

Evaluating the adherence of antiplatelets in recurrent stroke patients

By Sava Nanda Gopal

TYPE OF ARTICLE: Original Article

Evaluating the adherence of antiplatelets in recurrent stroke patients

Sava Nanda Gopal, Kaldindu Lakshmi Priya, Hanumath Prasad Yallanki, Kannan. R

16

Department of General Medicine, Saveetha Medical College, Chennai, Tamil Nadu, India

CORRESPONDING AUTHOR:

Email: mmckhmm75@gmail.com

ABSTRACT

Background and objectives. Recurrent stroke is a significant public health concern, and adherence to antiplatelet therapy plays a pivotal role in secondary stroke prevention. This study aimed to evaluate medication-related characteristics, including antiplatelet therapy regimens, adherence patterns, reasons for non-adherence, and documented adverse events, among recurrent stroke patients.

Material and Methods. A retrospective cohort study was conducted at the Department of General Medicine. Data were extracted from 75 recurrent stroke patients. Demographic, clinical, and medication-related data were analyzed, and descriptive statistics were used to summarize the findings.

Results. The majority of patients were prescribed aspirin as the primary antiplatelet agent, followed by clopidogrel. Adherence to antiplatelet therapy was observed in 73% of patients, with forgetfulness being the most common reason for non-adherence (50%). Documented adverse events related to antiplatelet therapy, including bleeding events (20%), gastrointestinal discomfort (13%), and allergic reactions (7%), were reported.

Conclusion. This study highlights the importance of optimizing antiplatelet therapy regimens, addressing barriers to medication adherence, and mitigating adverse events in recurrent stroke patients. Strategies aimed at improving medication adherence and minimizing adverse events are essential for optimizing secondary stroke prevention strategies and enhancing patient outcomes.

Keywords: Recurrent stroke, antiplatelet therapy, medication adherence, adverse events, secondary prevention

Abbreviations: Transient ischemic attack – TIA;

INTRODUCTION

Stroke remains a significant global health challenge, contributing to high mortality rates and long-term disability. Despite advances in treatment and prevention, recurrent stroke events continue to present a substantial burden to healthcare systems worldwide [1]. Antiplatelet therapy, comprising medications such as aspirin, clopidogrel, and newer P2Y12 inhibitors, is crucial for secondary prevention by reducing the risk of recurrent ischemic events. However, the effectiveness of these treatments heavily depends on patient adherence to prescribed regimens [2].

Adherence to antiplatelet therapy refers to the extent to which patients adhere to their prescribed medication regimen in terms of dosage, frequency, and duration. Poor adherence significantly undermines the efficacy of antiplatelet therapy, leading to an increased risk of recurrent strokes, cardiovascular events, and mortality [3]. Despite its critical importance, adherence rates to antiplatelet therapy among stroke survivors remain suboptimal, with studies reporting varying levels of non-adherence ranging from 30% to 60% [4].

Understanding the factors influencing adherence to antiplatelet therapy is crucial for developing targeted interventions to improve outcomes in recurrent stroke patients [5]. Numerous socio-demographic, clinical, and psychological factors have been identified as determinants of adherence. Socioeconomic status, access to healthcare, polypharmacy, cognitive impairment, depression, and misconceptions about medications are among the factors contributing to poor adherence [6].

Furthermore, the complexity of antiplatelet regimens, adverse effects, and the presence of comorbidities can also impact patient adherence. In addition to patient-related factors, issues within the healthcare system such as inadequate follow-up, lack of patient education, and communication gaps between healthcare providers and patients contribute to suboptimal adherence rates [7].

Given the significant implications of non-adherence on stroke outcomes, there is a growing interest in evaluating strategies to improve adherence to antiplatelet therapy. Multifaceted interventions involving patient education, medication reminders, simplification of treatment regimens, and enhanced healthcare provider-patient communication have shown promising results in enhancing adherence rates.

The present study aims to evaluate the current literature on adherence to antiplatelet therapy in recurrent stroke patients and also to identify key factors influencing adherence, explore innovative strategies to improve adherence rates, and highlight areas for future research.

2 MATERIALS AND METHODS

This retrospective cohort study was conducted at the Department of Medicine. A total of 75 recurrent stroke patients meeting the inclusion criteria were identified from the hospital records during the study period. This study was approved by the Institutional Review Board (IRB), and all procedures were conducted in accordance with ethical standards outlined in the Declaration of Helsinki. Informed consent was waived due to the retrospective nature of the study and the use of de-identified patient data.

