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THROMBOLYSIS WITH RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR IN RURAL INDIA: A PROSPECTIVE STUDY ON OUTCOMES AND BARRIERS IN ACUTE STROKE CARE

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Abstract

This study investigates the use of recombinant tissue plasminogen activator (rtPA) for acute ischemic stroke in a cohort of patients from rural India. **Background**: Despite the global burden of stroke as a critical driver of disability and mortality, access to timely thrombolytic therapy continues to be limited in rural settings due not only to socioeconomic factors but also to logistical barriers. The clinical profile, outcomes and challenges of rtPA treated stroke patients: A hospital-based study from a rural tertiary center of Malabar, Kerala. **Methodology**: The study was a prospective, observational design, and 28 patients presenting within the time window for rtPA were included. National Institutes of Health Stroke Scale (NIHSS) at admission, 1 h, 24 h, and discharge were used as clinical outcomes along with modified Rankin Scale (mRS) scores at 1 month and 3 months. **Results**: Among the 28 treated patients, a third experienced marked mRS score improvement at three months free of bleeding complications. However, treatment delays were observed, with a median door-to-needle time of 68 minutes, mainly reflecting decision-making impacted by socioeconomic characteristics. **Conclusion**: Thrombolysis with rtPA proved safe and effective in a rural setting. The study highlights the need for improved awareness, faster referral pathways, and enhanced financial accessibility to reduce delays in thrombolytic care. These findings underscore the potential for rtPA to be a viable stroke treatment option in rural areas, emphasizing the need for supportive policies to bridge healthcare disparities and improve stroke management outcomes across underserved regions.

Keywords: Acute ischemic stroke, Thrombolysis, Recombinant tissue plasminogen activator, Stroke management, Rural healthcare, Modified Rankin Scale, Stroke outcomes, Healthcare disparities, Socioeconomic barriers, Rural India, Stroke treatment accessibility, Tertiary care.

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Introduction

Stroke continues to be one of the leading causes of both morbidity and mortality globally, affecting particular population groups acutely in low-resource settings that may have poor access to specialists [1]. Recombinant tissue plasminogen activator (thrombolysis has been regarded as the backbone for treating acute ischemic stroke if given in a particular time window [2]. Several studies, such as the landmark NINDS and ECASS 3 trials, have shown that rtPA significantly decreases stroke-related morbidity, provided it is given early in the course of a stroke [3]. These clinical trials and subsequent urban-based studies may not reflect the challenges experienced in rural settings, where geography, poverty, and limited health infrastructure impede rapid access to care.

As a sizeable portion of the Indian population resides in rural areas, stroke patients living in such places experience different challenges [4]. The facilities in many rural hospitals — neuroimaging, appropriately trained specialists on hand, and 24-hour emergency services to administer rtPA within recommended time frames — do not exist [5]. In addition, their low socio-economic status and less awareness about stroke symptoms among the general public also prolong access to care [6]. Although some attempts have been made to develop stroke care in India, a significant void exists in the literature concerning the outcomes and feasibility of rtPA in rural tertiary care centers [7].

To fill this gap, this study assessed the outcomes of rtPA therapy in a rural Tertiary care center in Malabar, Kerala. Patients who received thrombolysis are evaluated for their NIHSS and mRS scores, and barriers to care are examined, including socioeconomic and logistical delays from call to intervention. We aim to provide insight into the challenges of stroke care in real-world settings, particularly those with limited resources and capabilities. We hope that some of this will be useful for developing new strategies to improve access to effective stroke care in rural locations. We aim to evaluate the effectiveness and safety of rtPA in a rural setting, delineate specific contributors to treatment delays, and identify areas of potential healthcare delivery improvement that could help close the urban: rural gap in stroke outcomes.

Materials and methods

This study was conducted as a prospective observational study at a rural tertiary care center in Malabar, Kerala, approved by the institutional ethics committee. Participants included consecutive ischemic stroke patients aged 18 years and above who presented to the emergency department within the 4.5-hour window period for thrombolysis and met the inclusion criteria for rtPA administration.

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Inclusion and Exclusion Criteria: Patients were eligible if they had a clinical diagnosis of acute ischemic stroke confirmed by a non-contrast CT scan, which ruled out hemorrhage, and no contraindications for rtPA use were present. Patients were excluded if they had large vessel occlusions requiring mechanical thrombectomy, were outside the thrombolytic window period, or had contraindications such as recent surgery, bleeding disorders, or other factors posing a high bleeding risk.

Procedure: Baseline clinical and demographic data, including age, gender, comorbid conditions (hypertension, diabetes, smoking status), and socioeconomic status, were recorded. Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) at baseline, and all patients underwent non-contrast CT imaging to exclude hemorrhage. RtPA was administered intravenously for eligible patients according to standard protocols following informed consent. Post-treatment, patients received an MR angiogram to evaluate for any residual occlusion; those who subsequently underwent thrombectomy were excluded from analysis.

