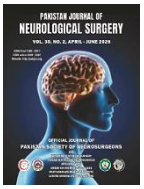

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Original Research

Outcome Analysis of tPA Administration in Acute Ischemic Stroke Patients at Nishtar Hospital, Multan

Muhammad Fahad Saleem[1], Ubaid Ullah Ansari[2], Sohaib Hassan[1], Muhammad Hamza Khan[1], Muhammad Wazir Ali Khan[3], Muhammad Wahab Qureshi[1], Meer Wasiq[1], M Wasay[4]

[1]*Neurology Department, Nishtar Medical University Hospital, Multan*
[2]*Neurology Department, Multan Medical & Dental College*
[3]*Neurology Department, Sheikh Zayed Medical College/Hospital*
[4]*Neurology Department, Aga Khan University, Karachi - Pakistan*

ABSTRACT

Objectives: To assess the efficacy (clinical outcome), recovery (disability), and safety of rtPA use through an investigation of patients who were treated at a tertiary hospital for acute ischemic stroke.

Materials & Methods: A retrospective observational study included 115 adults aged>18 with an acute ischemic stroke who were treated with intravenous rt-PA at Nishtar Hospital, Multan, over a year. Data were obtained from medical records regarding demographics, vascular risk factors, stroke subtype, time to presentation, door-to-needle time, and NIHSS scores at presentation and 90 days after treatment. ANOVA and Pearson correlation were used to test for associations between age, stroke severity, and outcomes.

Results: Mean age was 55 years, and the majority of patients suffered from hypertension (62.6%) or diabetes (42.6%). The highest incidence of stroke was as a result of a cardioembolic cause (40%). The majority of patients, 70.4%, still met the 10-minute thrombolysis goal, even though they presented late. The majority of patients, 92(80%), showed improvement, recovery, and symptoms did not worsen during the next 72 hours of hospital stay, whilst 14.8% had limited improvement and 5.2% died from stroke. The relationship of age and stroke severity was highly significant at both the time of presentation and at 90 days post-stroke ($r > 0.89$, $p < 0.01$).

Conclusion: Intravenous rt-PA was associated with improved neurological outcomes and low mortality in this cohort; however, given the retrospective single-arm design, causal efficacy cannot be established, and findings require confirmation in controlled prospective studies.

Keywords: Stroke, Thrombolysis, rt-PA, Acute Ischemic Stroke, NIHSS (National Institutes of Health Stroke Scale).

Corresponding Author: Muhammad Fahad Saleem
Neurology Department
Nishtar Medical University Hospital, Multan
Email: drfahad@msn.com

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INTRODUCTION

Stroke is characterized by focal neurological deficits that occur suddenly due to diminished blood flow to the brain. Stroke is a leading cause of mortality and long-term disability globally and imposes a substantial burden on healthcare systems, particularly in low- and middle-income countries.[1] Approximately 85-87% of all strokes are ischemic in nature, resulting from thromboembolic occlusion of cerebral arteries.[2] At the cellular level, cerebral ischemia leads to adenosine triphosphate depletion secondary to hypoxia, disruption of neuronal ionic gradients, membrane depolarization, and, without timely reperfusion, irreversible neuronal injury.[3] With increasing life expectancy and rising prevalence of cardiovascular risk factors such as hypertension, diabetes mellitus, and dyslipidemia, the incidence of ischemic stroke continues to increase globally.[4] Survivors of acute stroke frequently experience persistent neurological deficits, leading to significant disability, reduced quality of life, and long-term dependency. Therefore, timely and effective acute-phase management is essential to restore cerebral perfusion, improve functional outcomes, and reduce stroke-related morbidity and mortality.[5-6]

Current standard management for eligible patients with acute ischemic stroke includes intravenous thrombolysis using recombinant tissue plasminogen activator (rt-PA), commonly known as alteplase.[7] Tissue plasminogen activator is a serine protease that catalyzes the conversion of plasminogen to plasmin, initiating fibrinolysis and thrombus dissolution. Recombinant formulations of tPA exhibit improved fibrin specificity and prolonged half-life compared to endogenous tPA due to resistance to plasminogen activator inhibitor-1 (PAI-1).[8] Early restoration of cerebral perfusion through thrombolysis can significantly limit infarct size and improve neurological recovery. Evidence from clinical and experimental studies supports that rt-PA administration within guideline-recommended time windows improves functional outcomes in acute ischemic stroke.[9]