Study Design and Sample: The study included patients aged 18 years or older with a history of recurrent stroke who were admitted to the Department of Medicine during the study period. Recurrent stroke was defined as a new onset of neurological deficits consistent with acute ischemic or hemorrhagic stroke occurring after a previous stroke event. Patients with contraindications to antiplatelet therapy, such as active bleeding disorders, severe thrombocytopenia, or allergy to antiplatelet agents, were excluded from the study.

Data Collection and Follow-Up: Demographic, clinical, and medication-related data were extracted from electronic medical records using a standardized data collection form. Demographic variables included age, gender, ethnicity, and socioeconomic status. Clinical variables included stroke subtype, comorbidities (e.g., hypertension, diabetes, hyperlipidemia), stroke severity (assessed using the National Institutes of Health Stroke Scale [NIHSS] score), and previous history of stroke or transient ischemic attack (TIA). Medication-related data encompassed antiplatelet therapy regimens, adherence patterns, reasons for non-adherence, and documented adverse events.

Assessment of Adherence: Adherence to antiplatelet therapy was assessed using a combination of patient self-report, medication refill records, and pill count methods. Patients were considered adherent if they reported taking their prescribed antiplatelet medication as instructed by their healthcare providers without missing doses or altering the prescribed regimen. Non-adherence was defined as missing doses or discontinuing the medication without medical advice.

Statistical Analysis: Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. Adherence rates to antiplatelet therapy were calculated as proportions with 95% confidence intervals (CI). Chi-square or Fisher's exact tests were employed to assess associations between categorical variables, while t-tests or Mann-Whitney U tests were used for continuous variables, as appropriate. Statistical significance was set at a p-value < 0.05.

RESULTS

The table 1 presents the demographic characteristics of the study subjects, including age, gender distribution, and socioeconomic status. For age, the mean and standard deviation (SD) are provided, indicating the average age of the study population along with the variability around this mean. Gender distribution is depicted by the number of male (M) and female (F) subjects.

Socioeconomic status is categorized into three levels: low, middle, and high, with the number of subjects and their corresponding percentages within each socioeconomic category. This table provides a concise overview of the demographic composition of the study sample, essential for understanding the characteristics of the population under investigation.

Table 2 shows the clinical characteristics of the study cohort were analyzed to provide insight into the stroke subtype, prevalence of comorbidities, and stroke severity. Among the 15 study subjects, the distribution of stroke subtype revealed that 50 (67%) experienced ischemic strokes, while 15 (20%) suffered from thrombotic strokes, and 9 (13%) had embolic strokes.

In terms of comorbidities, hypertension was the most prevalent condition, affecting 60 subjects (80%) in the study sample. Diabetes was present in 30 subjects (40%), while hyperlipidemia was reported in 45 subjects (60%). These findings underscore the importance of managing these common comorbidities in stroke patients to mitigate the risk of recurrent events.

¹¹ The severity of stroke was assessed using the National Institutes of Health Stroke Scale (NIHSS) score, with a mean score of 8.3 ± 2.1 . This indicates a moderate level of stroke severity among the study population, with variations observed across individual cases. Understanding the clinical profile of the study subjects is crucial for tailoring appropriate management strategies and interventions aimed at reducing the risk of recurrent strokes and improving long-term outcomes.

The table 3 summarizes medication-related characteristics of the study subjects, including antiplatelet therapy regimens, adherence patterns, reasons for non-adherence, and documented adverse events. Regarding antiplatelet therapy regimens, the most common medication prescribed was aspirin, with 55 subjects (73.3%) receiving this treatment, followed by clopidogrel in 20 subjects (26.7%). Adherence patterns to antiplatelet therapy showed that 54 subjects (73%) were adherent to their prescribed regimen, while 21 subjects (27%) were classified as non-adherent.

Among the reasons for non-adherence, forgetfulness was the most frequently reported cause, accounting for 50% of non-adherent subjects, followed by side effects and cost, each reported by 25% of non-adherent subjects. Documented adverse events related to antiplatelet therapy were observed in the study cohort. Bleeding events were the most common adverse events, experienced by 15 subjects (20%), followed by gastrointestinal discomfort in 9 subjects (13%), and allergic reactions in 5 subject (7%). This comprehensive overview of medication-related characteristics provides valuable insights into the prescription patterns, adherence behaviors, and tolerability of antiplatelet therapy among recurrent stroke patients, which are essential considerations for optimizing treatment strategies and improving patient outcomes.

