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Factors Affecting Management of Acute Ischemic Stroke with Reference to Intravenous Thrombolysis and its Impact on Short Term Outcome

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Abstract: ***Background*: Stroke is a major global health concern, ranking second in terms of fatality worldwide, following ischemic heart disease. However, few stroke patients arrive at the hospital within the optimal time for thrombolysis, and even among those who do, not all receive this therapy. Therefore, the objective of the study was to examine the factors that influence the treatment of acute ischemic stroke, particularly with intravenous thrombolysis, and to evaluate the short-term outcomes. *Methods*: This prospective observational study was carried out between August 2019 to August 2021 in the emergency department of tertiary care hospital. Patients with acute ischemic stroke (AIS) who were eligible for intravenous thrombolysis within 4.5 hours of the beginning of symptoms were included in the study. Comprehensive assessments, including history, examinations, and blood investigations, were conducted. Thrombolytic treatment was administered if within the specified time frame, while antiplatelets were given in other cases. Follow-up evaluations were conducted at discharge and 90 days. *Results*: The age distribution, comorbidities, and CT-MRI findings were similar between individuals who received thrombolysis and those who did not. Among the thrombolysis group, 84% had no complications, while 8% experienced intracerebral hemorrhage, and 8% had an extension of the infarction. The overall mortality rate was 13.33% for non-thrombolysis patients and 12% for thrombolysis recipients, with no statistically significant difference between the two groups. *Conclusion*: The results highlight the need for careful consideration when deciding to use thrombolysis for AIS cases. Additionally, they emphasize the importance of actively monitoring and effectively managing any potential treatment complications.***

Keywords: Stroke, thrombolysis, acute stroke, ischemic stroke, tissue plasminogen activator

1. Introduction

Stroke, a significant worldwide health concern, is a prominent contributor to death and disability in developed countries, and its incidence is on the rise in lower-income and middle-income countries [1]. The rise in India's life expectancy, which now exceeds 60 years, has resulted in higher occurrence of age-related, non – communicable like stroke [2, 3]. Thus, strokes have emerged as the fourth leading cause of death and fifth leading cause of disability of India [4, 5]. Ischemic stroke is distinguished by the abrupt reduction of blood flow to the particular area of the brain leading to corresponding impairment of neurological function in that affected region [6]. Hypertension, alcoholism, smoking, diabetes mellitus, and dyslipidemia are the primary factors contributing to stroke [7].

The majority of ischemic strokes are caused by thromboembolism often originating from conditions such as large artery atherosclerosis and cardiac disorders, notably **atrial** fibrillation and small vessel disease [6].

Medications that disrupt hemostasis and clot formation, such as anticoagulants and platelet antiaggregant, are commonly employed in the management of cerebrovascular diseases due to the substantial involvement of thrombosis in the pathophysiology of ischemic stroke. These drugs are also used to prevent the recurrence of stroke [8].

The treatment of acute ischemic stroke (AIS) with intravenous thrombolysis (IVT) using tissue plasminogen activator (tPA) has been shown to lead to improved functional outcomes in patients. [9]. Acute stroke treatment is still difficult in the modern era. Several countries currently regularly provide thrombolytic therapy to all eligible participants who had an acute ischemic stroke within the designated time frame without any contradictions. Recombinant tissue plasminogen activator (r-tPA), when given intravenously within 4.5 hours of stroke after the initial onset of stroke, has been linked to positive predictive results [8, 10].

The therapeutic window for IVT is quite narrow, hence prompt hospital admission for IVT with t-PA is essential for the successful treatment of ACS. Unfortunately, few number of cases with ischemic stroke reperfusion therapy using IVT, because of delayed hospital presentation, which is a key limiting factor. Furthermore, even within the therapeutic

time frame, the early administration of thrombolysis is linked to better clinical outcomes than the delayed administration of thrombolysis [11, 12]. Thus, the aim of the current research was to study the factors **influencing the management of AIS by** intravenous thrombolysis and study its short-term outcomes.

2. Materials and Methodology

This prospective observational study was performed in the emergency ward of Medical Department of a tertiary care hospital from 1 August 2019 to31 August 2021. The present study included the patients with AIS who met the eligibility criteria for intravenous thrombolysis. The individuals who arrived at the hospital within the designated window period of 4.5 hours from the beginning of symptoms. The participants were provided with information and given informed written consent. The research protocol obtained approval from the Institutional Ethical Committee.

Criteria for inclusion:

- Patients between the ages of 18 to 80 years including male and female.
- Patients diagnosed with ischemic stroke who were admitted to the hospital within 4.5 hrs from the beginning of symptoms.

