



A PROSPECTIVE STUDY ON THE EFFECTIVENESS AND BARRIERS OF RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR IN RURAL STROKE MANAGEMENT

Dr. Befin K¹, Dr. Subramonia Subin C²

¹Associate Professor, Department of Emergency Medicine, Sree Mookambika Institute of Medical Sciences, Kanniyakumari, Tamilnadu, India.

²Junior Resident, Department of Emergency Medicine, Sree Mookambika Institute of Medical Sciences, Kanniyakumari, Tamilnadu, India.

Corresponding Author: Dr. Subramonia Subin C

Junior Resident, Department of Emergency Medicine, Sree Mookambika Institute of Medical Sciences, Kanniyakumari, Tamilnadu, India.

ABSTRACT

Background: Acute ischemic stroke is a leading cause of mortality and long-term disability worldwide. Recombinant tissue plasminogen activator (rtPA) remains the standard thrombolytic therapy when administered within the recommended therapeutic window. However, rural healthcare settings face significant barriers that may delay timely thrombolysis. This study aimed to evaluate the outcomes and barriers associated with rtPA therapy in acute ischemic stroke patients managed at a rural tertiary care center.

Methodology: This prospective observational study was conducted in the Department of Emergency Medicine at Sree Mookambika Institute of Medical Sciences, Kulasekharam, from May 2025 to February 2026. Patients with CT-confirmed acute ischemic stroke eligible for intravenous rtPA were included. Baseline demographic, clinical, imaging, and socioeconomic data were recorded. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS). Outcomes were evaluated using NIHSS at discharge and modified Rankin Scale (mRS) at one and three months follow-up. Treatment delays including door-to-imaging and door-to-needle times were analyzed. Statistical analysis was performed using SPSS version 25.0.

Result: Among 28 patients treated with rtPA, no major bleeding complications were observed. Meaningful functional improvement at three months follow-up was seen in 35.7% of patients. Mean door-to-imaging time was 21 minutes, while mean door-to-needle time was 68 minutes. Delays were mainly related to socioeconomic factors, delayed decision-making, and limited awareness regarding stroke symptoms and thrombolytic therapy.

Conclusion: Thrombolysis with rtPA is safe and feasible in rural tertiary care settings. Improving public awareness, reducing treatment delays, and strengthening rural stroke care systems may further improve outcomes in acute ischemic stroke patients.

Keywords: Acute Ischemic Stroke, Recombinant Tissue Plasminogen Activator, Thrombolysis, Rural Healthcare, NIHSS, Modified Rankin Scale.

INTRODUCTION

Stroke is one of the leading causes of mortality and long-term disability worldwide and poses a major public health burden, particularly in low- and middle-income countries. Acute ischemic stroke accounts for nearly 80–85% of all stroke cases and results from sudden occlusion of cerebral blood vessels leading to interruption of blood supply to the brain. Early diagnosis and timely intervention are crucial in reducing neurological damage and improving functional outcomes.

The burden of stroke is especially significant in resource-limited settings where access to specialized stroke care remains inadequate. [1]

Recombinant tissue plasminogen activator (rtPA) has emerged as the cornerstone of acute ischemic stroke management. Intravenous thrombolysis with rtPA has been shown to restore cerebral perfusion by dissolving thrombi when administered within the recommended therapeutic time window. Landmark clinical trials such as the National Institute of Neurological Disorders and Stroke (NINDS) trial and the European Cooperative Acute Stroke Study (ECASS III) demonstrated that early administration of rtPA significantly improves neurological recovery and reduces long-term disability in patients with acute ischemic stroke. These studies established thrombolysis as the standard evidence-based therapy for eligible stroke patients. [2,3]

Despite the proven efficacy of thrombolytic therapy, the utilization of rtPA in developing countries such



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as India remains limited, especially in rural regions. Rural populations face unique challenges including delayed transportation, poor road connectivity, lack of awareness regarding stroke symptoms, financial constraints, and inadequate healthcare infrastructure. Many peripheral healthcare centers lack facilities such as neuroimaging services, stroke units, trained neurologists, and round-the-clock emergency care necessary for timely thrombolysis. Consequently, a large number of patients fail to reach hospitals within the therapeutic window period, thereby losing the opportunity for effective treatment. [4,5]

India has a predominantly rural population, and stroke care disparities between urban and rural healthcare systems continue to remain substantial. Public awareness regarding the warning signs of stroke and the importance of early hospital presentation is often poor in rural communities. In addition, socioeconomic limitations and dependency on local healthcare providers further contribute to treatment delays. Even when patients arrive at tertiary care hospitals, barriers such as affordability of rtPA, lack of trained personnel, and delayed neuroimaging may affect timely administration of thrombolytic therapy. [6]

