

Factors Affecting Thrombolysis of Stroke in Emergency Department of a Tertiary Care Hospital

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Abstract

Introduction: Stroke is leading cause of disability in adults and each year millions of stroke survivors has to adopt life with restriction in activities of daily living as a consequence of stroke. Time is brain, early recognition of acute ischemic stroke is important because IV fibrinolytic treatment should be provided as early as possible, generally within 3 to 4.5 hours of onset of symptoms. Delay in presentation resulting in increased morbidity and mortality. **Methods:** All patients with age above 18, suspected stroke, fulfilling the Inclusion criteria at the Emergency Medicine department Bangalore Baptist Hospital, during one and half years period were enrolled in study. Diagnosis can be made on neurological assessment and neuroimaging. Data collection – Administration of questionnaire and data entry. The data collected will be entered into an excel sheet and the analysis will be done using relevant statistical methods. The characteristics of patients' with acute stroke will be analyzed by using chi-square analysis for categorical variables and the *t*-test for continuous variables. Statistical analyzes will be performed using the Statistics Package for Social Scientists. **Results:** Out of 184 patients in the study, there were a total of 46 patients who arrived hospital within 6 hours of onset of symptoms and the rest arrived after 6 hours of onset of symptoms. A *p*-value of ($p < 0.0005$) as arrived, which is significant for this study. In our study out of 184 patients who presented to emergency with symptoms of stroke, 183 patients were identified within 25 minutes. One patient was not identified who was presented beyond 6 hours of symptom onset. Once we identified that patient arrived in window period ($n=5$), we performed CT scan within 25 minutes ($p < 0.0005$) and interpretation within 45 minutes ($p < 0.0005$) and thrombolysis of these patients started within one hour ($p < 0.0005$) which is statistically significant. **Conclusion:** We found that in our study prehospital factor the distance from hospital is significant factor associated with delay in arrival to hospital. It is recommended that creating awareness among general public about stroke symptom and thrombolysis is at most need of the hour. Strengthen of ambulance services and training people (paramedics and EMT) who are involved in first contact with the patient, so that identification of stroke will happen at field.

keywords: Stroke; Pre hospital; Thrombolysis

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Introduction

Stroke is one of the important causes of mortality, morbidity and disability all over the world in both

developed and developing nations. In 2008, it was estimated that cerebrovascular disease accounted for 6.1 million deaths worldwide equivalent to 10.8% of all deaths. Developing countries account

for the maximum number of cases. It is leading cause of disability in adults and each year millions of stroke survivors has to adopt life with restriction in activities of daily living as a consequence of stroke. Prevalence rate of strokes in India is about 1.54 per thousand and death rate about 0.6 per thousand. The Disability-Adjusted Life Years (DALYs) lost is about 597.6 per lakh.¹

Stroke is defined as any disease process that interrupts blood flow to the brain and is classified into two major types: ischemic and hemorrhagic strokes. Ischemic stroke accounts for 87% whereas hemorrhagic stroke accounts for 13% of the cases. Fibrinolytic therapy is contraindicated in hemorrhagic type of stroke and anticoagulants are better avoided.²

Neurons are exquisitely sensitive to changes in cerebral blood flow and the final common pathway in the pathophysiology of these types of strokes is by the mechanism of altered neuronal perfusion. Early identification of symptoms and presentation to hospital is the key to better outcome.

This study has been done in an effort to study the pre-hospital and in-hospital factors which cause a delay in thrombolysis leading to poor outcome and compromised quality of life. The results derived can be used to extrapolate a multi-centric and multi-disciplinary protocol for stroke management in a resource limited setting.

Materials and Methods

The study was conducted in the emergency department of a tertiary care teaching hospital in India from 25th September 2015 to 31st May 2017 after approval by the institutional ethics committee. All patients with age >18 years presenting with facial droop, arm drift, abnormal speech, sudden numbness or weakness of face, arm or leg, sudden confusion or aphasia and sudden visual deficits were included in the study. Time of stroke onset was defined as the time when the patient or an observer first noticed a neurological deficit. If the symptoms were present on waking, it was assumed that stroke had occurred during the night and the time of onset was taken when the patient was last seen without symptoms.

The exact time of arrival at hospital was routinely marked. A standard structured questionnaire was completed by interviewing the patient (if possible) and accompanying attendant/relative after taking informed consent. The questionnaire documented the patient's age, sex, educational level and

financial status. Information regarding the mode of transport to the hospital and the presence of any relative or friend during the time of onset of stroke was also gathered. Neurologic findings and the type of stroke were documented. Consciousness was assessed by Glasgow Coma Scale (GCS). The stroke severity was documented using the National Institute of Health Stroke Scale (NIHSS). In our study we defined the window period as 4.5 hours based on ECASS 3 study. The statistical software SPSS 16.0 was used for the analysis of data and Microsoft word and excel have been used to generate graphs and tables.