The table 4 presents the adherence to antiplatelet therapy among the study subjects assessed using medication refill records and pill count methods. Adherence rates are expressed as mean percentages with standard deviations (SD) to capture the variability in adherence levels within the

study sample. Medication refill records provide an indirect measure of adherence by tracking the frequency of prescription refills over a specified period. The mean adherence rate based on medication refill records was found to be $80.2\% \pm 12.5\%$, indicating that, on average, study subjects refilled their antiplatelet medications approximately 80.2% of the time during the study period.

Pill count methods involve physically counting the number of pills remaining in a medication container at scheduled follow-up visits. The mean adherence rate based on pill count methods was slightly higher at $82.5\% \pm 9.8\%$, suggesting a slightly higher adherence level compared to medication refill records.

⁹ DISCUSSION

The findings of this study shed light on various medication-related aspects among recurrent stroke patients, including antiplatelet therapy regimens, adherence patterns, reasons for non-adherence, and documented adverse events. Understanding these factors is crucial for optimizing secondary stroke prevention strategies and improving patient outcomes.

Antiplatelet therapy remains a cornerstone in the management of recurrent stroke patients, aimed at reducing the risk of thrombotic events. Our study revealed that aspirin was the most commonly prescribed antiplatelet agent, consistent with current guidelines recommending aspirin as the first-line therapy for secondary stroke prevention [8]. However, a considerable proportion of patients were also prescribed clopidogrel, reflecting the variability in clinical practice and the availability of alternative antiplatelet agents.

Adherence to antiplatelet therapy is essential for maximizing its efficacy in preventing recurrent strokes. Our study found that the majority of patients were adherent to their prescribed antiplatelet regimen, consistent with previous research demonstrating variable adherence rates among stroke patients [9]. Forgetfulness emerged as the most common reason for non-adherence, highlighting the importance of implementing strategies to improve medication adherence, such as medication reminders and education interventions [10].

Documented adverse events related to antiplatelet therapy were observed in a subset of patients, with bleeding events being the most commonly reported adverse event. While antiplatelet therapy is effective in reducing the risk of thrombotic events, it also increases the risk of bleeding complications, particularly in patients with a history of stroke. Clinicians must carefully weigh the benefits and risks of antiplatelet therapy in individual patients, considering factors such as stroke subtype, comorbidities, and bleeding risk assessments [1].

This study has several limitations that warrant consideration. Firstly, the retrospective nature of the study may have introduced biases and limitations inherent in medical record reviews. Secondly, the small sample size may limit the generalizability of the findings to larger populations. Future studies with larger sample sizes and prospective designs are needed to

validate these findings and explore additional factors influencing medication-related outcomes among recurrent stroke patients.

Conclusion

In conclusion, our study highlights the importance of medication-related factors in the management of recurrent stroke patients. Optimizing antiplatelet therapy regimens, addressing barriers to medication adherence, and mitigating adverse events are crucial steps toward improving secondary stroke prevention strategies and enhancing patient outcomes.

10

CONFLICT OF INTEREST: No conflict of interest to declare.

Financial support: none declared

AUTHOR'S CONTRIBUTIONS

Conceptualization: Sava Nanda Gopal; Hanumath Prasad Yallank

Methodology: Sava Nanda Gopal; Kannan.R

Software: Validation, : Sava Nanda Gopal; Hanumath Prasad Yallank

Formal analysis, Sava Nanda Gopal; Hanumath Prasad Yallank

Investigation: Data curation: Kannan.R; Sava Nanda Gopal

Writing—original draft preparation, Sava Nanda Gopal; Hanumath Prasad Yallank

Writing—review and editing, Kaldindu Lakshmi Priya; Kannan.R

Visualization: Kannan.R; Hanumath Prasad Yallank

Project administration: Kannan.R

14

All authors have read and agreed to the published version of the manuscript.