Several urban-based studies from India have evaluated the effectiveness and safety of rtPA in acute ischemic stroke; however, there is limited literature assessing outcomes and barriers associated with thrombolysis in rural tertiary care settings. Understanding these barriers is essential for developing strategies aimed at improving stroke care delivery in underserved populations. Identification of factors contributing to treatment delay and poor accessibility may help in designing effective stroke awareness programs and strengthening rural healthcare systems. [7]

Therefore, the present prospective study was undertaken to evaluate the clinical outcomes of thrombolysis with recombinant tissue plasminogen activator in patients with acute ischemic stroke in a rural tertiary care center. The study also aimed to identify the major barriers affecting timely thrombolysis and acute stroke care delivery in rural India.

Aim

To evaluate the outcomes of thrombolysis with recombinant tissue plasminogen activator (rtPA) in patients with acute ischemic stroke in a rural tertiary care setting and to identify the barriers affecting timely stroke care.

Objectives

1. To assess the clinical outcomes of acute ischemic stroke patients treated with recombinant tissue plasminogen activator.

2. To evaluate the improvement in neurological status following rtPA administration using standard clinical assessment scores.

3. To identify the demographic and clinical factors associated with thrombolytic therapy outcomes.

METHODOLOGY

This prospective observational study was conducted in the Department of Emergency Medicine at Sree Mookambika Institute of Medical Sciences, Kulasekharam, from May 2025 to February 2026. The study included patients presenting with acute ischemic stroke who were eligible for thrombolytic therapy with recombinant tissue plasminogen activator (rtPA). Patients were included if they had a clinical diagnosis of acute ischemic stroke confirmed by non-contrast computed tomography (CT) scan demonstrating absence of intracranial hemorrhage and had no contraindications to rtPA administration. Patients with large vessel occlusion requiring mechanical thrombectomy, those presenting outside the recommended thrombolytic window period, and patients with contraindications such as recent surgery, bleeding disorders, uncontrolled hypertension, or other high-risk bleeding conditions were excluded from the study.

Detailed baseline demographic and clinical data including age, gender, smoking status, socioeconomic status, and associated co-morbidities such as hypertension and diabetes mellitus were recorded using structured data collection forms. Stroke severity was assessed at admission using the National Institutes of Health Stroke Scale (NIHSS). All patients underwent non-contrast CT brain imaging prior to thrombolysis to exclude intracranial hemorrhage. Eligible patients received intravenous recombinant tissue plasminogen activator according to standard stroke thrombolysis protocols after obtaining informed consent from the patient or their relatives. Following thrombolytic therapy, magnetic resonance angiography (MR angiogram) was performed to assess residual vascular occlusion. Patients who subsequently underwent mechanical thrombectomy were excluded from the final analysis.

Clinical outcomes were assessed using NIHSS score at discharge as the primary outcome measure, while the modified Rankin Scale (mRS) at one month and three months post-treatment was used as the secondary outcome measure. Significant clinical improvement was defined as an 8-point reduction in NIHSS score, a 3-point reduction in mRS score, or a final mRS score of 0–1. Mild and moderate improvements were categorized based on predefined NIHSS and mRS criteria. Treatment intervals including onset-to-door time, door-to-imaging time, and door-to-needle time were recorded to identify delays in stroke care delivery and thrombolysis administration.

All collected data including clinical, epidemiological, imaging, and outcome variables were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 25.0. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical

variables were presented as frequencies and percentages. Independent sample t-test, Chi-square test, and correlation analysis were used to assess associations between baseline variables and treatment outcomes. A p-value of less than 0.05 was considered statistically significant.

RESULT

Table 1: Baseline Features of Patients Thrombolysed with RtPA

Parameter	Number	Minimum	Maximum	Mean	Std. Deviation
Age	28	42	85	63.4	9.39
Onset to Door Time (minutes)	28	30	240	151.4	50.97
Door to Imaging Time (minutes)	28	5	50	21.6	12.1
Door to Needle Time (minutes)	28	20	160	68.8	32.56
NIHSS at Admission	28	4	27	10.4	5.64
NIHSS at Discharge	28	1	42	9.8	9.9
mRS at 1 Month	28	0	6	2.89	1.59
mRS at 3 Months	28	0	6	1.74	1.74

Treatment Times: The average time from stroke onset to hospital arrival was 151 minutes, reflecting challenges associated with rural healthcare accessibility. The door-to-imaging time it averaged 21 minutes, while the door-to-needle time was 68 minutes. The prolonged door-to- needle time was attributed to socioeconomic factors that impacted patient decision-making and consent processes.

