>0.05$). This means that an increase in medication adherence by one level, either from low to moderate or from moderate to high, reduces the risk of recurrent stroke in stroke patients by 57.1%. Meanwhile, for the depression level variable, an Odds Ratio of 2.060 ($p<0.05$) was found, indicating that an increase in depression by one unit, from low to mild or from mild to moderate, increases the relative risk of recurrent stroke in stroke patients by 106%. This statistically significant result provides compelling evidence supporting a true association between depressive symptoms and stroke recurrence, rather than a finding attributable to random variability.

Table 3. Analysis of Depression Level – Medication Adherence on Stroke Recurrence

Variable	OR (95% CI)	p
Medication Adherence		
Low	0.429 (0.103-1.783)	0.236
Moderate		
High		
Depression		
Low Depression	2.060(1.117 -3.797)	**0.007***
Mild Depression		
Moderate Depression		
Moderate-Severe Depression		
Severe Depression		

DISCUSSION

Recurrent stroke constitutes a major focus in secondary stroke prevention, aiming to improve long-term patient prognosis. As illustrated in Table 1, the frequency of physiotherapy sessions and the predominance of hypertension are notably higher among patients with recurrent stroke. The decision to administer more intensive physiotherapy to this group, compared to patients without recurrence, may be

influenced by several clinical factors. One contributing factor is stroke severity, as more severe cases often necessitate intensive rehabilitative efforts to optimize recovery outcomes. Additionally, the patient's level of physical activity may also play a role, given that physical inactivity has been associated with an increased risk of stroke recurrence.

Among post-stroke patients, both groups were found to have a history of hypertension. This finding is consistent with data from the HDSS survey, which indicates a high prevalence of stroke associated with advancing age, hypertension, and diabetes mellitus[15]. Hypertension is the leading modifiable risk factor for stroke[16], with approximately 50% of stroke cases being attributed to it. Lowering blood pressure is the most effective and comprehensive strategy for preventing recurrent strokes. Clinical guidelines recommend reducing blood pressure to below 140/90 mmHg, and if well tolerated, to below 130/80 mmHg[17]. Reducing blood pressure following a stroke has been shown to decrease the likelihood of recurrent stroke by approximately 25–30%[18].

The level of medication adherence among patients in the non-recurrent stroke group was classified as high, with a percentage of 41.7%. High adherence to medication in post-stroke patients has been associated with a lower risk of stroke recurrence. However, in this study, medication adherence among post-stroke patients was not significantly associated with stroke recurrence ($p > 0.05$). Nevertheless, one study reported that 83% of stroke patients adhered to their medication regimen, which is consistent with findings from other studies[19]. Medication adherence is independently associated with risk factor control, and factors such as local availability, daily reminders, and family support and care have been identified as facilitators of medication adherence[20]. In addition, high adherence to antihypertensive medication within the first six months post-stroke is associated with a lower risk of major adverse cardiovascular events (MACE) and fall-related hospitalizations[21].

Meanwhile, in the recurrent stroke group, the predominant level of medication adherence was moderate, at 41.7%. Although this does not fall into the high adherence category, patients with suboptimal adherence to pharmacological therapy in this study experienced stroke recurrence. Suboptimal medication adherence among stroke survivors has been previously reported, and poor adherence to secondary stroke prevention therapy has been associated with an increased risk of recurrence. Furthermore, higher medication adherence has been linked to a lower incidence of recurrent stroke and improvements in quality of life[22].

While numerous studies suggest that adherence to medication can help lower the risk of stroke recurrence, our findings did not establish a significant link between medication adherence and recurrent stroke. This discrepancy may be attributed to the narrow focus of our research, which evaluated only the degree of adherence without accounting for other influential factors such as patients' educational background, social support, or beliefs regarding medications[23]. Previous studies highlight that these contextual factors may have a stronger impact on preventing recurrent strokes than adherence alone. Additionally, the use of observational questionnaires without any accompanying intervention in our data collection process may have limited our ability to detect significant associations. This aligns with

existing literature reviews that point to inconsistencies in findings due to varying and often subjective adherence measurement methods, which can obscure statistical significance[24].