Inclusion Criteria

Age >18 yrs

Diagnosis of Acute ischemic stroke based on clinical examination and confirmation with CT brain

Exclusion Criteria

Head trauma within 3 months

Acute bleeding diathesis

Evidence of hemorrhagic on CT brain

Results

During the study period, 42,246 patients reported to our emergency department, of whom 224 were stroke. Out of 224 stroke cases we have studied, 184 satisfied the inclusion criteria and of 184 patients 120 (65.2%) were males and 64 (34.8%) were females (Fig. 1; Table 1).

Out of 184 patients included in the study, 46 patients who arrived within 6 hours of onset of symptoms to hospital had to travel a mean distance of 41 kilometres, whereas the rest 138 patients had to travel a mean distance of 76.88 kilometers, which was found to be significant ($p < 0.0005$) (Fig. 2; Table 2).

In our study involving 184 patients with acute ischemic stroke, the mean GCS for the patients presented within 6 hours and more than 6 hours is 12.84 and 13.9. This value is statistically significant with a p -value of 0.0005 (Fig. 3; Table 3).

A majority of patients were provisionally diagnosed by physicians within 25 minutes of encounter. However, 46 patients (25.1%) reached the hospital within 6 hours of symptom onset, and 1 patient was misdiagnosed among patients presented beyond 6 hours. A p -value of 0.563 made

Table 1: Patient Characteristics in the Study Group

Parameter	Number of patients reaching hospital within <6 hrs of symptom onset (n=46)	Number of patients reaching hospital >6 hrs of symptom onset (n=138)
Co-Morbidities		
Diabetes	23 (50%)	76 (55%)
Hypertension	28 (60.8%)	85 (61.6%)
Ischemic heart disease	33 (71.7%)	104 (75.3%)
Arrhythmia	2 (4.3%)	3 (2.1%)
Dyslipidaemia	15 (32.6%)	33 (23.9%)
Symptom Awareness		
Hemiplegia	19 (41.3%)	56 (40.5%)
Speech disturbance	8 (17.3%)	13 (9.4%)
Vertigo	0	0
Numbness	0	0
Headache	0	0
Education Status		
Illiterate	3 (6.5%)	9 (6.5%)
High school	28 (60.8%)	94 (68.1%)
Graduate	7 (15.2%)	23 (16.6%)
Postgraduate	8 (17.4%)	12 (8.7%)

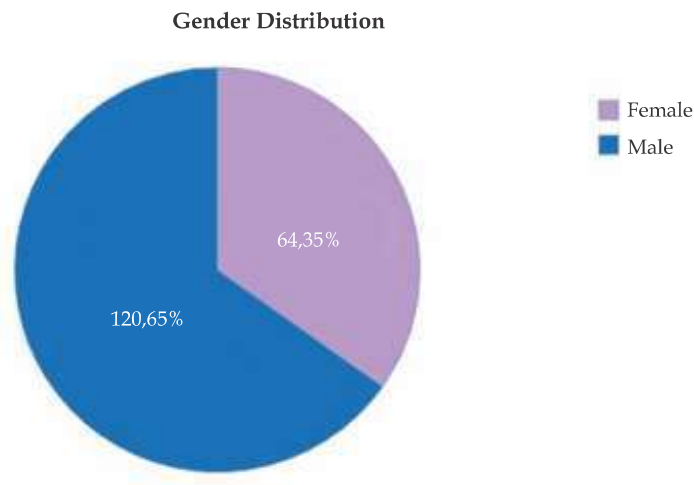


Fig. 1: Gender distribution in study population.

this insignificant (Fig. 4).