Clinical Outcomes: At admission, the mean NIHSS score was 10.4, indicating a moderate level of stroke severity among patients. By discharge, the mean NIHSS score had decreased to 9.8. Improvements in NIHSS scores were categorized as follows:

No improvement: 32.1%

Moderate improvement: 21.4%

Mild improvement: 32.1%

Moderate improvement: 10.7%

Major improvement (defined as a reduction of 8 points or more in NIHSS): 25.0%

These outcomes are displayed in Table 2 and are visually represented in the NIHSS improvement bar chart.

Follow-up Outcomes: The modified Rankin Scale (mRS) score at one-month post-treatment had a mean of 2.89, which decreased to 1.74 at the three-month follow-up. By three months, the improvement in mRS scores was classified as:

No improvement: 25.0%

Mild improvement: 17.9%

Major improvement (defined as an mRS score reduction of 3 points or final mRS of 0- 1): 35.7%

Table 2: Improvement Based on NIHSS at Discharge

NIHSS Outcome	Frequency	Percent (%)
No Improvement	9	32.1
Mild Improvement	9	32.1
Moderate Improvement	3	10.7
Major Improvement	7	25

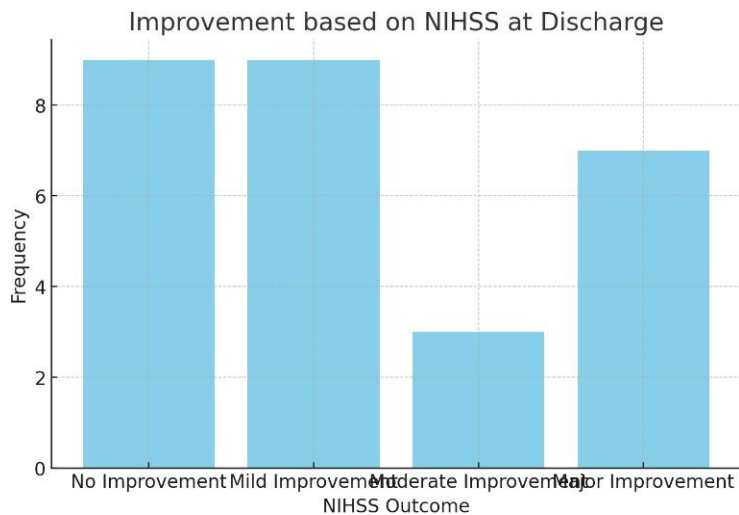
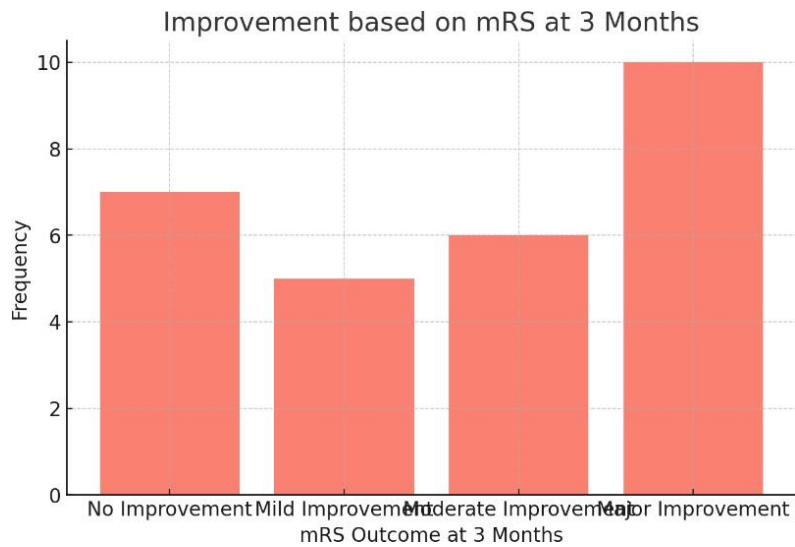


Table 3 Provides a Detailed Breakdown of Mrs Outcomes, and These Results are Also Depicted in the Mrs Improvement Bar Chart

Safety Outcomes: Importantly, no adverse effects, including symptomatic or asymptomatic bleeding, were observed within 24 hours post-thrombolysis. This supports the safety of rtPA administration in a rural tertiary care setting, even with potential delays.

