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# Pre-Hospital and In-Hospital Delay of Acute Ischemic Stroke Patients in India

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*Keywords:* *acute ischemic stroke, delay, thrombolytic, contraindication.*

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*Strictly as per the compliance and regulations of:*

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*Abstract-* Diseases that take place in developing countries could owing to poverty, lack of healthcare infrastructure, restricted access to the hospital. Many developing countries like India growing well economically and extending urbanization in recent years despite this large Indian population lives in poverty. However, risk factors for stroke in urban populations are like other developed nations. Stroke is the third common cause of death due to disease in India. The acute ischemic stroke has to be treated within few hours after the beginning of symptoms; if time goes beyond >4.5 after the onset of symptoms, thrombolytic drugs ineffective not only time, other contraindications also equally contribute to thrombolytic therapy. The use of thrombolytic in contraindication patients would further exaggerate the stroke. The various factors could cause a delay the management of acute ischemic stroke from pre-hospital delay to delay in diagnosis and treatment. An effective strategy is needed to meet the challenges in India.

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## I. Introduction

Stroke is the most complicated global public health complication. Report of the Global Burden of Diseases study conducted in 1990. In developing countries like India, both communicable and non-communicable diseases are a double burden. Globally, stroke is the third general cause of death after CHD and cancer. In recent times the incidence of stroke in India mounts higher than in western countries in India, the actual incidence rate of stroke is between 145-154/1,00,000 persons in a year. The major reason for increasing stroke incidence in India due to poor medical facilities in rural most populations are living. Few factors are certainly associated with a delay in the management of acute ischemic stroke-like pre-hospital delay due to late arrival, long-distance, rural living, poor knowledge, and Community awareness, along with other factors like delay in a hospital due to lack of CT scan facilities in rural and remote areas, inadequate infrastructure, delays often seen in the treatment of patients with acute ischemic stroke. Thrombolytic therapy for acute ischemic stroke was being approved in 1996 However, only 1% to 2% of patients with ischemic stroke have estimated to be eligible for it because of the time window. The beneficial effect of thrombolytic in acute ischemic stroke up to 4.5 hours of stroke symptom onset; previous guidelines were suggested 3 hours of thrombolytic also have some contraindication so, checking inclusion and exclusion is vital before starting therapy.

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*a) Pre-delay into the hospital*

The pre-hospital delay not declined since 2006 in India, with the many patients unsuccessful to arrive before 3 hours. Most population in developing countries like India living in rural areas where the health system is poor. one of the reason for emergency department arrival beyond 3 hours is a delay in transportation, transportation delay in urban areas due to excess of traffic, in the rural area due to shortage of ambulance service and distance from the hospital. Knowledge of stroke is relatively poor among people in India, especially in rural areas. A Study in Northwest India revealed both patients and their relatives did not have enough knowledge about the stroke and its symptoms, ignoring, personally thinking the symptoms would resolve quickly. Living or being alone during the onset of stroke, Stroke while sleeping, especially at mid-night, also contributes to factors in the pre-hospital delay.

*b) Delay in hospital*

Stroke units in the hospital provide a multi-regulated approach by neurologists, stroke physicians, stroke nurses, physiotherapists, speech therapists, and occupational therapists involve in cohesive and organized care of the patients. The number of strokes–care hospitals and those with obligated stroke units is not many in India. Insufficiency of imaging facilities and extremely high cost of thrombolytic agents and mechanical thrombectomy are the major hindrances in the proper management of acute ischemic stroke.

*c) Delay in diagnosis*

Indian government hospitals divided into PHC, CHC, SDH, and DH among these; only DH have a CT scan facility. Patients should be transported into DH or medical college hospital or multi-specialty hospital because other categories of hospitals do not have CT scan facility. It is certainly a timely process if patients reach into non-CT scan hospital. CT scan in-hospital admission also the factor causing the in-hospital delays; it is strongly impacted by factors such as patient admission process delay, shortness of staff, the distance between hospital stroke unit or causality, and CT room.

*d) Delay in management*

The decision-making process for thrombolytic selection should be a factor affecting in-hospital delay. The study revealed that the process of decision-making for intravenous thrombolytic contributed to a prominent factor in-hospital delay. Acute ischemic patients firstly examined by an emergency unit followed by being informed to the neurologist. Once a definite diagnosis made, medical professionals should communicate with their family members, informing the risk of intravenous thrombolytic and collecting information about the present and the previous history of patients to determine inclusion or exclusion criteria are necessary. If a patient contraindication to the thrombolytic agents; a mechanical thrombectomy is an alternative option. It takes more time because it is a surgical procedure. The high cost of thrombolytic therapy and mechanical thrombectomy makes it inaccessible to economically backward patients.

*e) Management of acute ischemic stroke*

The only pharmacological agent approved for the management of acute ischemic stroke is IV- (rt-PA).A reperfusion therapy that should be administered well inside a time 4.5 hrs right after symptom onset. It officially approved for management in acute ischemic stroke in 1996. The limitation on IV-rt-PA treatment beyond 4.5 hrs rules out most stroke patients admitted beyond this time-window as a result, dramatically restrain the eligible population. Tissue plasminogen activator within 4.5 hrs of the onset of symptoms remarkably boosts clinical outcomes in patients with acute ischemic stroke. Thrombolytic dissolve thrombi in the vascular bed by converting plasminogen to form plasmin. Plasmin is a proteolytic enzyme that burst the cross-links across fibrin molecules to break the structure of clots. The most important thrombolytic drugs used in ischemic stroke to stimulate plasminogen are urokinase/streptokinase and tissue plasminogen activators. The major pharmacological agent in tissue plasminogen activators is alteplase, which is converts plasminogen to the proteolytic enzyme plasmin, which is ruptures fibrin to dissolve. Apart from the pharmacological agents, mechanical thrombectomy also an indication in the management of acute stroke if time limits cross 4.5 hrs. In recent times reperfusion therapies also have been performed in mechanical embolus disruption or removal of a fibrin clot. Mechanical thrombectomy devices resolve the ischemic but not fully occluded clot. It is regaining perfusion through the earlier occulted artery. The application of retrievable stents into the ischemic part of blood vessels promptly relieves the block and improves the blood circulation. Now the day's most neurologists prefer mechanical thrombectomy to bring off reliable results similar to those seen by cardiologists in the treatment of myocardial infarction by angioplasty(stent).