In Table 3, the Odds Ratio (OR) analysis reveals an OR value of depression level was 2.060 with a p-value of < 0.05. The significant OR value indicates a strong association between depression levels and recurrent stroke incidence. In other words, individuals experiencing depression are 2.060 times more likely to have a recurrent stroke. This finding is consistent with previous studies indicating that post-stroke depression significantly increases the risk of stroke recurrence. This study's findings align with those of a meta-analysis indicating that people suffering from depression are 1.47 times more likely to experience a stroke[25]. A randomized clinical trial found that stroke patients with untreated depression had nearly twice the likelihood of experiencing a recurrent stroke compared to those receiving antidepressant therapy, such as citalopram[26]. The underlying mechanisms are not solely biological but also functional in nature. Depression has been shown to hinder patients' participation in post-stroke rehabilitation programs and worsen existing neurological impairments, thereby indirectly increasing vulnerability to recurrent stroke events[27]. Moreover, post-stroke depression tends to be persistent and has a high relapse rate. An 18-year longitudinal study found that two-thirds of patients who initially recovered from depression experienced a recurrence, particularly within the first five years after a stroke. These findings underscore that depression is a long-term risk factor that must be continuously managed to prevent stroke recurrence[28]. In line with this, the concept of "stroke depression" has been introduced to describe the complex bidirectional relationship between stroke and depression. This concept emphasizes that depression is not merely a post-stroke complication but a critical component in the comprehensive management of stroke patients aimed at reducing recurrence and mortality rates[29]. Therefore, PSD warrants more clinical attention and further research. Early screening and treatment of depressive symptoms may offer potential benefits in reducing the rate of stroke recurrence.

Several limitations of this study include the use of retrospective data, which introduces the possibility of information bias due to limitations in documentation accuracy or patient recall. Additionally, this study only analyzed specific variables and did not explore other factors such as genetics, social environment, or differences in medical therapies that may influence stroke recurrence. The limited study duration may not be sufficient to assess long-term outcomes related to stroke recurrence and the effects of risk factors. Lastly, the impact of non-medical interventions, such as health education or psychosocial therapy, was not specifically measured in this study.

Based on these findings, future studies should focus on clarifying the patterns and predictors of stroke recurrence. Investigations into lifestyle, psychosocial factors, and intervention strategies—particularly in the context of post-stroke depression—are critical to enhancing long-term patient outcomes. Further research should focus on determining the optimal dosage and intensity of physiotherapy, including the selection of physical activities for recurrent stroke patients with varying degrees of severity. Additionally, analysis of factors influencing patient adherence, such as daily

reminders, family support, and local availability, should be considered to improve adherence and reduce the risk of recurrence. Exploration of the effectiveness of psychological interventions, such as cognitive therapy or pharmacological treatments, in managing post-stroke depression is crucial. In the context of post-stroke depression, further studies are needed to evaluate the relationship between depression levels and the likelihood of stroke recurrence. Intervention strategies focused on Post-Stroke Depression (PSD), along with the benefits of early screening and management of depressive symptoms, should be further elucidated to reduce the risk of stroke recurrence. Overall, it is hoped that future research will provide deeper insights, support the development of more effective interventions, and improve long-term outcomes for post-stroke patients.

CONCLUSIONS AND RECOMMENDATIONS

The results of this study indicate that medication adherence reduces the risk of stroke recurrence with an OR of 0.429, though it was not statistically significant. In contrast, depression levels were significantly associated with stroke recurrence, with an OR of 2.060 ($p < 0.05$), where patients with severe depression were at a higher risk of experiencing recurrent stroke. It is recommended to implement a comprehensive approach that includes the identification and management of depression through early screening, psychological therapy, and appropriate social support for stroke patients to prevent recurrent strokes.

ACKNOWLEDGMENTS

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