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FACTORS CAUSING DELAY IN TIME TO DOOR AT EMERGENCY DEPARTMENT(ED) IN CASES OF ACUTE STROKE AND IT'S IMPACT ON OUTCOME AT TERTIARY CARE CENTRE

Neurology

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ABSTRACT

BACKGROUND: The effectiveness of stroke management is highly dependent on post onset time of treatment. The study hypothesized that perceptual, social and behavioral factors affect delay in seeking help after symptom onset and worsen the outcome and recovery.

OBJECTIVE: To look at the causes of delay in arrival to definitive care hospital ED after symptoms of acute stoke and its impact on patient's clinical outcome.

METHODS: An observational prospective study conducted on 63 patients with signs and symptoms of acute stroke (CPSS/NIHSS positive) reported to ED. Reasons for delay in arrival to ED observed. Patients divided into two groups, those who came within 4.5 hours of onset of acute stroke symptoms and those who came after 4.5 hours. Impact of delay on patient's outcome studied at time of discharge as primary end-points in terms of average length of stay (ALOS), complications and death. Secondary end-points evaluate in terms of improvement, deterioration and death within 30th day. Statistical analysis using Chi-square or Fisher's exact test applied to compare both the groups. Odds ratio with 95 % confidence limit was also calculated.

RESULTS: There were multiple overlapping causes of delay; most frequently was "first went to physician who doesn't treat stroke (8; 38.1%) and non-availability of nearby stroke centre (8; 38.1%)". Total 21 (33.34%) patients came after window period (4.5hours). Primary endpoints in terms of ALOS (8 days compared to 9 days, p=0.48), complications (OR=1.4, 95%CI:0.2-8.8, p=0.74) and death (OR=3, 95%CI:0.4-19.3, p=0.24) at time of discharge. Secondary endpoints in terms of improvement (OR=2.8, 95%CI:1.0-7.8, p=0.03), deterioration (OR=6.0, 95%CI:1.4-24.5, p=0.01) and death within 30 days (OR=1.2, 95%CI:0.2-5.5, p=0.81).

CONCLUSION: Inadequate knowledge of stroke identification and management causes delay in arrival to hospital. This delay can cause significant impact on patient outcome and recovery.

KEYWORDS

Acute Stroke, Time To Door, Emergency Department, Outcome Of Stoke, Cpss/nihss Score.

INTRODUCTION

The effectiveness of stroke management is highly dependent on post onset time of treatment. Recent reports have established the importance of aggressive medical and surgical intervention in hyper-acute stage[1]. Despite availability of reperfusion therapy for acute ischemic stroke, most patients remain ineligible, mainly because of late hospital arrival. This study hypothesized that perceptual, social and behavioral factors may affect delay in seeking help after symptom onset[2].

Annually an estimated 15 million people worldwide suffer from stroke, resulting in 5 million deaths and another 5 million with permanent disability. Over the next decade, the stroke burden projected to rise, particularly in developing countries. Timely access to effective medical treatment will be an important element to combat this public health challenge[3].

Early admission to stroke unit (SU) and factors that may cause admission delay represent relevant issues to obtain an optimal management of acute stroke. Human nervous tissue is rapidly lost as stroke progresses and emergent evaluation and therapy are required. Recent advances in quantitative neurostereology and stroke neuroimaging permit calculation of just how much brain is lost per unit time in acute ischemic stroke[4]. New drugs optimally curative in stroke therapy administered quickly after the appearance of the symptoms[5].

Early treatment is a critical determinant of successful intervention in acute stroke[6]. In addition, there is paucity of Indian studies on reasons for prehospital delay in arrival after acute symptoms of stroke and its impact. This study will help us to assess public awareness of warning symptoms, factors causing delay in their arrival and its impact on their outcome and to understand the need for stroke awareness program, which have hardly depicted in other Indian studies.

METHODS

Study Design:

The study was a prospective observational study, conducted at Fortis Hospital, Noida (UP) India for a period of one year (April 2016-April 2017). All patients with history of acute stroke (Cincinnati Prehospital Stroke Scale/ National Institutes of Health Stroke Scale (CPSS/ NIHSS) positive)[7] who came to ED were taken and total 63 patients were enrolled after applying exclusion criteria (patients not having any symptoms or signs of stroke, not willing to participate in study and in whom time zero can't be established).

Institutional ethical committee approval obtained and consent duly signed by patient or relatives taken before enrolment.