*Less than 3 hrs*

If within 3 hrs use intravenous alteplase therapy, well-defined manifestations are observed.

*3 to 4.5 hrs*

Intravenous alteplase therapies shold be provided that treatment initiated within 3 to 4.5 hrs of well-defined manifestations will be observed. Patients in this period will also determine if they are candidates to mechanical thrombectomy.

*4.5 to 6 hrs*

Patients within 4.5 to 6 hrs from stroke manifestation onset must not receive intravenous alteplase because of contraindication, but patients might be eligible for mechanical thrombectomy.

*6 to 24 hours*

Patients beyond 6 hrs from ischemic stroke symptom onset could not entitle for treatment with intravenous alteplase. Nevertheless, mechanical thrombectomy might be eligible if the hospital using an imaging-based selection of patients.

*Beyond 24 hrs*

Patients beyond 24 hrs from ischemic stroke symptom onset could entitle neither alteplase nor mechanical thrombectomy.

So timing is more important in the application of alteplase or mechanical thrombectomy in acute ischemic stroke.

## II. Inclusion and Exclusion Criteria for Thrombolytics

*a) Inclusion Criteria*

*Within 3 hrs of stroke symptom onset:*

Ischemic stroke diagnosis with mild to severe but impairs stroke symptoms, the onset of symptoms <3 hrs before proceeding treatment, age > 18 years.

*Between 3-4.5 hrs after stroke symptom onset:*

Age < 80 years, without any previous history of diabetes mellitus and prior stroke, NIHSS score < 25, presently not taking any oral anticoagulants, CT scan Imaging does not establish the involvement of > ⅓ of middle cerebral artery territory.

*If otherwise eligible:*

Blood pressure range below < 185/110 mm Hg, patients taking an anti-platelet drug-like (aspirin or clopidogrel or aspirin and clopidogrel) if the benefit outweighs the small risk of symptomatic intracerebral hemorrhage.

*Exclusion Criteria (Table 1)*

*Table 1*

**Absolute contraindication**

- Present condition of acute Intracranial Haemorrhage
- Past History of any Intracranial Haemorrhage
- Brain tumour, arteriovenous malformation, or aneurysm
- Just recent intracranial or intra-spinal surgery
- Severe to very Hypertension (systolic >185 mmHg or diastolic >110 mmHg)
- Arterial puncture at incompressible part in past 7 days
- Thrombocytopenia and Coagulopathy
- Severe Hypoglycaemia or Hyperglycaemia<50 or >400 mg/dL
- Advanced Age>80
- Severe Stroke and Coma
- Recent Major Surgery
- Central Nervous System Structural Lesions
- Dementia
- Platelet count <100000/mm3
- Heparin received within 48 h resulting in abnormally elevated aPTT above the upper limit of normal
- Currently or recently application of anticoagulant with INR >1.7 or PT >15 s
- Currently or recently application of direct thrombin inhibitors or direct factor Xa inhibitors
- CT scan established multi-lobar infarction (hypodensity>1/3 cerebral hemisphere)

**Relative contraindication**

Current proof proposes that under some situation, with caution consideration and measuring of the risk to benefit, patients might receive thrombolytic therapy despite≥1 relative contraindications.

- Just minor or rapidly improving stroke symptoms (clearing automatically)
- Pregnancy at all trimesters
- Onset of seizure with neurological destruction
- Major surgical operations or serious injuries (within past 14 day)
- Recent GIT tract or urinary tract bleeding (within past 21 days)
- Recent acute coronary infarction (within past 3 months)

## III. Meeting the Challenges of Stroke in India

Improving stroke knowledge and education, Improving awareness about risk factors and warning symptoms to the general population, sharing of knowledge as well as technical between research institutions, Increasing more number of stroke units and trained professionals to tackle the high Indian population, enhanced quality of care for stroke patients in India by improving guidelines and designated hospitals infrastructure, train research facilities for basic and clinical research regarding stroke.

## IV. Conclusion

The management of acute ischemic stroke has a time window due to delay by factors like pre-hospital delay and delay in-hospital have contributed patients into ineligible candidates for the thrombolytic therapy. The factors contributing to delay could not easily minimize because of greater challenges in developing countries like India. The challenges should be meeting by-improving stroke education, infrastructure, and guidelines.

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*Conflict of Interest*

The author declares that there are no conflicts of interest.

*Abbreviations*

CHD: Coronary heart disease; CT: Computed tomography; PHC: Primary health centre; CHC: Community Health Centre; SDH: Sub-District Hospitals; DH: District Hospitals; IV: Intravenous; (rt-PA): Recombinant tissue plasminogen activator; NIHSS: The national institutes of health stroke scale; PTT: partial thromboplastin time; INT: International normalized ration; PT: Prothrombin time

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