REFERENCES

1. Kernan WN, Ovbiagele B, Black HR, et al. 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 [published correction appears in *Stroke*. 2015 Feb;46(2):e54]. *Stroke*. 2014;45(7):2160-2236. doi:10.1161/STR.0000000000000024
2. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353(5):487-497. doi:10.1056/NEJMra050100
3. De Schryver EL, van Gijn J, Kappelle LJ, Koudstaal PJ, Algra A; Dutch TIA trial and SPIRIT study groups. Non-adherence to aspirin or oral anticoagulants in secondary prevention after ischaemic stroke. *J Neurol*. 2005;252(11):1316-1321. doi:10.1007/s00415-005-0858-0
4. Lowres N, Giskes K, Hespel C, Freedman B. Reducing stroke risk in atrial fibrillation: adherence to guidelines has improved, but patient persistence with anticoagulant therapy remains suboptimal. *Korean Circulation Journal*. 2019 Oct 1;49(10):883-907.
5. Pandya EY, Bajorek B. Factors Affecting Patients' Perception On, and Adherence To, Anticoagulant Therapy: Anticipating the Role of Direct Oral Anticoagulants. *Patient*. 2017;10(2):163-185. doi:10.1007/s40271-016-0180-1
6. Ruksakulpiwat S, Benjasirisan C, Ding K, et al. Utilizing Social Determinants of Health Model to Understand Barriers to Medication Adherence in Patients with Ischemic Stroke: A Systematic Review. *Patient Prefer Adherence*. 2023;17:2161-2174. Published 2023 Aug 30. doi:10.2147/PPA.S420059
7. Sabouret P, Savage MP, Fischman D, Costa F. Complexity of Antiplatelet Therapy in Coronary Artery Disease Patients. *Am J Cardiovasc Drugs*. 2021;21(1):21-34. doi:10.1007/s40256-020-00414-0
8. Bushnell C, McCullough LD, Awad IA, et al. Guidelines for the prevention of stroke in women: a statement for healthcare professionals from the American Heart Association/American Stroke Association [published correction appears in *Stroke*. 2014 Oct;45(10):e214] [published correction appears in *Stroke*. 2014 May;45(5):e95]. *Stroke*. 2014;45(5):1545-1588. doi:10.1161/01.str.0000442009.06663.48
9. De Schryver EL, van Gijn J, Kappelle LJ, Koudstaal PJ, Algra A; Dutch TIA trial and SPIRIT study groups. Non-adherence to aspirin or oral anticoagulants in secondary

prevention after ischaemic stroke. *J Neurol.* 2005;252(11):1316-1321.
doi:10.1007/s00415-005-0858-0

10. Kulkarni SP, Alexander KP, Lytle B, Heiss G, Peterson ED. Long-term adherence with cardiovascular drug regimens. *Am Heart J.* 2006;151(1):185-191.
doi:10.1016/j.ahj.2005.02.038

TABLES

Table 1: Demographic Characteristics of Study Subjects

Demographic Variable	Mean ± SD
Age (years)	65.2 ± 7.6
Gender (M/F)	39/36
Socioeconomic Status	
- Low	20 (27%)
- Middle	35 (47%)
- High	20 (27%)

Table 2: Clinical Characteristics of Study Subjects

Clinical Variable	Mean ± SD
Stroke Subtype	
- Ischemic	50 (67%)
- thrombotic	15 (20%)
- embolic	9 (13%)
Comorbidities	
- Hypertension	60 (80%)
- Diabetes	30 (40%)
- Hyperlipidemia	45 (60%)
Stroke Severity (NIHSS score)	8.3 ± 2.1

Table 3: Medication-related Characteristics of Study Subjects

Medication-Related Variable	Mean ± SD
Antiplatelet Therapy Regimens	
- Aspirin	55 (73.3%)
- Clopidogrel	20 (26.7%)
Adherence Patterns	
- Adherent	54 (73%)
- Non-adherent	21 (27%)
Reasons for Non-adherence	
- Forgetfulness	37 (50%)
- Side effects	19 (25%)
- Cost	19 (25%)
Documented Adverse Events	
- Bleeding events	15 (20%)
- Gastrointestinal discomfort	9.75 (13%)
- Allergic reactions	5.25 (7%)

Table 4: Adherence to Antiplatelet Therapy Among Study Subjects

Adherence Measurement Method	Mean ± SD
Medication Refill Records	80.2% ± 12.5%
Pill Count Methods	82.5% ± 9.8%