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Original Article

Internal Medicine Section

A Prospective Observational Study of Short-term Mortality Indicators in Acute Stroke Patients

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ABSTRACT

Introduction: Stroke is the second leading cause of death worldwide, causing 6.2 million deaths in 2011. There is a lack of uniform consensus regarding the predicting factors for mortality associated with stroke.

Aim: To determine the various factors which influence the mortality in acute stroke.

Materials and Methods: This was a prospective study conducted between November 2017 to February 2020 at the hospitals attached to Bangalore Medical College and Research Institute, Bangalore, Karnataka, India. All the patients diagnosed with Cerebrovascular Accident (CVA) using neuroimaging of brain within 24 hours of a symptoms were enrolled and followed-up for 28 days. After obtaining informed consent, demographic, clinical, laboratory and radiological data was recorded. Patients were assessed using standardised data sheet containing different variables and treated appropriately for ischaemic and haemorrhagic stroke.

Results: The study included 100 patients; 33 died during follow-up. The mean age of the patients was 55.35±15.78 years; there were 54 males and 46 females. Male gender (p-value <0.001), poor Glasgow Coma Scale (GCS) (p-value <0.001), severe neurodeficit (p-value <0.001), raised intracranial pressure (p-value <0.001) and complication like delayed recovery of GCS (p-value <0.001), aspiration pneumonia (p-value<0.001), Acute Kidney Injury (AKI) (p-value <0.001), fever (p-value <0.001), dysphagia (p-value <0.001), bedsore (p-value <0.001) and seizure (p-value <0.001) were the predictors of mortality in acute stroke.

Conclusion: The factors like poor GCS, severe neurodeficit, raised intracranial pressure at the time presentation of patient and occurrence of complication like delayed recovery of GCS, aspiration pneumonia, AKI, fever, dysphagia, bedsore and seizure can be used as prognostic marker in acute stroke. Comprehensive neurological care wherever feasible involving neurologist, neurosurgeon, interventional radiologist, physiotherapist which take care of the immediate need and to prevent the long term complication would help to decrease mortality in acute stroke.

Keywords: Aspirational pneumonia, Cerebrovascular accident, Prognostic marker

INTRODUCTION

A stroke, or CVA, is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause [1]. The second most common cause of death and the predominant cause of disability worldwide is stroke [2]. In 2018, one in every six deaths from cardiovascular disease was due to stroke [3]. In India, there is a scarcity of evidence regarding the epidemiology of the neurological disorder. According to India State-Level Disease Burden Initiative there is nearly two times increase in the rate of non communicable neurological disorder from 4-8.2% between 1990 and 2019 [4]. Stroke (37.9%), headache disorders (17.5%), and epilepsy (11.3%) are the leading contributors to neurological disorders burden in India, with stroke having caused 6,99,000 deaths in India in 2019, which was 7.4% of the total deaths in the country. About 68% of deaths due to neurological disorders is due to stroke, followed by Alzheimer's disease and other dementias (12%) and encephalitis (5%) [4].

The predictors for early mortality following stroke have been less intensively studied compared to risk factors for medium to long term mortality after stroke. There is a necessity for early prognostication of poor outcome including death following an acute event. In high income countries the 30 mortality rate following ischaemic stroke has been estimated to be around 15% [5-7]. Hence, knowledge regarding the early predictors of mortality following an acute event would impact on the management decisions, which can range from recognising the need for intensified monitoring to withdrawal from maximal therapy.

National Institute of Health (NIH) Stroke Scale by Adams HP et al., is the most accepted score for predicting outcome after ischaemic stroke. A score of >25 out of 42 on NIHSS carries grave prognosis however this scale does not consider other factors like neurological and medical complications e.g., recurrent stroke, delayed recovery, raised Intracranial Tension (ICT), increased mass effect and size of lesion or new onset Acute Myocardial Infraction / Atrial Fibrillation / Congestive Cardiac Failure (AMI/AF/CCF) or aspiration pneumonia during hospital stay [8].