Of the 184 patients, only 5 patients got a CT within 25 minutes from time of arrival, due to high suspicion and being within window period. However, 138 patients who arrived after 6 hours did not get a CT within 25 minutes as the need for fast-tracking such a patient had already surpassed

the window period. A *p*-value of <0.0005 made this factor significant (Fig. 5). A similar profile was seen with respect to the interpretation of the CT with significant *p*-value of <0.0005. Of all the patients within window period, the CT was reported within 45 minutes. With a *p*-value of <0.0005, making it significant (Fig. 6), all the patients who reached the hospital during window period were subjected to

Table 2: Distance from Hospital

	Time (hours)	N	Mean distance in kilometers	Std. Deviation	T	p-value
Distance	>6	138	76.88	51.110	4.515	<0.0005
	<6	46	41.00	29.346		

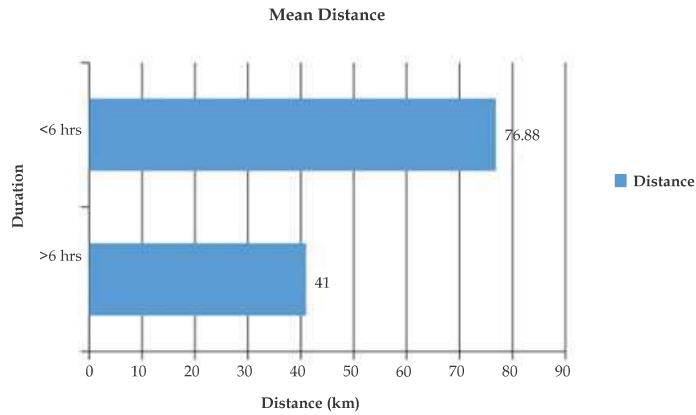


Fig. 2: Distance from hospital

Table 3: Assessment of Glasgow Coma Scale (GCS) in Patients with Acute Ischemic Stroke

	Time (hours)	n (number)	Mean GCS	Std. Deviation	T (t test)	p-value
GCS	>6	138	13.9420	1.20684	5.749	0.0005
	<6	46	12.8478	0.78789		

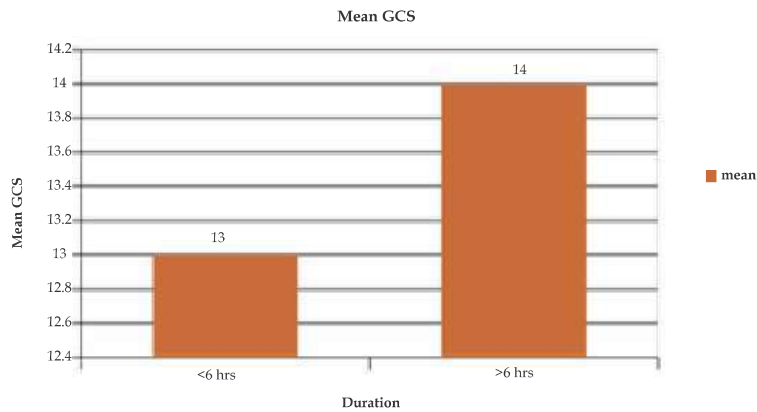


Fig. 3: Mean GCS of patients with acute ischemic stroke.

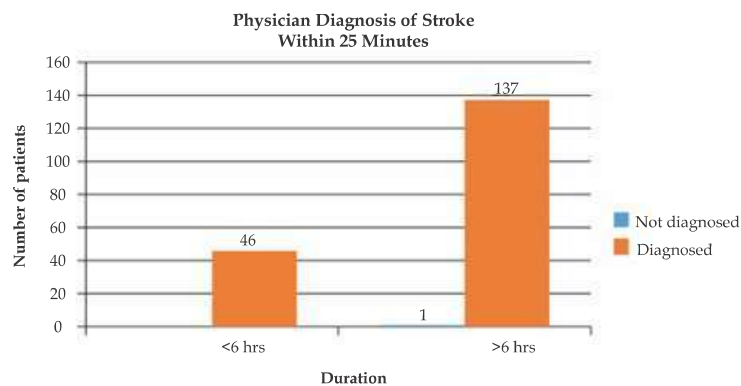


Fig. 4: Physician diagnosis of stroke within 25 minutes.

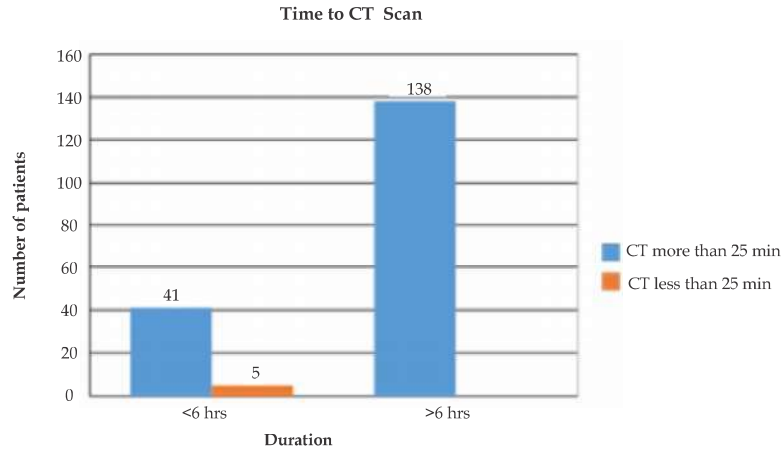


Fig. 5: CT obtained in less than 25 minutes.