Criteria for exclusion:

- Pregnant females
- Patients with intracranial hemorrhage
- Patients with head trauma
- Patients with stroke mimics including Todd's paralysis in the post-ictal phase, migraine, hypoglycemia

A comprehensive assessment was conducted for the patients, including a detailed history which includes addictions, comorbidities, and time taken to reach the hospital. Systematic and central nervous system (CNS) examinations were performed. Blood investigations were conducted, including hemoglobin, total white blood cell count, platelets, blood urea, serum creatinine, serum bilirubin, SGPT, and prothrombin time.

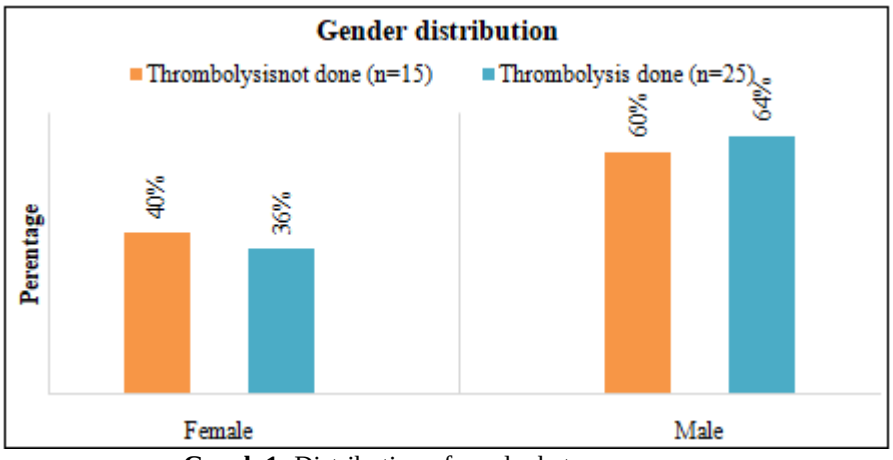
Methodology

Upon encountering a hyper-acute stroke patient, the emergency room physician conducted essential blood tests and non-contrast CT scan/MRI while notifying an on-call neurologist. CT scan/MRI findings were categorized as early ischemic or non-ischemic. Patients with intracranial hemorrhage were excluded. Thrombolytic treatment with intravenous (rTPA) was administered if family members agreed and the stroke onset was within 4.5 hours. Antiplatelets were given if contraindications or refusal for thrombolysis existed. Neurological assessments, including National Institute of Health Stroke Scale (NIHSS) and MRS scores were recorded before and after treatment. Repeat CT scans were scheduled at 24 hours, with additional scans for neurological deterioration. Symptomatic intracranial hemorrhage was determined by clinical deterioration. Modified rankin scale (MRS) evaluations were conducted at discharge and 90 days for thrombolysed patients.

Statistical analysis

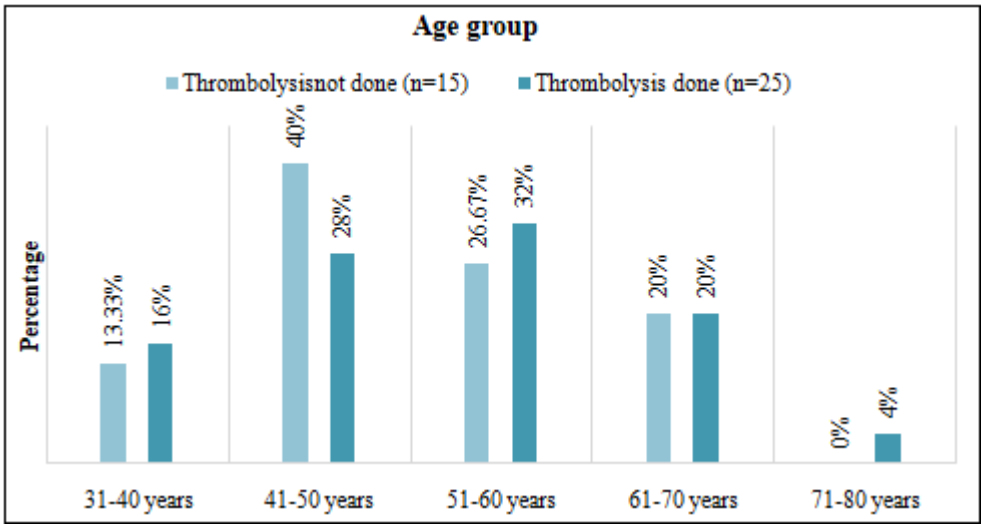
The collected data was entered and organized in a spreadsheet using Microsoft Excel. Statistical analysis was performed using SPSS version 20.0. Continuous variables were summarized using descriptive statistics, such as mean and standard deviation, while categorical variables were expressed as proportions. The chi-square test was utilized to examine the relationship between categorical variables, and the t-test was used to assess the association between continuous variables. A p-value of less than 0.05 was considered statistically significant.

