Original Research Paper

Volume - 16 | Issue - 11 | November - 2026 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Neurology

MEDICATION NON-ADHERENCE AND RECURRENT ISCHEMIC STROKE: AN EXPLORATORY POST-HOC ANALYSIS OF A PROSPECTIVE SINGLE-CENTER COHORT IN EASTERN INDIA

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ABSTRACT **Background:** Secondary prevention following ischemic stroke requires sustained adherence to prescribed medications. The relationship between documented non-adherence and recurrent ischemic stroke was evaluated in a hospital-based cohort. **Methods:** This exploratory post-hoc analysis draws on a prospective observational study cohort of 105 adults with first-ever ischemic stroke followed for six months. The exposure was recorded drug non-compliance, and the outcome was documented recurrent ischemic stroke. **Results:** The study reports recurrent ischemic stroke in 20/105 (19.0%) participants. Non-compliance was reported in 14/105 (13.3%), with recurrence in 10/14 (71.4%) compared with 10/91 (11.0%) compliant patients. The reported unadjusted odds ratio was 20.25, and the adjusted odds ratio was 20.379 (95% CI 4.794–86.626; p<0.001). **Conclusions:** Recorded non-adherence was strongly associated with recurrence in the study analysis.

KEYWORDS : Ischemic Stroke; Recurrent Stroke; Medication Adherence; Secondary Prevention

INTRODUCTION

Stroke is one of the leading causes of mortality and long-term disability worldwide, imposing a substantial healthcare burden in both developed and developing countries. Ischemic stroke accounts for approximately 70–80% of all strokes and occurs due to obstruction of cerebral blood flow, resulting in focal neurological deficits. Ischemic stroke survivors remain vulnerable to recurrent cerebrovascular events. Secondary prevention is guided by stroke mechanism and includes appropriate antithrombotic treatment, control of blood pressure and diabetes, lipid lowering, and smoking cessation[1,2]. Adherence to prescribed regimens is necessary for intended preventive treatment to be delivered, yet the observed relationship between adherence and recurrence can be confounded by disease severity, access to care, treatment indications, and the timing of exposure ascertainment. Patient education, caregiver involvement, regular follow-up, and sustained lifestyle modification are therefore essential to improve adherence and reduce recurrence risk [3,4].

The present study at a tertiary neurology centre in eastern India examined demographic, radiological, etiologic, and vascular factors associated with recurrence. It reported an especially large association between drug non-compliance and recurrent stroke.

Objective: To describe the association between chart-recorded medication non-adherence and recurrent ischemic stroke within six months.

MATERIALS AND METHODS

The parent study was a prospective observational, single-centre study in the Department of Neurology, Kalinga Institute of Medical Sciences, Bhubaneswar.

Inclusion Criteria: All patients presenting with a first episode of ischemic stroke, aged greater than 18 years, and who provided informed consent for participation.
Exclusion Criteria: Patients aged less than 18 years, patients with recurrent stroke at presentation, patients with prior history of intracranial haemorrhage, patients with imaging evidence of venous infarction.

It reports 136 screened, 7 declining participation, 24 excluded, and 105 enrolled. Six-month follow-up was described.

Study Procedure

Patients presenting with symptoms suggestive of ischemic stroke were evaluated clinically and radiologically. After confirmation of diagnosis and eligibility screening, written informed consent was obtained. A detailed history was recorded, including demographic details, risk factors, and prior medical history. Clinical examination was performed thoroughly, and stroke severity was assessed using standardised scoring systems such as NIHSS and GCS. Baseline investigations were conducted, including blood tests and imaging studies. Patients were followed up over 6months to monitor for the occurrence of recurrent ischemic stroke. During follow-up visits, clinical status, adherence to medications, and control of risk factors were assessed. Any new neurological deficit suggestive of recurrence was evaluated and confirmed with imaging.

Statistical Methods

The parent study measured age, sex, hypertension, diabetes, dyslipidemia, smoking, alcohol use, baseline NIHSS, MRI territory, vascular imaging, TOAST subtype, and six-month functional outcome. The study reports univariate comparisons and multivariable logistic regression including age, baseline NIHSS, hypertension, diabetes, non-compliance, and cardioembolism.

Ethics

The study describes Institutional Ethics Committee approval and written informed consent from participants or legally authorized representatives.