Several studies are done for the past 25-30 years in India and other parts of the world to find out the prognostic marker of acute stroke. German stroke collaboration study predicted that a NIHSS score >25, higher age group and fever was associated with increased mortality following ischaemic stroke [9], whereas another study by Weimar C et al., found that apart from NIHSS score and higher age, low GCS has the poor outcome [10]. The most significant predictors of mortality according to a study in India regarding short-term mortality in acute stroke were delay in recovery of consciousness and new onset myocardial infraction / heart failure and aspiration pneumonia [11]. So, there is no uniform consensus regarding the most important factors which predict mortality and many studies failed to consider the complete profile of the patients from clinical to radiological aspect.

The present study aimed to include all the important factors in stroke including clinical, radiological aspects along with complications, risk factors and co-morbidities in stroke (either ischaemic or haemorrhagic). To find out most influential factors involved in four weeks mortality in acute stroke.

MATERIALS AND METHODS

It was a prospective observational study with a follow-up period of 28 days, and conducted between November 2017-February 2020. All the data was collected from patients who were admitted in Victoria Hospital and Bowring and Lady Curzon Hospital attached to Bangalore Medical College and Research Institute, Bangalore, Karnataka, India. Ethical Committee clearance was taken on 26/10/2017, Ref no BMC/PG/170/2017-18

Sample size calculation: Based on a previous study by Das S et al., electrolyte imbalance (one of the prognostic marker) was 51.8% in stroke patient. So, sample size calculated was as follows [11]:

$$n = \frac{z_\alpha^2 pq}{d^2}$$

where, z_α=1.96, p= 51.8, q= 100- 51.8=48.2, d=20% of p

$$n = \frac{(1.96)^2 \times 51.81 \times 48.2}{(10.3)^2} = 90.4$$

So, sample size of 100 patients of acute ischaemic stroke was selected for the study.

Inclusion criteria

- Acute stroke cases which has been confirmed by Neuroimaging of Brain,
- Admitted within 24 hours of onset of symptoms,
- Age >18 years.

Exclusion criteria

- Subarachnoid haemorrhage/subdural haematoma,
- Asymptomatic CVAs/transient ischaemic attack/ onset of symptoms >24 hours,
- Head injury,
- Previous brain lesions like neurocysticercosis, tuberculoma, meningitis, encephalitis or hydrocephalus.

Methodology for data collection: After obtaining informed consent, detail demographic, clinical, laboratory (routine blood investigation and Electrocardiogram (ECG)) and radiological (Computed Tomography (CT)/ Magnetic Resonance Imaging (MRI) brain, chest radiograph, 2D Echocardiography (ECHO)) data were recorded [Appendix-1,2]. Patients were assessed using standardised data sheet containing different variables and treated appropriately for ischaemic and haemorrhagic stroke.

STATISTICAL ANALYSIS

Data was entered and analysed using Microsoft Excel and the Statistical Package for the Social Science (SPSS) software, version 21.0. Various categorical variables frequencies, various numerical variables, means and standard deviations were used in data analysis. To test association between stroke outcome and various categorical variables Chi-square test was used. Fisher's-Exact test was used where chi-square was not applicable. A p-value <0.05 was considered statistically significant with 95% CI.

RESULTS

During the study period, a total of 100 patients who fit into the inclusion criteria were studied and patients were followed-up for a period of 28 days or till the mortality. Out of 100 patients, 33 died during the study. The mean age of the patients in present study was 55.35±15.78 years. Nineteen patients were below the age group of 45 year (stroke in young) and majority of patients were male (n=54). [Table/Fig-1] shows that among the dead most common risk factor were diabetes and hypertension (100%), majority of the patient had severe neurological deficit (70%) and GCS 7-9 (54%) at the time of presentation. Most common complication in present study was aspiration pneumonia and bedsores (24 patients each) [Table/Fig-2].