3. Results



Graph 1: Distribution of gender between groups

In the "Thrombolysis not done" group, out of the 15 individuals, 40% were female and 60% were male. In the "Thrombolysis done" group, which consisted of 25 individuals, 36% were female and 64% were male. The p-value of 0.8 indicates that there is no statistically significant difference in the distribution of genders between the two groups.



Graph 2: Age group distribution of patients between the groups

The table presents the distribution of age groups among individuals who did or did not receive thrombolysis, along with corresponding statistical analysis. In the "Thrombolysis not done" group, the percentage distribution of individuals across different age groups was as follows: 13.33% in the 31-40 years age group, 40% in the 41-50 years age group, 26.67% in the 51-60 years age group, 20% in the 61-70 years age group, and none in the 71-80 years age group. In the "Thrombolysis done" group, the percentage distribution of individuals across different age groups was as follows: 16% in the 31-40 years age group, 28% in the 41-50 years age group, 32% in the 51-60 years age group, 20% in the 61-70 years age group, and 4% in the 71-80 years age group. The p-value of 0.36 for mean age indicates that there is no statistically significant difference in the mean age between the two groups.

Table 1: Distribution of comorbidities and Ct-MRI findings between the groups

Comorbidities	Thrombolysis notdone (n=15)	Thrombolysisdone (n=25)	Total (n=40)	p-value
Hypertension	10 (66.67%)	16 (64%)	26 (65%)	**0.864**
Diabetes	04 (26.67%)	08 (32%)	12 (30%)	**0.722**
IHD	01 (6.67%)	05 (20%)	06 (15%)	**0.253**
Hypothyroidism	02 (13.33)	02 (4%)	04 (10%)	**0.586**
CT-MRIfinding				
Lacunarstroke	07 (46.67%)	07 (28%)	14 (35%)	-
Anteriorcirculationstroke	07 (46.67%)	13 (52%)	20 (50%)	-
Posteriorcirculationstroke	01 (6.66%)	05 (20%)	06 (15%)	-

The presented table illustrates the distribution of comorbidities and CT-MRI findings among individuals who underwent thrombolysis compared to those who did not. In the group without thrombolysis (15 individuals), the incidence of hypertension was 66.67%, diabetes was 26.67%, IHD was 6.67%, and hypothyroidism was 13.33%. For the thrombolysis-receiving group (25 individuals), the respective percentages were 64%, 32%, 20%, and 4%. Statistical analysis revealed no significant differences in comorbidity distribution between the two groups.

Regarding CT-MRI findings, among the 15 individuals without thrombolysis, 46.67% had lacunar stroke, 46.67% had anterior circulation stroke, and 6.66% had posterior circulation stroke. In the thrombolysis group (25 individuals), the percentages were 28%, 52%, and 20%, respectively.

By providing the total counts for each CT-MRI finding, the table enables comparison between the two groups. Overall, among the total of 40 individuals, 35% had lacunar stroke, 50% had anterior circulation stroke, and 15% had posterior circulation stroke.

Table 2: Complications in thrombolysis group

Complications	Thrombolysis done (n=25)
No complication	21 (84%)
Intracerebral Hemorrhage	02 (8%)
Extension of infarction	02 (8%)

According to the data provided, among the group of individuals who received thrombolysis (a treatment for stroke), 84% (21 individuals) did not experience any complications. Among the remaining individuals, 8% (2 individuals) developed intracerebral hemorrhage, which refers to bleeding within the brain. Another 8% (2 individuals) experienced an extension of the infarction, which is the expansion of the area of tissue damage caused by reduced blood supply. These complications indicate potential adverse effects associated with thrombolysis treatment.

Table 3: Comparison of onset to door time and door to needle time among study participants

Variables	Thrombolysis not done (n=15)	Thrombolysis done (n=25)	Total (n=40)
Mean Onset to door time	1.30 ± 0.73	1.36 ± 0.77	1.33 ± 0.74
Mean Door to needle time	-	1.55 ± 0.63	-

Based on the data provided in Table 3, the study observed that the mean time elapsed from the onset of symptoms to hospital arrival was 1.33 hours. However, the analysis did not indicate any significant difference in time between individuals who received thrombolysis and those who did not.