Stroke patients receiving thrombolytic therapy derive the greatest benefit when treatment is administered promptly.[6] Current international guidelines recommend intravenous rt-PA within 3 hours of symptom onset, with an extended window of up to 4.5 hours in carefully selected patients.[10] However, in low- and middle-income countries, utilization of thrombolytic therapy remains limited due to delayed hospital presentation, inadequate public awareness of stroke symptoms, and resource constraints. Moreover, concerns regarding complications, particularly symptomatic intracranial hemorrhage, necessitate careful patient selection and close monitoring.

In contemporary acute stroke management, mechanical thrombectomy has emerged as an essential complementary reperfusion strategy alongside intravenous thrombolysis. It involves endovascular retrieval of large-vessel occlusions using stent retrievers or aspiration systems and has demonstrated superior functional outcomes in appropriately selected patients, particularly those with large vessel occlusions. This advancement has significantly reshaped acute ischemic stroke treatment paradigms globally.[1-3] Furthermore, most major stroke outcome studies and thrombolysis registries from South Asia, including regional stroke registry data, have demonstrated variable rates of rt-PA utilization and outcome disparities compared to high-income settings. These regional findings highlight persistent gaps in thrombolysis access, delays in door-to-needle time, and differences in stroke care infrastructure, underscoring the need for locally generated evidence.[3-4]

Stroke subtype classification in this study is based on the TOAST (Trial of Org 10172 in Acute Stroke Treatment) criteria, which categorizes ischemic stroke into large-artery atherosclerosis, cardioembolism, small-vessel occlusion (lacunar), stroke of other determined etiology, and stroke of

undetermined etiology.[5-6] This classification ensures standardized etiological grouping and improves comparability with international stroke research. Thus, the purpose of this study was to analyze the clinical outcomes of patients with acute ischemic stroke after administration of intravenous rt-PA (tPA) at Nishtar Hospital, Multan, with specific emphasis on functional recovery and treatment-related complications. The findings aim to contribute context-specific evidence on thrombolytic therapy outcomes in a resource-limited setting and help guide improvements in acute stroke care in Pakistan.

MATERIAL AND METHODS

Study Design and Setting

An observational retrospective design study was performed at Nishtar Hospital Multan, a tertiary care teaching hospital that serves as a primary referral center for patients who have an acute stroke in Southern Punjab, Pakistan, during one calendar year (October 2024 to October 2025) by reviewing the medical record data of those patients who were treated with intravenous thrombolysis because of an acute ischaemic stroke.

Study Population

During the set amount of time, all patients who were adults and who had a diagnosis of acute ischemic stroke and who received intravenous tissue plasminogen activator (tPA) were included in this study. A total of 115 have submitted their information to be considered for this analysis. Patients were excluded if they were missing their pertinent medical records or the required information about their outcomes.

Clinical Assessment and Imaging

Patients presenting to the emergency department with suspected acute ischemic stroke underwent immediate neurological evaluation using the National Institutes of Health Stroke Scale (NIHSS). Non-contrast computed tomography (CT) of the brain was performed in all patients to exclude intracranial hemorrhage before thrombolysis. In selected cases, CT angiography (CTA) was additionally performed to identify large vessel occlusion (LVO) and to guide further management decisions. Patients identified with LVO on CTA were assessed for eligibility for mechanical thrombectomy and, when appropriate, were referred to a higher-level neurointerventional center through a structured referral pathway**.** The diagnosis of acute ischemic stroke was confirmed based on clinical presentation and imaging findings before administration of thrombolytic therapy.

Thrombolytic Therapy

Eligible patients received intravenous alteplase (tPA) at a dose of 0.9 mg/kg (maximum 90 mg), with 10% administered as an IV bolus over 1 minute and the remaining 90% infused over 60 minutes.[11] Door-to-needle time and symptom-to-hospital presentation time were recorded as continuous variables.

Data Collection

Structured data collection forms were used to collect medical record data from participating hospitals. With respect to demographic profile, there were important variables, which were based on "age" and "sex." Other variables collected include whether the patient was admitted to an emergency department; whether there were vascular risk factors (hypertensions, DX As, atrial fibrillation, previous anticoagulation); the type of stroke presented for treatment; the time of presentation; the time from door-to-needle; and the National Institutes of Health Stroke Scale (NIHSS) scores recorded at the time of initial admission and at 90 days post-stroke. Other information collected included the use of carotids for imaging, details of carotid endarterectomies,

treatment success/failure, and complications, including hemorrhagic transformation and bleeding due to anticoagulants.