Data Collection: After enrolment, data was recorded using a standard form and assessment was done at three steps. Firstly at admission, the clinical characteristic of each patients were recorded including demographics, symptoms and signs, its time of onset and reasons for delay in arrival to hospital. Study cases categorized into two Groups: **Group-1** includes patients who came after 4.5 hours after symptom onset of acute stroke and **Group-2** includes the patients who came within 4.5 hours after symptom onset of acute stroke.

Next assessment for impact of delay in terms of ALOS, complications and death during hospital stay done at time discharge of patients. Final assessment done telephonically at 30th day in terms of change in clinical status (improvement, deterioration or same status) and death.

STUDY OBJECTIVES:

Study Approach (primary Objective)

Cause Of delay in hospital arrival after onset of acute stroke symptoms shown in figure 1.

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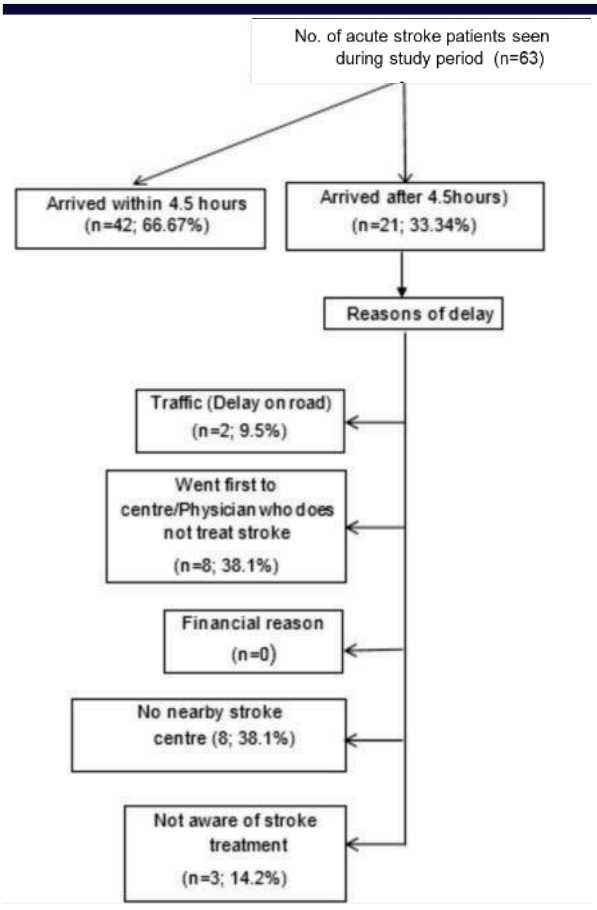

Figure 1. Study Approach-showing Reasons Of Delay In Hospital Arrival After Symptoms Of Acute Stroke

Secondary Objective (Study approach)

Impact of delay in patient's outcome assessed between both the groups with -

Primary endpoint at the time of discharge in terms of ALOS, complications and death.

Secondary endpoint at 30th day follow up done in terms of improvement, deterioration, same status or deth. (Figure-20).

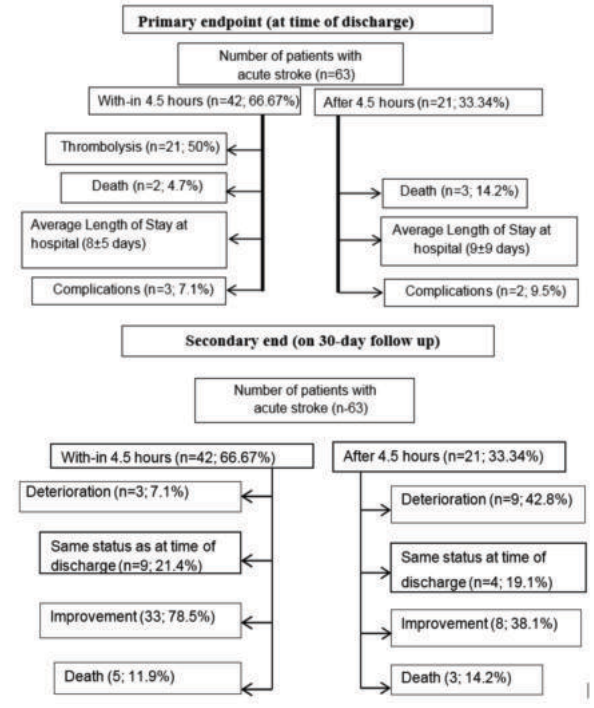

Figure 2. Study Approach-showing Impact On Delay In Patient's Outcome

STATISTICAL ANALYSIS:

The study designed to include 63 patients. SPSS version 17 (SPSS, Inc., Chicago, IL, USA) was used for data analysis. Data entered in Microsoft Excel spreadsheet. Continuous data presented as mean and standard deviation (SD) whereas categorical data expressed in terms of frequencies and percentages. Patients divided into two groups, those who came within 4. 5 hours of onset of acute stroke symptoms and those who came after 4.5 hrs. Chi square or Fisher's exact test applied to compare both the groups at the time of discharge and on 30 day follow up. Odds ratio with 95 % confidence limit was also calculated. Student t test or Mann-Whitney (non- parametric) test applied for comparison of means of two independent groups. For measuring, the quantum of association, the Odds ratio (OR) with 95% confidence interval (CI) presented and statistical significance at p-value of < 0.05 considered throughout.

RESULTS

During study period, 438 patients presented to the Emergency Department(ED) with complaint of neurological deficit or altered sensorium and after applying inclusion and exclusion criteria, 63 patients enrolled for the study. Excluded patients includes149 (34 %) patients in whom final diagnosis was other than stroke like hypoglycemia, seizure, brain tumor and psychiatric causes, 123(28 %) patients were not willing to participate in study, 65(14.8 %) patients had suspected transient ischemic attack and 38 (8.6%) patients in whom time zero could not be established.

PATIENT DEMOGRAPHY:

Total 63 patients enrolled in the study out of which 41 (65.1%) patients were male and 22(34.9%) patients were females. Figure 3 showing age distribution of patients. Most of the patients belong to 66 - 75 years old followed by 56 - 65 years old and least number of cases are from up to 35 years of age group. Mean age of subjects was 59.1 ± 14.7 years and the youngest patient was 29 year old, however the oldest was 90 year old.

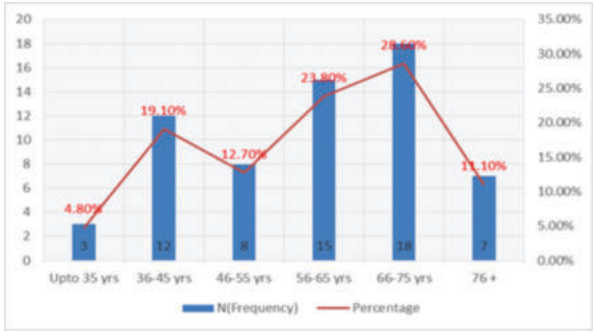

Figure 3. Showing Age Distribution Of Patients

PRIMARY OBJECTIVE

Out of 63 patients, 42(66.66%) patients came within 4.5 hours and 21(33.34%) patients came after window period (4.5 hours) as shown in figure 4.

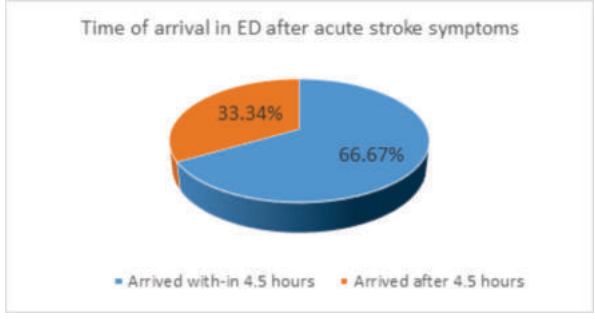

Figure 4. Showing Distribution Of Patients According To Time Of Arrival In Ed After Symptoms Of Acute Stroke.

NCCT head findings in patients who arrived within 4.5 hours and after

4.5 hours study group observed. It was found that in patients, who came within 4.5 hours, 61.9% had ischemic stroke and 38.1 % had hemorrhagic stroke. Patients who came after 45 hours, 52.4 % patients had ischemic stroke and 47.6 % had hemorrhagic stroke. Figure 5 showing various reasons of delay in patients There were multiple overlapping causes of delay; most frequently stated cause of delay was "went first to physician who doesn't treat stroke" (38.09%) and "non-availability of nearby stroke centre" (38.09%). However, none of the patients stated financial reason as cause of delay.

