Online Journal of Health and Allied Sciences
Peer Reviewed, Open Access, Free Online Journal
Published Quarterly : Mangalore, South India : ISSN 0972-5997
Volume 9, Issue 3; Jul-Sep 2010

Original Article:

A study of factors delaying hospital arrival and predictors of mortality in patients presenting to emergency department with Stroke: A developing state scenario

Ganraj Bhat Sankapithilu, Research Assistant,
Vinayak Nagaraja, Research Assistant,,
Mudassir Azeez Khan, Professor and Head,
Department of Community Medicine, Mysore Medical College and Research Institute, Mysore.

Address For Correspondence:
Dr. Ganraj Bhat Sankapithilu,
Research Assistant,
Department of Community Medicine,
Mysore Medical College and Research Institute,
Mysore, India.
E-mail: gansi.bhat@gmail.com

Citation: Sankapithilu GB, Nagaraja V, Khan MA. A study of factors delaying hospital arrival and predictors of mortality in patients presenting to emergency department with Stroke: A developing state scenario. *Online J Health Allied Scs.* 2010;9(3):2
URL: http://www.ojhas.org/issue35/2010-3-2.htm
Open Access Archives: http://cogprints.org/view/subjects/OJHAS.html and http://openmed.nic.in/view/subjects/ojhas.html

Submitted: Sep 2, 2010; Accepted: Sep 27, 2010; Published: Oct 15, 2010

Abstract:
Background: Thrombolytic therapy for acute ischemic stroke has recently become available in India but its success depends on initiating the treatment in the narrow therapeutic time window. There is commonly a delay of several hours before patients with acute stroke seek medical attention. **Materials and Methods:** A prospective study was conducted to assess the factors influencing this delay in admission of acute stroke cases. 134cases (101 males, 33 females) of acute stroke that arrived within 72 hours at our hospital casualty were recruited. A standardized structured questionnaire was given to patients or their attendants. **Results:** The median time to casualty arrival was 9 hours with 13.4% cases arriving within 3 hours and 36.5 % cases within 6 hours. Distances from hospital, referral, belief in myths and alternate medicine and low threat perception of symptoms of stroke were independent factors associated with delay in arrival. Living in city, day time onset, urgency shown by attendant, availability of transport and presence of family history were associated with early arrival. There was no correlation with patients' or attendants' sex, educational status, history of previous stroke or transient ischemic attack, subtype or severity of stroke, time of stroke and availability of transport. 134 patients (65.7% were from rural population, 55.22%-smokers, 46.76%-alcoholics) with mean (SD) age of 53.83+/-18.02years [significantly lower in females (mean difference=9.73years p=0.002)], were admitted and diagnosed to have stroke. 87.3% had first episode of stroke and 12.7 had more than one episode of stroke. ICF rate was 26.1%. ICF rate has no relation with age (p=0.516), sex (p=0.460), number of episodes (0.795), underlying hypertension (p=0.905). Odds of diabetics dying were 12 times higher than non-diabetics. Inpatient mortality was also significantly higher in smokers compared with non-smokers (p=0.004), in patients with right-sided compared with left-sided hemiplegic (p=0.029) and who couldn't afford computed tomography (CT) scan (p=0.007). Kaplan Meier curve in Image-1 shows the survival following admission to emergency ward. **Conclusion:** Adequate measures need to be taken to improve the public awareness of stroke and the role of local doctors. Our study has shown that active smokers, involvement of the right side and non performance of CT were independent predictors of mortality which have not been shown earlier. Also, we found that diabetes mellitus is independent predictor of mortality in stroke, which has been seen in earlier studies too.
Key Words: Epidemiology; Stroke; Thrombolytic therapy

Introduction:
Stroke is predicted as the second leading cause of death and disability in developed nations.[1] In India, the prevalence of stroke was reported as 471.58 per 100,000 and (545.10 per 100,000 when age is standardized to the world standard population) with the annual incidence rate of 123 per 100,000 (145 per 100,000 on standardization to the world stand population).[2] This is higher than in studies reported from the developed nations.[3-6] Indian studies have also reported 30-day case fatality rate of over 41%. Despite such high prevalence and fatality, in the year 2000, India was ranked amongst the countries lacking sufficient research data on stroke.[7] With growing evidences of improved outcome in stroke with timely thrombolytic therapy, reaching the hospital early after stroke onset becomes an issue of high priority. Several studies have emphasized on delay in reaching the hospital but evidences from India are still lacking. We sought to determine this delay in reaching the hospital after stroke onset and in-hospital mortality in South Indian population.