There was a statistically significant difference (p-value <0.001) in mortality between males and females but not among different age group [Table/Fig-1]. Low GCS, severe neurodeficit and raised ICT showed statistical significance in affecting mortality [Table/Fig-1], whereas, type of the lesion [Table/Fig-3], site of the lesion [Table/Fig-4], size of the lesion [Table/Fig-5], mass effect [Table/Fig-1] and previous co-morbidities didn't show any statistical significance [Table/Fig-2]. Complication like delay in GCS recovery, aspiration pneumonia, AKI, fever, dysphagia, bedsores and seizures showed statistically significant mortality difference in patients after one month of follow-up [Table/Fig-2].

DISCUSSION

The lifetime risk of ischaemic or haemorrhagic stroke in adults is 25% and the risk of ischaemic stroke is 18% from the age of 25 years onward [12]. In North America and western Europe population the incidence of stroke ranges from 90-180 per 100,000 population, whereas in East Asia, Eastern Europe and Central Asia, it ranges from 241–360 per 100,000 population [13].

The cumulative incidence of stroke ranged from 105 to 152 per 100,000 persons per year, and the crude prevalence of stroke ranged from 44.29 to 559 per 100,000 persons in different parts of the country during the past decade. These values were higher than those of high-income countries [14].

In India, age-adjusted stroke mortality is 192 per 100,000 per person, which is one of the most frequent cause of death in the country [15]. Total six studies reported mortality rates of stroke in India; three studies from urban population [16-18] and three from rural population [19-21]. According to the data available

Demography and clinical features	Alive (n=67)				Dead (n=33)				p-value
Age (years)	57.7±15.9				59.6±15.5				0.8
Gender (Male:Female)	42:25				12:21				<0.001
Clinical Features	Grade 0	Grade 1	Grade 2	Grade 3	Grade 0	Grade 1	Grade 2	Grade 3	
GCS*	0	58 (87%)	7 (10%)	2 (3%)	0	3 (10%)	18 (54%)	12 (36%)	<0.001
Neurodeficit	58	10 (15 %)	37 (55%)	20 (30%)	0	0	10 (30%)	23 (70%)	<0.001
Raised ICT†	58 (87%)	7 (10%)	2 (3%)	0	20 (61%)	8 (24%)	4 (12%)	1 (3%)	<0.001
HTN (hypertension)	0	44 (66%)	16 (24%)	7 (10%)	0	18 (54%)	7 (21%)	8 (25%)	0.19
DM (Diabetes Mellitus)	1 (1%)	56 (84%)	6 (9%)	4 (6%)	0	23 (70%)	5 (15%)	5 (15%)	0.275
Hyperlipidaemia	58 (87%)	5 (7%)	2 (3%)	2 (3%)	29 (87%)	0	1 (3%)	3 (10%)	0.786
Carotid Artery Stenosis	56 (84%)	6 (9%)	5 (7%)	0	32 (97%)	0	1 (3%)	0	0.127
Mass Effect	54 (81%)	6 (9%)	4 (6%)	3 (4%)	21 (64%)	4 (12%)	4 (12%)	4 (12%)	0.266
Delay in Recovery of GCS	15 (22%)	24 (36%)	17 (25%)	11 (17%)	26 (79%)	2 (6%)	1 (3%)	4 (12%)	<0.001

[Table/Fig-1]: Demography and clinical features.
*Glasgow Coma Scale, †Intracranial tension; Grading was done considering the impact of each components in the table on the prognosis of stroke; Chi- square test and Fischer's-Exact test