RESULTS

Cohort Characteristics

The study reports a mean age of 59.6 ± 11.6 years; 70 participants (66.7%) were male. Hypertension occurred in 83 (79.0%), diabetes in 62 (59.0%), and hyperlipidemia in 50 (47.6%). Twenty participants (19.0%) had recurrent ischemic stroke. The mean age of recurrent cases was 64.2 ± 7.8 years versus 58.5 ± 12.2 years in non-recurrent cases (reported p=0.051).

Primary Exposure-outcome Association

The study reports 14 non-compliant and 91 compliant participants. Recurrence was recorded in 10/14 and 10/91, respectively. The reported unadjusted OR was 20.25 (p<0.001).

Table 1. Drug Compliance Status and Recurrence(N=105)

Compliance Status	Total n	Recurrence n (%)	No recurrence (%)
Compliant	91	10 (11.0%)	81 (89.0%)
Non-Compliant	14	10 (71.4%)	4 (28.6%)
Total	105	20 (19.0%)	85 (81.0%)
Fisher's exact test: OR = 20.25, p < 0.001* (statistically significant).			

Multivariate Logistic Regression

Drug non-compliance was the only statistically significant independent predictor of stroke recurrence in the multivariate model (OR = 20.38, 95% CI: 4.79–86.63, p < 0.001).Non-compliant patients had more than 20 times the odds of recurrent stroke compared to compliant patients, after adjusting for all other predictors. Each additional year of age was associated with a 5.5% increase in recurrence odds (p = 0.076, borderline significant). Patients with cardioembolic stroke had over four times the adjusted odds of recurrence (OR =4.16) though this did not reach significance given the small subgroup (n=12). DM showed a 2.2-fold increase in recurrence odds after adjustment (p = 0.243).

Table 2. Multivariate Logistic Regression — Predictors of Stroke Recurrence (N=105)

Variable	Adjusted OR	95% CI	p
Drugnon-compliance	20.379	4.794–86.626	<0.001
Age (per year)	1.055	0.994–1.120	0.076
Admission NIHSS	0.959	0.870–1.058	0.404
Hypertension	1.873	0.329–10.678	0.480
Diabetes mellitus	2.241	0.579–8.673	0.243
Cardioembolism	4.162	0.751–23.050	0.103

Secondary Outcomes

The study reports mean six-month mRS of 2.40 among recurrent cases versus 2.04 among non-recurrent cases (p=0.095 for mean comparison). Admission NIHSS correlated with six-month mRS (Spearman rho=0.599; p<0.001).

DISCUSSION

In this cohort, documented non-compliance showed a large positive association with recorded recurrence. It was present in 14 patients (13.3%) of whom 10 patients (71.4%) developed recurrence compared with only 10 of 91 compliant patients (11.0%). The univariate association was highly significant with OR = 20.25 and p < 0.001. In multivariate logistic regression drug non-compliance remained the only independent predictor of recurrence with β = 3.014, SE = 0.738, adjusted OR = 20.379, 95% CI: 4.794–86.626 and p & lt; 0.001. This indicates that non-compliant patients had more than 20times higher odds of recurrent stroke after adjustment for other variables. Antiplatelets, anticoagulants,lipid-lowering drugs, antihypertensives, and diabetes medications have distinct indications; therefore, a single binary adherence variable may combine heterogeneous behaviors and treatment opportunities [2,5,6,7]. Future analyses should differentiate prescribed drug classes and distinguish non-initiation, intermittent missed doses, and permanent discontinuation if such data exist. The findings arise from one tertiary centre and a six-month observation period. The sample is small; generalizability to community stroke populations and other care settings is therefore uncertain. Nonetheless, the cohort provides a useful foundation for examining real-world secondary-prevention gaps in an Indian setting. Strengths include the prospective parent design, structured neurological assessments, imaging and TOAST characterisation. Medication adherence is a critical determinant of successful secondary prevention. Non-compliance with prescribed therapies, including antiplatelets, anticoagulants and antihypertensives, significantly increases the risk of recurrent stroke. Factors contributing to poor adherence include lack of awareness, financial constraints, side effects and inadequate follow-up. In many cases, patients discontinue medications once symptoms improve, leading to uncontrolled risk factors and subsequent recurrence. Addressing these challenges through patient education, counselling, and regular follow-up is essential to ensure sustained therapeutic benefit [8][9].

CONCLUSIONS

The study reports a strong association between recorded medication non-compliance and recurrent ischemic stroke over six months. Drug non-compliance emerged as the most powerful and actionable predictor. Therefore, effective secondary prevention should prioritise strict medication adherence, patient education, caregiver involvement, and regular follow-up

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