Table 4: Comparison of Outcome among study participants (n=40)

Discharged/ Death	Thrombolysis not done (n=15)	Thrombolysis done (n=25)	Total (n=40)	p-value
Discharged	13 (86.67%)	22 (88%)	35 (87.5%)	0.902
Death	02 (13.33%)	03 (12%)	05 (12.5%)	

According to the findings presented in Table 8, the study observed a mortality rate of 13.33% among patients who did not undergo thrombolysis, while the proportion of deaths was 12% among patients who received thrombolysis. The difference in mortality between the two groups did not show statistical significance based on the observed data.

4. Discussion

The probability of experiencing a stroke rises as individuals get older, with the risk doubling for each successive decade after the age of 45 [13]. The full consequences of a stroke may not be immediately apparent and can take time to fully comprehend. Stroke can have significant physiological, economic and physiological effects on patients. There is substantial evidence supporting the potential benefits of thrombolysis in improving survival rates [14]. Thrombolysis administered within a specific time frame has been shown to reduce the size of infarctions and minimize the occurrence of complications, including cardiopulmonary complications. Thrombolysis has the potential to decrease the duration of hospitalization and lower the risk of pneumonia, thereby reducing deaths with AIS. However, thrombolysis also carries the risk of inducing hemorrhagic complications [15, 16].

This study aimed to investigate the factors contributing to the non-treatment among patients who presented to the institute within 4.5 hours. Additionally, the demographic characteristics of thrombolysed and non-thrombolysed patients were examined, as well as the outcomes in both groups within the 4.5-hour window.

In the study of Mehrpour M et al. [17] 66% of the cases were male and 34% were female. The age range of the cases in the research was 31 to 90 years. In the present study, the thrombolysis group 64% was male and 36%w were female. The age ranges of the patients in the thrombolysis were 41-50 years. The under-60 age group, primarily consisting of men, plays a significant role in generating income and bears a greater financial burden associated with stroke in India. Furthermore, this age group faces a higher risk of stroke due to lifestyle choices, addictions, and the presence of common co-existing medical conditions, which are more prevalent compared to women in the premenopausal age group. However, after menopause, the risk of developing co-morbidities becomes nearly equal between men and women.

In the present study, hypertension emerged as the most prevalent comorbidity, affecting approximately 65% of the patients. Similarly in the study done by Kannan V et al. [18] hypertension was the major cause for ischemic stroke patients and hemorrhagic patients. In the present study diabetes mellitus (DM) was found to be 30% followed by ischemic heart disease (IHD) 15% and hypothyroidism which was found to be 10%. In the study of Nepal G et al. [19] hypertension was found to be 56.1% and DM was found to be 17.5%. Another study done by Lei et al. [20] hypertension was found in 47.3% of patients, diabetes mellitus was found to be 24.5% of patients and IHD was found in 14.5%.

The CT-MRI findings in the present study among 40 patients 35% had lacunar stroke, 50% had anterior circulation stroke, and 15% had posterior circulation stroke. Similarly, in the study of Kannan et al. [18] strokes occurring in the anterior circulation accounted for the majority of cases, contributing to approximately 88.27% of total. On the other hand, strokes within posterior circulation constituted a smaller proportion, with just over 137 cases, making up approximately 11.72% of the total.

Out of the total participants, 84% did not encounter any complications. Among the remaining participants, 8% experienced the development of intracerebral hemorrhage and another 8% experienced an extension of the infarction. In research performed by Dharmasaroja PA et al. [21], 11% of patients reported to experienced early clinical deterioration after receiving rt- PA thrombolysis. The main reasons for this deterioration were symptomatic intracerebral hemorrhage and the development or expansion of infarction in the malignant middle cerebral artery stroke.

According to the study findings, the mortality rate among patients who did not undergo thrombolysis was observed to be 13.33%. On the other hand, the proportion of deaths among patients who received thrombolysis was 12%. In the research conducted by Li H et al. [22] among the 31 patients included, 12 deaths occurred during the hospital stay, with an equal number in both the rt-PA and control group. During the period between discharge and the third month, a total of four patients from the rt-PA group and two patients from the control group experienced mortality. No deaths were recorded in the rt-PA group between months 3 and 6, whereas seven deaths occurred in the control group.

5. Conclusion

Acute ischemic stroke faces several challenges globally, leading to delayed treatment. These challenges stem from various factors such as lack of public awareness, delayed response times, late presentation of patients, and inadequately equipped hospitals for managing these cases. Enhancing emergency medical services, including infrastructure development, offering more affordable alternatives to thrombolytic agents, and ensuring strict adherence to inclusion and exclusion criteria, are vital steps toward improving outcomes in acute ischemic stroke.

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