Materials and Methods:
This prospective observational hospital based study has been conducted in the emergency ward of Department of Medicine, K. R. Hospital, Mysore, Karnataka, India. The study protocol has received institutional ethical clearance. Our hospital is a 1,330-bed hospital which includes 335 beds in General Medicine. It is a tertiary care and academic center, located in Southern India. K. R. Hospital serves as major referral center for middle to low socioeconomic strata population. Its catchment area includes 5 districts, Mysore, Mandya, Chamrajnagar, Hassan and Kodagu encompassing 5,467,316. Most patients from rural area are being seen first at primary health centers and are then referred to higher centers. The referral to government versus private hospital mainly depends on financial af-

fordability. Availability of ambulance service in Indian suburban and rural area is very poor and only 12% of patients reach hospital by ambulance.[8]

Acute care to all patients is being provided at the emergency ward in department of medicine. Since, our institution does not have neurologists, stroke cases are managed under department of medicine. Thrombolytic therapy for stroke is being administered in our hospital but in very low fraction as is the case in majority of government hospitals in India which have patient input form middle to low socio-economic strata.[9]

Subject selection: Patients presenting to the emergency ward with stroke over a period of one and half year, December 2007 through May 2009, were selected. Stroke was defined as a neurological deficit of cerebrovascular cause that persists beyond 24 hours or is interrupted by death within 24 hours. Diagnosis was made by the physician on duty. Subject identification has been done by manual search of emergency ward admission log. Case sheets of patients with following diagnoses were screened to identify all the potentially eligible subjects; stroke, transient ischemic attacks (TIA), cerebrovascular accidents (CVA), cerebral or cerebellar or pontine or medullary or internal nuclear or intracranial or infarction or ischemia or thrombosis or hemorrhage and were reviewed further. Subject enrollment has been done for 1 day a week, 9:00 AM to 5:00 PM, by the study investigators. Informed consent was obtained from the all the subjects at the time of enrollment to the study.

Data Collection and Follow-up: Data collection has been done using pre-determined data collection form. Demographic and clinical characteristic of enrolled subjects were collected at the time of admission; duration since onset of symptoms as noticed by the patient or relatives, source of referral, state of patient at the time of presentation, age, gender, socioeconomic status, smoking behavior, alcohol intake, medications, previous stroke episodes, initial blood pressure (mean of three readings), side of involvement and clinical impression. All the patients were subsequently followed up till their discharge or death, whichever came first, and notes were made regarding hospital course and outcome. Primary outcome variable was death during current hospitalization.

Data Analysis: Data was entered into Microsoft excel-2003 from the data collection form. Distribution of observation for individual has been described using percentage, mean with standard deviation and median with range. Pearson's' chi-square or Fishers exact test and independent sample t-test were used to see the relation between categorical versus categorical and categorical versus continuous, respectively. Survival was calculated using Kaplan-Meier curve. Cox proportional hazards model was constructed to identify independent predictors of inpatient mortality. All data analyses were performed using SPSS (Statistical Package for the Social Sciences) for windows, version 11.5

Results:

Over the period of 18 months, 164 patients were admitted to the emergency ward during the specified recruitment time. 14 subjects denied consent, 16 were missed and 134 subjects were enrolled in this study. Clinical and demographical characteristics of studied subjects are shown in Table 1. More than half of the patients (51.5%) presented to the hospital directly and the rest were referred, majority from primary health centers (28.4%). Sixty eight percent were from rural areas and 78 (58.2%) patients never attended school. CT scan in first 12 hours was performed in 48 patients and 7 (5.2%) patients received thrombolytics, 31% received anti hypertensive and all subjects received Aspirin. Only 7 subjects were thrombolysed by neurologists. All the patients who received thrombolysis survived. All the patients were followed up till their discharge or death.