Outcome Measures: The primary outcome was measured as the NIHSS score at discharge, while the secondary outcome was the modified Rankin Scale (mRS) score at 1- and 3 months post-treatment. Significant improvement was defined as an 8-point reduction in NIHSS a 3-point reduction in mRS or a final mRS of 0-1. Mild and moderate improvements were also categorized based on predefined NIHSS and mRS criteria.

Data Collection and Analysis: Structured data collection forms were used to record clinical, epidemiological, imaging, and outcome variables. Treatment intervals were recorded to assess delays, including door-to-imaging and door-to-needle times. Statistical analysis was conducted using SPSS software, where descriptive statistics summarized baseline characteristics, and outcomes were analyzed for significant associations with demographic and clinical factors.

Results

A total of 28 patients were included in this study, with ages ranging from 42 to 85 years and a mean age of 63. The patient cohort consisted of 57.1% males. The most common comorbid conditions observed were hypertension (46.4%) and diabetes mellitus (39.3%), with 17.9% of patients reporting a history of smoking. Baseline characteristics, such as onset-to-door time, door-to-imaging time, and NIHSS scores, are summarized in Table 1.

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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%
- 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%

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- Moderate improvement: 21.4%
- 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

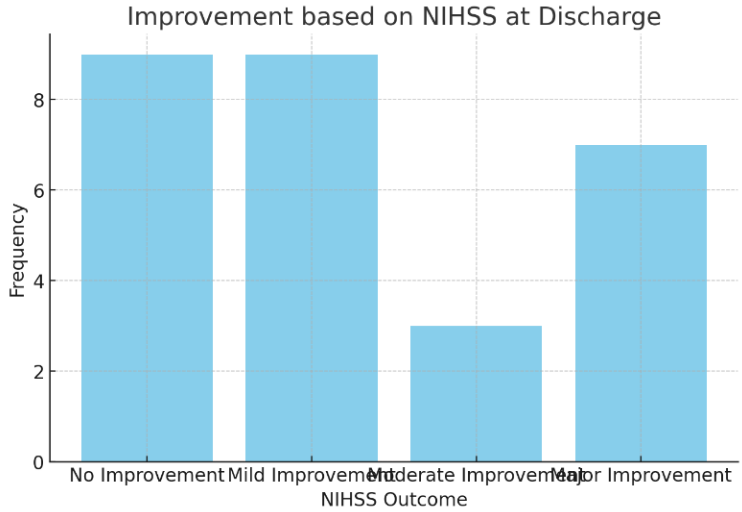

Table 3 provides a detailed breakdown of mRS outcomes, and these results are also depicted in the mRS improvement bar chart.

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 at 3 Months	Frequency	Percent (%)
No Improvement	7	25
Mild Improvement	5	17.9
Moderate Improvement	6	21.4
Major Improvement	10	35.7

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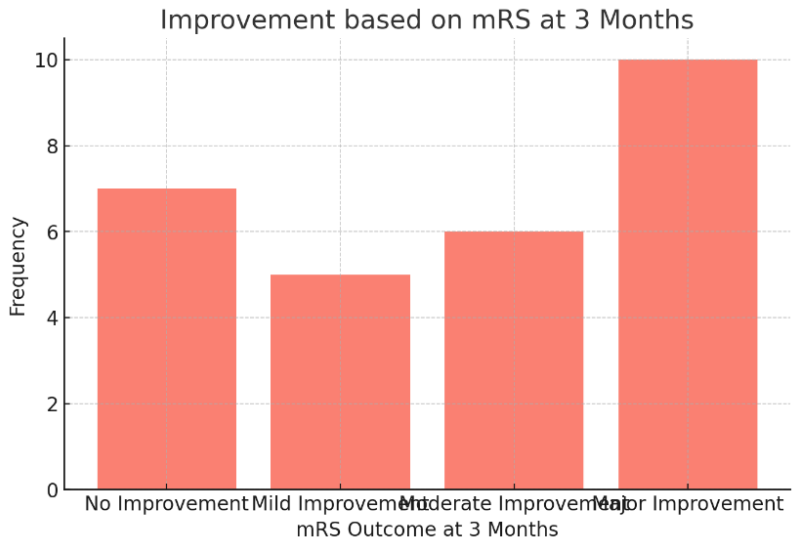

These data show that rtPA therapy can be efficacious and safe in a rural setting for the acute treatment of ischemic stroke but has struggled with delays to treatment. The findings call to action the need for intervention strategies that address socioeconomic barriers and logistical delays to improve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

Discussion

The main aim of this study was to examine the clinical outcomes and complications associated with intravenous rtPA when given for acute ischemic stroke at a rural tertiary care center in Kerala, India. Out of 28 patients treated, all had no adverse bleeding events, and 35.7% achieved meaningful mRS improvement at three months of follow-up. Although the door-to-imaging time was a modest average of 21 minutes, it appeared that door-to-needle times were much longer at 68 minutes, primarily attributed to socioeconomic issues surrounding patient decision-making. Our study conclusions regarding the feasibility and safety of rtPA in a rural setting reinforce center findings while underscoring the need for more timely intervention.