Outcome Measures

The primary outcome that was measured in this trial was improvement in clinical status based on the difference in the National Institutes of Health Stroke Scale (NIHSS) score from the beginning to the end of the study (90 days). Secondary outcomes included the frequency of hemorrhagic complications, as well as the need for carotid procedures after treatment. In addition, treatment outcomes were classified as either having recovered/improved, not having improved as expected, or dying.

Definition of Symptomatic Intracranial Hemorrhage (SICH)

Symptomatic intracranial hemorrhage (SICH) was defined as any intracranial hemorrhage associated with clinical deterioration, indicated by an increase of ≥4 points in the NIHSS score, or resulting in death within 24-36 hours following thrombolytic therapy. This definition is consistent with established stroke research and thrombolysis registry criteria.[12]

Statistical Analysis

Using SPSS Statistics version 25, the dataset was collected and evaluated in the following ways: Qualitative data were reported as frequencies and percentages; quantitative data were reported as Mean ±SD. A one-way analysis of variance (ANOVA) was used to compare NIHSS scores between age groups. Pearson correlation coefficient was used to evaluate the relationship between age, NIHSS scores at time of onset, and 90 days after onset. Statistical significance was assigned to all tests with p-values <0.05.

Ethical Considerations

Approval was received from the institutional review board for this study from Nishtar Medical University and Hospital, Multan (Reference no: 18813/NW; Dated: 25-10-2025). Informed consent was waived since this was a retrospective study based on review of existing records. The confidentiality of patients was maintained, and no personal identifiers were recorded for any patients. All procedures conducted by participating institutions complied with regulatory guidelines and institutional policy.

RESULTS

Demographic and Clinical Characteristics

The mean age of patients in this study was 55 years, with 33% of patients in the 50-59 age range and 22% in the 60-69 age range. Only 15% of patients were aged 70 or older. There was a slightly higher number of male than female patients (63 % vs 52%), representing a male predominance of 54.8% vs 45.2%. The majority of patients were admitted to the Neurology Ward (44.3%) and 40.9% to the Critical Care Unit. The most prevalent vascular risk factor amongst patients included hypertension (62.6%), diabetes mellitus (42.6%), and Atrial Fibrillation (25.2%). Of all patients studied, 27% were previously using anticoagulants before their stroke. Cardioembolic stroke was the most prevalent type of stroke (40%), followed by Lacunar Infarct (30.4%) and Large Artery Atherosclerotic Stroke (20%). The other subtypes accounted for the remaining 9.6% of total strokes (Table 1).

Time Metrics and NIHSS Scores

Time-related variables and stroke severity (assessed via NIHSS scores) at the time of admission and at 90 days are summarized in Table 2. The majority of the patients had arrived

at an ED within >2 hours of symptom onset (69.6%). Only 20.0% of the patients had arrived at an ED within <2 hours, and only 10.4% of the patients had arrived within <1 hour of the onset of their symptoms. Despite these delayed presentations, most of the patients received early in-hospital thrombolysis (70.4% of the patients received intravenous tPA within 10 minutes of arrival to an ED; 30.4% received it within 5 minutes, and 40.0% received it within 10 minutes of their arrival to the ED). At the time of admission, the majority of the patients had moderate stroke severity (NIHSS 5-15) (50.4%), with 29.6% of the patients presenting with severe stroke (NIHSS ≥16) and 20.0% of the patients presenting with mild stroke (NIHSS 0-4). Upon 90-day follow-up, the majority of the patients had moderate residual neurological deficits (47.8%), with 33.0% having mild residual neurological deficits and 19.1% having severe residual neurological deficits.