Table 1: Demographical and clinical characteristics of studied cohort

Variables	**Observations** (n=134)
Age (mean ± SD*)	53.8 ± 18.0
Gender	
Male	101 (73.4%)
Female	33 (26.6%)
Smokers (current smokers %)	76 (90.1%)
Alcoholics	62 (46.3%)
Referrals	
Came directly	69 (51.5%)
PHCs	38 (28.4%)
District Hospital	9 (6.7%)
Nursing home/general practitioner	18 (13.4%)
First ever episode of Stroke	117 (87.3%)
Repeated episode of stroke	17 (12.7%)
Known Hypertensive	52 (38.8%)
Known Diabetics	19 (6.7%)
Side of involvement	
Right	72 (53.7%)
Left	24 (17.9%)
Bilateral	38 (28.4%)
*Standard Deviation	

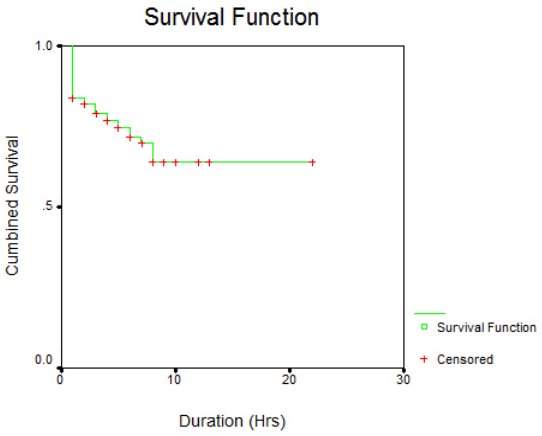

Figure 1: Kaplan Meir curve showing overall survival in stroke patients

Median delay in reaching to hospital from the time of onset of stroke was 9 hours, 18 (13.4%) patients reached the hospital within 3 hours and 31 (23.1%) reached within 6 hours. This delay was more in females compared to males but the difference was not statistically significant (p = 0.71).

Of the 134 subjects, 67 had shown improvement in neurological deficits during hospitalization, 30 had stable deficits, 2 had shown worsening and 35 subjects expired. Figure 1 shows the Kaplan–Meier curves for survival. Majority of deaths occurred early during the course of hospitalization. Subjects who survived till 9th day of hospitalization, in-hospital mortality was nil. In univariant analysis, in-hospital mortality was found to have no relation with age (p = 0.516), gender (p = 0.460), prior stroke episodes (p = 0.528), underlying hypertension (p = 0.536), and involvement of right side compared with left side (p= 0.4). There was no significant difference in mortality between patients reaching hospital within 3 hours versus patients who reached hospital after three hours (p = 0.532). Inpatient mortality was significantly higher in smokers compared with non-smokers (p = 0.003), diabetics compared with non-diabetics (p = 0.001) and those who could not afford Computed Tomography (CT) scan (p = 0.007). Table 2 shows res-

ult of Cox proportional hazards models which identify smoking and diabetes as independent predictors of in-hospital mortality.

Table 2: Independent Predictors of inpatient mortality				
	Hazard ratio	95.0% CI		Significance
		Lower	Upper	
Age	2.066	.988	4.31	0.054
Gender	1.752	0.627	4.896	0.285
DM	4.661	1.406	15.458	0.012
HTN	1.471	0.546	3.963	0.446
Smoking	3.995	1.393	11.463	0.010
Delay in reaching hospital	.999	0.994	1.005	0.797
Number of episode	.990	0.339	2.890	0.986
CT scan	.548	0.195	1.540	0.254
Side of involvement	1.289	0.867	1.918	0.209

Table 3-Univariant analysis of in- patient mortality	
Univariant analysis, In-hospital mortality	**Significance (p value)**
Age	0.516
Gender	0.460
Before and after 3 hours	0.532
Prior stroke episodes	0.528
Hypertension	0.536
DM	0.001
Smoking	0.003
Involvement of right side compared with left side	0.400
Patients who could not afford Computed Tomography (CT) scan	0.007
Early Arrival	**p value**
Living in city	(0.027)
Distance<10 km	(0.03)
Day time onset	(0.01)
Family history	(0.01)
Male attendant	(0.56)
Attendant's Relationship with the patient	(0.34)
Urgency shown by attendant	(0.01)
Prior stroke episodes	(0.883)
Availability of transport	(0.01)
GCS score	(0303)
Aphasia	(0.338)
H/O hypertension, diabetes, IHD	(0.834)
Late Arrival	**p value**
Female gender	(0.71)
Educational status of patient	(0.84)
Attendant's educational status	(0.89)
Lack of knowledge about stroke	(0.83)
Low threat perception	(0.01)
Belief in Myths and alternate medicine	(0.01)
Below Poverty Line	(0.377)
Referral	(0.017)