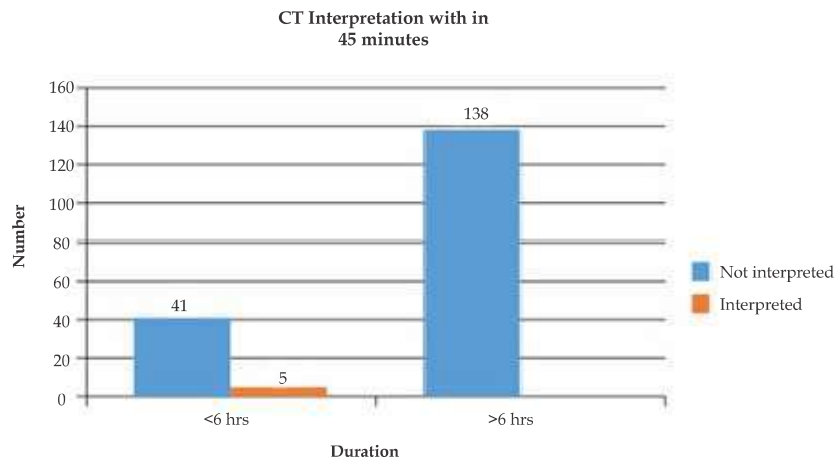


Fig. 6: CT interpretation in less than 45 minutes.

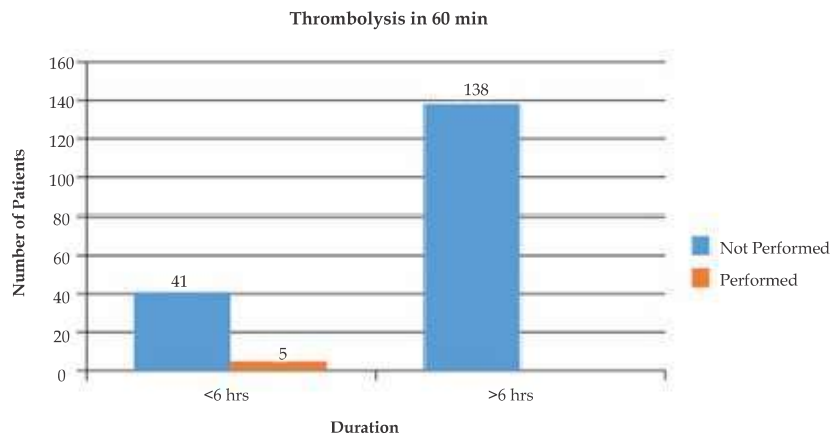


Fig. 7: Fibrinolytic therapy performed within the study group.

fibrinolytic therapy/ thrombolysis within an hour of arrival (Fig. 7).

Discussion

Early detection of stroke must begin within among the general public as they are the first to identify stroke symptoms. The Cincinnati Prehospital Stroke Scale (CPSS) identifies stroke on the basis of 3 physical findings namely facial droop, arm drift and abnormal speech. If any 1 of these 3 signs is present, the probability of stroke is 72%. The presence of 3 findings indicates that the probability of stroke is greater than 85%.³ The timing of presentation of acute ischemic stroke to the hospital is crucial because intravenous fibrinolytic therapy should be provided as early as possible, generally within 3 to 4.5 hours of onset of symptoms. After that, it has not shown to have beneficial effects. Even within this narrow time period; quicker the therapy started, better are the chances of recovery. According to AHA (American heart association)/ ASA (American stroke association) the window period is less than 3 hours. People need to access emergency medical services quickly when early stroke symptoms occur. However, in most communities, only 1–7% of stroke victims arrive at the hospital in time for stroke revascularization therapies.⁴ It was found in China that only 37% of patients reached the hospital within the effective therapeutic time window for strokes, and the rate of thrombolytic therapy for an ischemic stroke is estimated at only 1–3%.⁵ Prehospital delay is the time from symptom onset to hospital arrival. This delay may be due to numerous reasons. For instance, many patients and their relatives do not consider their symptoms to be serious enough and a wait-and-see approach is adopted before seeking treatment. A serious stroke makes patients unable to ask for help themselves. The in hospital delays could be because of error in triaging the patient at the ED, time of arrival like during handing-over or change of shifts, availability of beds in ICU, financial status of patient, availability of on-call neurologist, etc. These factors increase delay in thrombolysis which decreases their therapeutic efficacy. Ashraf *et al.*⁶ performed a retrospective study in 2015 and found that 83% of patients presented to emergency room after 4 hours. Iosif *et al.*⁷ performed a retrospective study in 2012 and analyzed the social factors influencing hospital arrival time in acute ischemic stroke patients. They took a cut-off time period for arrival of patient as 6 hours. After due consideration of above-mentioned factors we arrived at a decision for a time limit of 6 hours