Table 1: *Demographic and Clinical Characteristics of Patients (n = 115).*

Variable	Category	n	%
Age (years)	30-39	12	10.4
	40-49	21	18.3
	50-59	38	33.0
	60-69	26	22.6
	≥70	18	15.7
Gender	Male	63	54.8
	Female	52	45.2
Admission Department	Neurology Ward	51	44.3
	Critical Care Unit	47	40.9
	Other	17	14.8
Risk Factors	Hypertension	72	62.6
	Diabetes Mellitus	49	42.6
	Atrial Fibrillation	29	25.2
	Prior Anticoagulant Use	31	27.0
Stroke Type	Cardioembolic	46	40.0
	Lacunar	35	30.4
	Large artery atherosclerosis	23	20.0
	Other	11	9.6

Table 2: *Time Metrics and NIHSS Scores.*

Variable	Category	n	%
Time to Presentation	≤1 hour	12	10.4
	≤2 hours	23	20.0
	>2 hours	80	69.6
Door-to-Needle Time	≤5 min	35	30.4
	≤10 min	46	40.0
	≤15 min	34	29.6
NIHSS at Onset	Mild (0–4)	23	20.0
	Moderate (5-15)	58	50.4
	Severe (≥16)	34	29.6
NIHSS at 90 days	Mild deficit	38	33.0
	Moderate deficit	55	47.8
	Severe deficit	22	19.1

Treatment Outcomes, Carotid Imaging, and Complications

Table 3 describes the treatment outcomes of intravenous thrombolytic therapy and carotid imaging results with complications of patients treated with intravenous thrombolytics. The majority of the stroke patients demonstrated a favorable clinical outcome, with 92(80%) showing improvement, recovery, and symptoms not worsening during the next 72 hours of hospital stay. Poor improvement was seen in 17 patients (14.8%), with mortality occurring in 6 patients (5.2%). Carotid imaging was completed in most instances (80%), with 10.4% of patients subsequently having carotid endarterectomy. In terms of safety outcomes, hemorrhagic transformation occurred in 5.2% of patients, and bleeding associated with anticoagulation occurred in 5.2% of patients. These results show a relatively low occurrence rate of significant hemorrhagic complications after thrombolysis.

In Table 4, researchers used one-way analysis of variance (ANOVA) and Pearson correlation analyses to evaluate how age related to stroke severity as measured by NIHSS scores on presentation and 90 days following stroke. A significant difference ($F = 41.967$; $p < 0.001$) was

found via one-way ANOVA in NIHSS scores by age group at presentation, indicating increasing stroke severity at presentation with increasing age. Pearson correlation analysis provided strong positive correlations between age and NIHSS scores on presentation ($r = 0.901$) and at 90 days post-stroke ($r = 0.894$; both $p < 0.01$). Additionally, there was also a strong positive correlation between NIHSS scores on presentation and 90 days following stroke ($r = 0.938$; $p < 0.01$). This finding indicates that increased stroke severity at presentation was correlated with poorer neurological outcomes at follow-up.

Table 3: *Treatment Outcomes, Carotid Imaging, and Complications.*

Variable	Category	n	%
Treatment Outcome	Improved/Recovered/Not worsened	92	80.0
	Poor improvement	17	14.8
	Mortality	6	5.2
Carotid Imaging	Performed	92	80.0
	Not performed	23	20.0
Carotid Endarterectomy	Yes	12	10.4
	No	103	89.6
Complications	Hemorrhagic transformation	6	5.2
	Bleeding due to anticoagulants	6	5.2

Table 4: *One-Way Anova and Pearson correlation for age, NIHSS scores at Onset, and 90 days.*

Source	SS	df	MS	F	p-value
One-way ANOVA (NIHSS at onset by age group)					
Between groups	108.174	4	27.043	41.967	<0.001
Within groups	109.672	110	0.997		
Pearson Correlation for Age, NHSS at onset, and 90 days					
Age	1		0.894$**	0.901**	
NIHSS at 90 days	0.894**		1	0.938**	
NIHSS onset	0.901**		0.938**	1	

DISCUSSION

The majority of patients were middle-aged men, but of these men, most had co-morbidities of either hypertension or diabetes, while cardioembolic strokes were also the most frequent subtype of strokes seen. Many patients delayed coming to the hospital for treatment; however, most patients received thrombolysis services quickly after arriving at the hospital. In fact, 80% of all patients improved after receiving treatment, and only 5% of patients died. Stroke severity and outcome were strongly era-related, with older patients more likely to have severe strokes and therefore death.