Table 3: Improvement Based on MRS at 3 Months

mRS Outcome at3 Months	Frequency	Percent (%)
No Improvement	7	25
Mild Improvement	5	17.9
Moderate Improvement	6	21.4
Major Improvement	10	35.7



These data show that rtPA therapy can be efficacious and safe in a rural setting for the acute treatment of ischemic stroke but has struggled with delays to treatment. The findings call to action the need for intervention strategies that address socioeconomic barriers and logistical delays to improve access to prompt stroke treatment in rural settings.

DISCUSSION

The present study evaluated the outcomes and barriers associated with thrombolysis using recombinant tissue plasminogen activator (rtPA) in patients with acute ischemic stroke managed at a rural tertiary care center in Kerala, India. Among the 28 patients who received thrombolytic therapy, no major adverse bleeding events were observed, and 35.7% of patients demonstrated meaningful improvement in modified Rankin Scale (mRS)

scores at three months follow-up. These findings support the safety and feasibility of rtPA administration in rural healthcare settings when appropriate patient selection and standardized treatment protocols are followed. Similar results were demonstrated in previous landmark stroke trials and observational studies evaluating intravenous thrombolysis. [8,9]

The absence of symptomatic intracranial hemorrhage or significant bleeding complications in the present study highlights the importance of careful patient screening and adherence to established thrombolysis guidelines. Intravenous rtPA remains the gold standard treatment for eligible patients with acute ischemic stroke when administered within the recommended therapeutic window. The National Institute of Neurological Disorders and Stroke (NINDS) trial and ECASS III trial demonstrated that early thrombolysis significantly improves neurological recovery and functional outcomes while maintaining an acceptable safety profile. [8,10]

An important observation in the present study was the relatively short mean door-to-imaging time of 21 minutes, indicating efficient initial emergency department evaluation and neuroimaging services. However, the average door-to-needle time was prolonged at 68 minutes. Delayed thrombolysis was primarily attributed to socioeconomic factors, delays in obtaining consent, lack of awareness regarding stroke treatment, financial concerns, and delayed decision-making by patient relatives. These findings emphasize the unique challenges encountered in rural healthcare settings where social and economic barriers may significantly affect timely stroke management. Similar barriers have been reported in several Indian studies evaluating stroke care accessibility in rural populations. [11,12] The present findings further reinforce the well-established concept that “time is brain” in acute ischemic stroke management. Previous studies have consistently shown that earlier administration of rtPA results in better neurological outcomes and reduced disability. The beneficial effects of thrombolysis decline progressively with treatment delay due to irreversible neuronal injury. Therefore, minimizing treatment delays remains a critical component of effective stroke care systems. [13]

Compared to urban tertiary stroke centers, rural healthcare facilities often face additional limitations including lack of trained stroke specialists, inadequate emergency transport systems, poor public awareness, and limited access to advanced neuroimaging. Despite these barriers, the current study demonstrated that thrombolysis can still be successfully implemented in rural tertiary care settings with appropriate infrastructure and protocol-based management. This finding is particularly important for developing countries such

as India, where a substantial proportion of the population resides in rural areas. [14]

The moderate functional improvement observed in 35.7% of patients at three months follow-up is clinically significant considering the delayed presentation and socioeconomic challenges faced by the study population. Public health initiatives aimed at increasing awareness of stroke symptoms, improving emergency referral pathways, strengthening peripheral healthcare systems, and reducing financial barriers may further improve thrombolysis utilization and outcomes in rural regions. [15]

Overall, the present study highlights that rtPA thrombolysis is both feasible and safe in rural tertiary care settings. However, significant barriers related to delayed presentation and socioeconomic factors continue to affect timely intervention and optimal outcomes. Strengthening stroke care infrastructure and improving community awareness are essential steps toward enhancing acute stroke management in rural India.

CONCLUSION

The present study demonstrated that thrombolysis with recombinant tissue plasminogen activator (rtPA) is both feasible and safe in the management of acute ischemic stroke in a rural tertiary care setting. A significant proportion of patients showed meaningful functional recovery at three months follow-up without major bleeding complications. Although efficient door-to-imaging times were achieved, delays in door-to-needle time remained a major challenge, primarily due to socioeconomic factors, delayed decision-making, lack of awareness regarding stroke symptoms, and limited access to timely healthcare services. These findings highlight the importance of strengthening rural stroke care infrastructure, improving public awareness, and establishing rapid referral systems to facilitate early thrombolysis. Early recognition and timely administration of rtPA can significantly improve neurological outcomes and reduce stroke-related disability in rural populations. Further large-scale studies are required to optimize acute stroke care delivery and overcome barriers affecting thrombolytic therapy in resource-limited settings.

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