The results of our study support prior findings that demonstrate the advantages of rtPA within a time-sensitive frame. By administering rtPA within 3 to 4.5 h of stroke onset, landmark trials, including the National Institute of Neurological Disorders and Stroke (NINDS) and ECASS III, have demonstrated its efficacy in reducing disability-related stroke [8]. This paper focuses a little more on the rural aspect. Still, it sets it in the context of urban door-to-negate studies reporting shorter times often attributed to patient socioeconomic status, access to care, and public awareness—the same variables in this study affecting time. Our findings are aligned with others focusing on rural strokes, emphasizing the different challenges compared to urban literature in which door-to-needle times are often less than 45 minutes [9].

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This study's strengths include its prospective design and focus on a rural population often underrepresented in stroke research. The study offers valuable insights into rtPA's application in underserved areas by documenting real-world barriers and outcomes. However, the small sample size limits generalizability, and as a single-center study, these results may not fully represent other rural areas with varying healthcare capacities and protocols.

In short, this study demonstrates that rtPA thrombolysis is a safe and potentially effective treatment for acute ischemic stroke in rural contexts. However, we must overcome the socioeconomic and logistical barriers to maximize these benefits. Improving public awareness, early treatment protocol, and infrastructure in rural areas will reduce the lag time and accessibility of stroke care. This study calls for focused policy interventions and resource allocation to reduce health inequities, thus enabling an equitable response to stroke delivery in rural India.

Conclusion

This study shows that rtPA can be given safely and has the potential to be effective in rural tertiary care environments for acute ischemic stroke. Even though the clinical outcomes show remarkable responses, the study identifies considerable treatment initiation delays due to socioeconomic and logistical factors, including inadequate patient awareness and inaccessibility to healthcare. These results highlight the requirement for tailored interventions such as community awareness strategies, a rapidly adaptable hospital protocol, and defense mechanisms to optimize access and timeliness of stroke care in rural regions. This is a critical step toward the timely delivery of care for stroke patients residing in rural or underserved areas, as addressing these issues can significantly enhance outcomes and help narrow the gap in access to healthcare resources between urban and rural communities.

References

1. Baatiema, L., Abimbola, S., Aikins, A., Damasceno, A., Kengne, A., Sarfo, F., Charway-Felli, A., & Somerset, S. (2020). Towards evidence-based policies to strengthen acute stroke care in low-middle-income countries. Journal of the Neurological Sciences, 418. https://doi.org/10.1016/j.jns.2020.117117.
2. Yang, Y., Zhou, Z., Pan, Y., Chen, H., & Wang, Y. (2020). Randomized trial of argatroban plus recombinant tissue-type plasminogen activator for acute ischemic stroke (ARAIS): Rationale and design.. American Heart Journal, 225, 38-43. https://doi.org/10.1016/j.ahj.2020.04.003.
3. Zhang, X., Gu, Y., Xu, W., Song, Y., Zhang, A., Zhang, Z., Jiang, S., Chang, S., & Ni, G. (2020). Early Electroacupuncture Extends the rtPA Time Window to 6 h in a Male

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Rat Model of Embolic Stroke via the ERK1/2-MMP9 Pathway. Neural Plasticity. https://doi.org/10.1155/2020/8851089.

4. Inamdar, A. (2022). Factors associated with hospital arrival time of acute stroke patients in rural India. European Journal of Preventive Cardiology. https://doi.org/10.1093/eurjpc/zwac056.073.
5. Moore, K., Liu, R., Wise, E., Shah, J., Calhoun, M., & Haboubi, M. (2020). Abstract 97: Cerebrovascular Trained Advance Practice Nurse Practitioners Can Safely and Accurately Administer Alteplase and Their Neurology Physician Colleagues via Telemedicine. Stroke. https://doi.org/10.1161/STR.51.SUPPL_1.97.
6. Nobel, L., Rasnick, E., Ding, L., Robinson, D., Ayala, F., Kissela, B., & Kleindorfer, D. (2023). Abstract WP35: Neighbourhood Effects on Knowledge Of Stroke Risk Factors And Stroke Warning Signs. Stroke. https://doi.org/10.1161/str.54.suppl_1.wp35.
7. Subir, A., Krishnadasn, C., Ghafoor, F., & Rafeeque, M. (2021). Outcome of thrombolysis with recombinant tissue plasminogen activator (rtPA) in a rural tertiary care center. IP Indian Journal of Neurosciences. https://doi.org/10.18231/J.IJN.2021.022.
8. Mendelson, S., & Prabhakaran, S. (2021). Diagnosis and Management of Transient Ischemic Attack and Acute Ischemic Stroke: A Review.. JAMA, 325 11, 1088-1098. https://doi.org/10.1001/jama.2020.26867.
9. Vargas, A., Zobel, R., Cherian, L., Dafer, R., Osteraas, N., Song, S., Cichon, M., & Conners, J. (2023). Mobile Stroke Unit Treatment Times and Transport Frequency in a Suburban Setting. https://doi.org/10.1101/2023.03.02.23286726.