Table 4 Type of Intracranial lesion among patients	
Thrombosis	70
Hemorrhage	51
Embolism	3
Trauma	0
Infection	3
SOL	7

Discussion:

Summary of Major Findings: Only thirteen percent patients reached hospital within 3 hours of onset of symptoms with median delay in reaching the hospital being 9 hours. Overall, in-hospital mortality was 26.1% and all deaths occurred within first 8 days of hospitalization. Smoking and diabetes were independent predictors of in-hospital mortality.

Delay in the Management: As per recommendations made by American Academy of Neurology in 1996, thrombolytics were not shown to be effective beyond 3 hours after onset of stroke.[10] In a pooled analysis of 6 randomized placebo-controlled trials of intravenous r-tPA by ATLANTIS, ECASS, and NINDS r-tPA study group investigators, beneficial effect of r-tPA was proved beyond 3 hours since the odds ratio for a favorable outcome was 1·40 (1·05–1·85) for those treated within 181–270 minutes.[11] However, the beneficial effect did not extend beyond 6 hours[11]. This was further supported by systematic review conducted by Wardlaw et al. and randomized controlled trial by ECASS Investigators.[12,13] On putting all these together, thrombolytic therapy within 3 hours of onset of stroke has advantage in terms of mortality and functional out come. Its use between 3 to 4.5 hours does not reduce the mortality but increases functional outcome at discharge and at 3 months.

To be able to benefit from thrombolytic therapy, patients need to reach hospital within the above mentioned duration. In our cohort, only 13.4% reached the hospital within duration of definitive benefit and 23.1% could reach in duration where use of thrombolytics could have improved the functional outcome. In other studies, percentage of patients reaching hospital within 3 hours have ranged between 28.0 to 61.4 with average delay in reaching to hospital ranging from 5.1 to 5.6 hours.[14-18] The maximum number of patients (61.4%) reaching the hospital within 3 hours were reported by Turin et al., from Takashima Stroke Registry, Japan. They perceived that higher stroke severity was associated with shorter delay in reaching hospital which is supported by other studies too.[15-18] Other factors reported to be associated with shorter duration of hospital arrival are use of Emergency Medical Services (EMS) or ambulance, time of stroke onset, female sex, perceived adequacy of income, whereas advanced age and living alone were associated with longer delay.[14-18]

In our cohort, majority of patients had low educational status and were from rural areas where transportation is not good and health facilities are located far away. Also, this population is not well aware of stroke symptoms. These factors were potential contributors in delay to reach the hospital. In addition, female gender had higher delay in our study which could be the result of females using health services less frequently than men, even when they are available. This could be because they do not recognize the need to seek medical attention or cannot overcome social and cultural barriers.[19]

In-hospital Mortality: Several studies have been reported on in-hospital mortality from across the globe. This was significantly lower in the western world when compared with developing nations.[4,20] There is only limited data available on stroke related mortality in India. The overall 30-day case fatality noted in the Kolkata study was 41.08% (men, 38.18%; women, 43.24%) which is significantly higher than Western countries (17 to 33%).[3-6,20] Our study results support higher in-hospital mortality associated with stroke in India.

In recent years, several factors have been described to independently predict in-hospital mortality in stroke which are advancing age, female gender, severity of stroke, associated comorbid conditions, atrial fibrillation, previous stroke/transient ischemic attack.[20-22] Our study supports DM and smoking to be independent predictors of in-hospital mortality in stroke.

One of the few limitations of this study was smaller sample size. Small number of subjects in each group decreased the strength of association. Stroke severity at the time of presentation which is well proven to have impact on mortality, was not recorded. Also, we had calculated delay in reaching hospital from the time of recognition of symptoms by patient or patient relatives. This may have underestimated the actual delay in

reaching the hospital from the time of onset of stroke as many patients could have had stroke in sleep. We did not enroll patients over weekends and nights where delay may be substantially different.