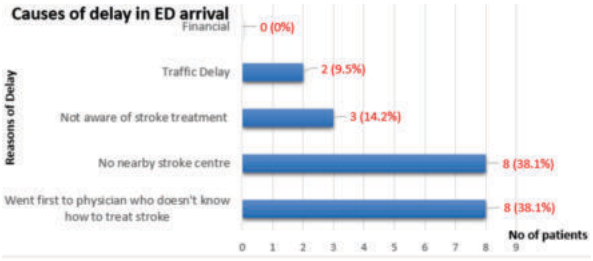

Figure 5. Showing Causes Of Delay In Hospital ED Arrival

SECONDARY OBJECTIVE

Impact of delay in patient's outcome assessed between both the groups in terms of –

Primary endpoint at the time of discharge in terms of average length of stay (LOS) (8 days compared to 9 days, p=0.48), complications (OR=1.4, 95%CI:0.2-8.8, p=0.74) and death (OR=3, 95%CI:0.4-19.3, p=0.24) as in table 1. Patients who came after 4.5 hour have 3 times increased chance of in-hospital mortality than those who came before 4.5 hours.

Table 1. Primary Endpoint At The Time Of Discharge.

	Group-1 After 4.5 hours(n=21)	Group-2 With-in 4.5 hours(n=42)	p-value	OR	CI (Min-Max)
Average length of stay(LOS) in days	9	8	0.48		
Complications n (%)	2 (9.5)	3 (7.1)	0.74	1.4	0.2-8.8
Death n (%)	3(14.2)	2(4.7)	0.24	3.0	0.4-19.3

Secondary endpoints in terms of improvement (OR=2.8, 95%CI:1.0-7.8, p=0.03)), deterioration (OR=6.0, 95%CI:1.4-24.5, p=0.01) and death within 30 days (OR=1.2, 95%CI:0.2-5.5, p=0.81) shown in table 2. Patients who came within 4.5 hours of acute stroke symptoms in ED improved three-fold more in comparison to patients who came after 4.5 hours. In addition, patients who came after 4.5 hour deteriorated 6 times more on 30 days follow up than those who came before 4.5 hours.

Table 2. Secondary Endpoint At The Time Of Discharge

	Group-1 After4.5 hours (n=21)	Group-2 With-in 4.5 hours (n=42)	p-value	OR	CI (Min-Max)
Improvement n(%)	8 (38.1)	33(78.5)	0.03	2.8	1.0-7.8
Deterioration n(%)	9 (42.8)	3 (7.1)	0.01	6.0	1.4-24.5
Same status n (%)	4 (19.1)	9 (21.4)	0.8	0.8	0.2-3.2
Death n (%)	3 (14.2)	5 (11.9)	0.81	1.2	0.2-5.5

DISCUSSION

At this centre, approximately 12000 - 14000 patients attended ED in a year, out of which 20 % patients are with symptoms of acute stroke as per last 3-year audit. This centre started thrombolysis program in 2011 and established code FAST in December 2014 to approach all patients as a team as per American Heart Association guideline. Many of patients could not be thrombolysed because they crossed allowed window period (3-4.5 hours)[8]. This study planned to analyze the factors causing delay in arrival to definitive care hospital from time of symptom onset in cases of acute stroke.

The treatment of stroke has progressed significantly since the early 1900's with improved outcomes. The first historical reference to the nervous system found in ancient Egyptian records dating back to 3500 B.C. Hippocrates in 400 B.C. first described paralysis and convulsion or seizures that resulted after brain injuries, along with the observation that paralysis to the opposite side of the body resulted when a section from one half of the brain was injured. In the 17 century, a detailed study of the brain and nervous system found in the works of Thomas Willis who studied at Oxford University. Willis did multiple experiments on cadavers, classified the nerves of the brain and described the communication of the arteries at the base of the brain that we now call the Circle of Willis. He also recognized that lesions in a specific part of the brain led to weakness in an associated part of the body[9].

Despite these advances, there were actually very few effective treatments for an acute stroke. In the early 1900's most of the treatments for stroke, patients were limited to rehabilitation after an acute stroke, and most patients usually left with permanent and severe deficits[9].

The discovery of thrombolytic agents goes back to the 1930's, when it was shown that substances derived from bacteria (streptokinase, staphylokinase), tissue (fibrinokinase), urine (urokinase) or bat saliva could activate the fibrinolytic system. The potential to treat arterial thrombosis with plasmin recognized, but it was not until 1958 that its first use in acute ischemic stroke (AIS) described. However, since computer tomography (CT) was not available until the mid-1970, optimal selection of patients was not possible. Early studies with streptokinase in AIS showed an increased risk of intracranial hemorrhage and lack of efficacy, which was associated with low fibrin specificity. The search for new agents with a better risk-benefit profile continued until 1979 when tissue plasminogen activator (t-PA) discovered. In 1983 it became possible to produce recombinant tissue Plasminogen Activator (rt-PA) by expression of a cloned gene which enabled clinical trials to be started, mainly for coronary thrombolysis[10].