The risk factor and demographic profile of this cohort are similar to other studies, both regionally and internationally, with all of these studies indicating a predominance of men, and that stroke patients have a significant burden of hypertension and diabetes.[13] Evidence also indicated that cardioembolic and lacunar infarction were by far the most common types of stroke in India and South Asia due to the increasing incidence of atrial fibrillation and small vessel disease in those areas.[14] However, in the present study, the proportion of cardioembolic stroke (40%) appears relatively high compared to the documented prevalence of atrial fibrillation (25%). This discrepancy may reflect limitations in etiological workup, including incomplete cardiac evaluation (e.g., lack of prolonged rhythm monitoring or echocardiographic assessment), which may have led to potential misclassification or under-detection of other stroke subtypes. Patients in this study who presented to the hospital with acute stroke symptoms and had delays in presenting, usually delays from 12 to 120 minutes; however, door-to-needle times were shorter in this study compared to previous studies, with delayed treatment times often limiting thrombolysis use.[15-16] Rapid thrombolysis in-hospital likely contributed to the positive neurological outcomes seen in most patients in this study.

Improvement of NIHSS scores from the time of baseline to 90-day follow-up was similar to the findings of landmark trials and observational studies that demonstrated the effectiveness of thrombolysis for the reduction of neurological deficits when administered during the time period of efficacy.[17-18] The mortality rate of this study (5%) was less than that of many regional cohorts (between 10% and 23%); therefore, patient care selection/criteria have improved, and protocol-guided care was more common. The occurrence of hemorrhagic transformation or bleeding due to anticoagulants was similar to the global safety profile of thrombolysis, indicating that thrombolytic therapy offers an accepted risk-benefit ratio in routine practice.[19] A strong positive correlation was observed between age and NIHSS scores at both baseline and 90-day follow-up. However, the very high correlation coefficients should be interpreted with caution. These values may reflect the relatively small sample size, limited variability within the study population, and potential influence of confounding factors such as baseline stroke severity and comorbid conditions. Therefore, while age remains an important predictor of stroke severity and outcomes, further multivariate analysis in larger cohorts is warranted to validate the strength of this association. The data from this cohort support the previous literature identifying a strong correlation between age and NIHSS score at both the beginning of treatment and at 90-day follow-up, and that both of these variables strongly correlate with negative outcomes.

LIMITATIONS

Due to the single-pass assessment and the small sample size, it was difficult to draw generalizable conclusions from the results of this study. Moreover, since no control group of patients did not receive thrombolysis, no comparative analysis could be performed. Moreover, patients will be followed for more than 90 days, therefore limiting the identification of other predictors of outcome and the development of optimal thrombolysis strategies in developing countries.

CONCLUSION

Patients who suffered an acute ischemic stroke (AIS) and were treated with intravenous thrombolysis demonstrated favorable neurological outcomes, with approximately 80% showing improvement or stabilization of symptoms during the initial 72 hours of hospital stay, and a low observed mortality rate. However, these findings should be interpreted cautiously, as this was a retrospective single-arm study without a control group, limiting the ability to establish definitive treatment efficacy. An increase in age was associated with greater stroke severity and poorer clinical outcomes. The results suggest an association between timely thrombolytic therapy and improved clinical outcomes, particularly when supported by structured in-hospital stroke care and adherence to established treatment protocols. While the findings are consistent with existing literature, causal inferences cannot be made, and further controlled, prospective studies are required to validate these observations.

ABBREVIATIONS

AIS: Acute Ischemic Stroke.
CT: Computed tomography.
CI: Confidence Interval.
mRS: Modified Rankin Scale.
NIHSS: National Institutes of Health Stroke Scale.
OR: Odds Ratio.
PAI-1: Plasminogen activator inhibitor-1.
SICH: Symptomatic Intracranial Hemorrhage.
tPA: Tissue Plasminogen Activator.

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AUTHOR CONTRIBUTION TABLE

Author Name	Contribution
Muhammad Fahad Saleem	Conceptualization, & Final Approval of Manuscript.
Ubaid Ullah Ansari	Study Design & Manuscript Writing.
Sohaib Hassan	Collection, Literature Review, Final Approval of Manuscript.
Muhammad Hamza Khan	Data Collection & Literature Review.
Muhammad Wazir Ali Khan	Data Collection & Draft Review.
Muhammad Wahab Qureshi	Recruitment & Clinical Supervision.
Meer Wasiq	Data Analysis.
M. Wasay	Statistical Work.