Even with these limitations, we believe these findings enhance our current knowledge regarding the epidemiology of stroke among South Indian population and provide an initial departure point for potential strategies for better management of stroke like strengthening EMS/ambulance service, increasing awareness about stroke symptoms and seeking health care.

References:

1. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet*. 1997;349(9064):1498-1504.
2. Das SK, Banerjee TK et al. A prospective community-based study of stroke in Kolkata, India. *Stroke.* Epub 2007 Feb 1;38(3):906-910.
3. Brown RD, Whisnant JP et al. Stroke incidence, prevalence, and survival: secular trends in Rochester, Minnesota, through 1989. *Stroke.* 1996;27(3):373-380.
4. Kolominsky R, Sarti C et al. A prospective community-based study of stroke in Germany--the Erlangen Stroke Project (ESPro): incidence and case fatality at 1, 3, and 12 months. *Stroke* 1998;29(12):2501-2506.
5. Rothwell PM, Coull AJ et al. Change in stroke incidence, mortality, case-fatality, severity, and risk factors in Oxford shire, UK from 1981 to 2004 (Oxford Vascular Study). *Lancet* 2004;63(9425):1925-1933.
6. Syme PD, Byrne AW et al. Community-based stroke incidence in a Scottish population: the Scottish Borders Stroke Study. *Stroke.* Epub 2005 Aug 4;36(9):1837-1843.
7. Stroke epidemiological data of nine Asian countries. Asian Acute Stroke Advisory Panel (AASAP). *J Med Assoc Thai.* 2000;83(1):1-7.
8. Pandian JD, Srikanth V et al. Poverty and stroke in India: a time to act. *Stroke*. Epub 2007 Oct 22;38(11):3063-3069.
9. Durai PJ, Padma V et al. Stroke and thrombolysis in developing countries. *Int J Stroke* 2007;2(1):17-26.
10. Practice advisory: thrombolytic therapy for acute ischemic stroke--summary statement. Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 1996;47(3):835-839.
11. Hacke W, Donnan G et al. Association of outcome with early stroke treatment: pooled analysis of ATLANTIS, ECASS, and NINDS r-tPA stroke trials. *Lancet.* 2004;363(9411):768-774.
12. Hacke W, Kaste M et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med* 2008;359(13):1317-1329.
13. Wardlaw JM, Murray V et al. Thrombolysis for acute ischemic stroke. *Cochrane Database Syst Rev* 2009(4):CD000213.
14. Derex L, Adeleine P et al. Factors influencing early admission in a French stroke unit. *Stroke* 2002;33(1):153-159.
15. Chang KC, Tseng MC et al. Pre hospital delay after acute stroke in Kaohsiung, Taiwan. *Stroke*. Epub 2004 Feb 12;35(3):700-704.
16. Maze LM, Bakas T. Factors associated with hospital arrival time for stroke patients. *J Neurosci Nurs* 2004;36(3):136-141, 155.
17. Maestroni A, Mandelli C et al. Factors influencing delay in presentation for acute stroke in an emergency department in Milan, Italy. *Emerg Med J.* 2008;25(6):340-345.
18. Turin TC, Kita Y et al. The time interval window between stroke onset and hospitalization and its related factors. *Neuroepidemiology* Epub 2009 Jul 27;33(3):240-246.
19. Key P. Women, health and development, with special reference to Indian women. *Health Policy and Planning.* 1987;2(1):58-69.
20. Sweileh WM, Sawalha AF et al. Predictors of in-Hospital Mortality after Acute Stroke: Impact of Gender. *Int J Clin Exp Med.* Epub 2009 Jan 30;2(1):41-47.
21. Heuschmann PU, Kolominsky PL et al. Predictors of in-hospital mortality and attributable risks of death after ischemic stroke: the German Stroke Registers Study Group. *Arch Intern Med.* 2004;164(16):1761-1768.
22. Carter AM, Catto AJ et al. Predictive variables for mortality after acute ischemic stroke. *Stroke.* Epub 2007 Apr 19;38(6):1873-1880