In 1995, the National Institute of Neurological Disorders and Stroke (NINDS) study group reported that patients with acute ischemic stroke who received alteplase (0.9 mg per kilogram of body weight) within 3 hours after the onset of symptoms were at least 30 % more likely to have minimal or no disability at 3 months than those who received placebo[11]. Two European trials, the European Cooperative Acute Stroke Study (ECASS-I) and ECASS II, investigated a time window of up to 6 hours but failed to show the efficacy of thrombolytic treatment, as defined by each trial[12,13,14].

A subsequent analysis of the NINDS study[15] and the combined analysis[16] of data from six randomized trials[11-14, 17-18] that investigated thrombolysis treatment for ischemic stroke in a total of 2775 patients, showed a clear association between treatment efficacy and the interval between the onset of symptoms and administration of the thrombolytic agent. In the pooled analysis, a favorable outcome observed even if treatment given between 3 and 4.5 hours, with an odds ratio of 1.4 for a favorable outcome with alteplase treatment as compared with placebo. This analysis also suggested that the longer time window, as compared with the shorter window, was not associated with higher rates of symptomatic intracranial hemorrhage or death[12].

This study-analyzed the factors that influence the interval from stroke onset to hospital arrival[19]. After applying inclusion and exclusion criteria, 63 patients studied out of which 65.1% were males and 34.9 % were females. It was comparable to study done by Teng Yeow et al in which 58.9% of study subjects were males and 41.1% were females[20]. In study done by Siddiqui et al, 52 % of study subjects were males and 47.9 % were female[21].

This study showed that only 66.6% of patients came to ED within 4.5 hours and 33.33% patients came after 4.5 hours of onset of acute stroke symptoms, it is in concordance with the study done by Yu RF et al in which 59% of the patients presented within 3 hours of symptom onset[22].

One of the major determinants of delay is the referral pattern. Contact with the local doctor is associated with significant delay[21]. This pattern is similar in other studies as well.[20-21]. Majority of our patients (38.1%), who came to our hospital after 4.5 hours had contacted their local general practitioner first which contributed to significant delay. It is in concordance to other studies[20-21]. Therefore, it is important to organize continuous medical education for health care professionals to increase awareness of importance of patient's t transfer to an organized stroke centre. Public awareness should also be increased that once they recognize the symptoms of stroke they directly transfer the patient to hospitals where facilities to handle such patients are present[21]. In this

study, 38.1% of the patients who came after 4.5 hours delayed because there was no nearby stroke centre. It is in concordance with the study done by Teng Yeow Tan et al[20] and Siddiqui et al[21]

Patients who came within 4.5 hours improved three-fold more in comparison to patients who came after 4.5 hours and it was statistically significant. Similarly, patients who came after 4.5 hour deteriorated 6 times more on 30 days follow up than those who came before 4.5 hours and it found statistically significant. It is in concordance with previous studies[11-13, 17-18, 23-25] where early arrival to hospital of both ischemic and hemorrhagic stroke patients is associated with better clinical outcomes and have hardly depicted in other Indian studies.

CONCLUSION

We concluded that inadequate knowledge of stroke identification and management causes delay in arrival to hospital for patients with acute stroke. This delay can cause significant impact on patient's outcome and recovery.

LIMITATIONS

30 day follow up was done by phone interview, clinical status of the patients was assessed by attendant and patient's subjective opinion. Modified Rankin Scale and NIHSS not used for follow up because of various reasons like patient/ attendants were not interested in long interviews, some had no time, and some had poor educational background so were unable to give interview as per this study requirement.

RECOMMENDATIONS-

- Stroke awareness campaigns should be organised on regular basis for helping society to recognise stroke symptoms and importance of early hospital arrival in acute stroke.
- General physicians should be aware of stroke symptoms so that they recognise the disease correctly and refer to nearby stroke centres as soon as possible.
- General physicians should be aware of location of stroke centres so that they can refer to the nearest stroke centre.
- Hospitals should develop stroke protocols so that patients with acute stroke identified early and treated in time as well.
- Hospitals in remote areas should be equipped with facilities for rapid transportation of patients with acute stroke to nearby stroke centres.

Conflict Of Interest

None

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