from the onset of symptoms as the best feasible time period for analysis of data and also to be more inclusive. Delay in presentation results in increased morbidity and mortality. However, not all people diagnosed with an ischemic stroke are suitable for thrombolytic treatment. Before the decision to treat is made, the patient must have a CT scan of brain done to rule out a hemorrhage and other possible causes of stroke like symptoms.

Diabetes, hypertension and ischemic heart disease are well-known risk factors for development of stroke. In our study, the prevalence of diabetes, hypertension and ischemic heart disease is 53%, 61.4% and 74.5% respectively but we also observed no relation between previous co morbidities and early arrival to hospital. Ashraf *et al.*⁶ found that patient with coronary artery disease had early arrival to hospital which did not translate into our study.

We also found a significant number of our patients to be illiterate (122/184, 66.3%) which we propose to be a major risk factor for delay in arrival to hospital. The awareness of symptoms was more with educated people. Iosif *et al.*⁷ also concluded that younger age and higher education status is associated with early arrival to hospital. In our study we found symptom awareness of stroke in patients was very less. Hemiplegia as stroke symptom is known to only 49% patients, so as speech disturbance which is known to only 17% patients. None of our study population identified vertigo, numbness and headache as stroke symptoms. Siddiqui, *et al.*⁸ postulated that patient and bystander's lack of awareness about stroke symptom is an important risk factor for delay in arrival to hospital which is reciprocated in our study.

There is a statistically significant correlation between GCS and subsequent hospital arrival of the patients in our study. The mean GCS of patients who arrived to hospital within 6 hours and above 6 hours is 13 and 14 respectively. This shows that lesser the GCS, earlier is the arrival to hospital (Fig. 3; Table 3).

The mean distance of patient's residence to hospital is significantly high in our study ($p=0.0001$). We think that it is one of the predominant factors for delayed presentation to hospital. The distance is more pronounced in patients who presented in more than 6 hours to hospital. Similar results are seen in multiple studies done on Indian population.^{6, 9, 10}

Number of patients who came with their own vehicle is 125 (67%) and those in ambulance are

59 (32%). More than half of the patients came in their own vehicle which might have caused delay in arrival. This may be due to non-availability of ambulance or trained EMS. Pandian *et al.*⁹ obtained similar conclusions in their study with respect to ambulance usage. In our study, more than 50% patients decided to wait and watch and not to seek medical attention immediately. Faiz *et al.*¹¹ found that hesitancy to contact medical services is a significant factor in delay to hospital arrival.

In patients who arrived to emergency room within window period (n=5), CT scan was obtained in 25 minutes which is statistically significant ($p=0.000$). Once a patient was identified to be in window period, CT scan was done within 25 minutes and interpreted within 45 minutes ($p=0.000$). Thrombolysis of these patients was initiated within one hour ($p=0.000$). This is in accordance with AHA guidelines for stroke thrombolysis. The in-hospital management by the doctors and staff has been excellent as reflected by their early identification and activation of hospital services resulting in thrombolysis of all the patients who arrived within window period.

Conclusion

We found that in our study, prehospital factors are the major cause for delay in presentation of stroke patients to the hospital. We also found that there was less awareness of stroke symptoms and stroke thrombolysis. The distance from hospital is a significant factor associated with delay in arrival. Patients with low GCS arrive early to the hospital. Lack of knowledge about the activation of EMS, poor educational status of patient and less utilization of ambulance services compounded the delay in arrival to the hospital. The patient's reaction towards symptoms also contributed to the delay in arrival to hospital. It is recommended that creating awareness among general public about stroke symptoms and thrombolysis is at most need of the hour. The government and social organizations need to take initiatives to create awareness among the general public using mass media. Strengthening of ambulance services and training of paramedics and emergency technicians who are first responders will ensure early identification of stroke and hospital transfer. Dedicated stroke units with imaging facilities and trained personnel have to be formed in all hospitals for early thrombolysis of patients who present within window period.

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