Complication and Previous Handicap	Alive	Dead	p-value
New onset ischaemic heart disease	4 (6%)	1 (3%)	0.39
New onset congestive cardiac failure	2 (3%)	2 (6%)	-
New Onset Arrhythmia*	2 (3%)	3 (9%)	-
Stress Ulcer	3 (5%)	4 (12%)	0.15
Aspiration Pneumonia	4 (6%)	20 (61%)	<0.001
Electrolyte Imbalance†	6 (9%)	11 (33%)	0.007
AKI (Acute Kidney Injury)	6 (9%)	12 (36%)	<0.001
Fever	8 (12%)	14 (42%)	<0.001
Dysphagia	6 (9%)	12 (36%)	<0.001
Bedsores	13 (19%)	11 (33%)	<0.001
Seizure	4 (6%)	9 (27%)	<0.001
Previous Handicap‡	10 (15%)	10 (30%)	0.14

[Table/Fig-2]: Comparison of complication and previous handicap in alive and dead patient after one month follow-up.
*All the patient had Atrial fibrillation, †All the patient had hyponatraemia; ‡10 patients had old CVA, 5 had chronic kidney diseases, 2 had Atrial fibrillation, 3 had mitral stenosis

	Haemorrhage	Infarct	Infarct+ Haemorrhage	p-value
Alive	15 (22%)	47 (70%)	5 (8%)	0.44
Dead	11 (33%)	19 (58%)	3 (9%)	

[Table/Fig-3]: Type of the lesion.
Chi-square test

	Grade 1	Grade 2	Grade 3	p-value
Haemorrhage				
Alive	11 (16%)	3 (4%)	0	0.8
Dead	9 (27%)	2 (6%)	1 (3%)	
Infarct				
Alive	29 (43%)	13 (19%)	5 (7%)	0.11
Dead	7 (21%)	7 (21%)	5 (15%)	
Infarct+ Haemorrhage				
Alive	0	3 (4%)	2 (3%)	0.33
Dead	1 (3%)	2 (6%)	0	

[Table/Fig-4]: Site of the lesion.
Fischer's-Exact test

	Grade 1	Grade 2	Grade 3	p-value
Haemorrhage				
Alive	2 (3%)	9 (13%)	4 (6%)	0.12
Dead	0	4 (12%)	7 (21%)	
Infarct				
Alive	7 (10%)	21 (31%)	24 (35%)	0.86
Dead	2 (6%)	9 (27%)	11 (33%)	

[Table/Fig-5]: Size of the lesion.
Both Chi- square test and fisher exact test

from these studies, the proportional mortality rates of stroke were 13-14.3% but there is no concrete data available on mortality of subtypes of strokes [20]. In the present study, the mortality rate was 33% which was above the national average (13-14.3%) [20] and out of 33 death, 20 happened within one week of presentation. Mortality rate was 33% in haemorrhagic stroke and 58% in ischaemic stroke, whereas according to the study by Henon H et al., overall mortality in ischaemic stroke was 4.9% and 18% in haemorrhagic stroke [22].

With regards to age and gender, at young ages, women have a higher risk of stroke then men, while at older ages the relative risk reverses [23]. Overall, strokes are commonly reported among women because of their longer life span compared with men [24,25]. A study found that among Europeans the risk of stroke increased by 9% per year in men and 10% per year in women [26]. In India, Joshi R et al., recorded the deaths occurring in 45 villages in Andhra Pradesh for a period of 12 months, it was found that 13% of the total deaths were due to stroke, 14% in females and 12% in males [20]. In this study, it was found that mortality was 36% in male and 64% in female. The mean age of death in this study was 59.6±15.5 years, whereas it was 67.47±11.8 years as reported by Kalkonde YV et al., [21].

A study by Henon H et al., which used 18 variables concluded that, level of consciousness at the time of presentation and delay in the recovery of GCS >7 days was the most important predictors of mortality in acute stroke [22]. In the present study, GCS <7 (36%) and delay in the recovery of GCS >7 days (12%) were the major contributors of mortality. It was found that among stroke patients with grade 3 neurodeficit, the mortality rate was 70%. In another study, the risk of death with a severe focal neurodeficit was 53% [9]. Another study observed that raised intracranial pressure is an important predictor of mortality (53%) in ischaemic stroke followed by pulmonary embolism and pneumonia [27]. The present study observed that raised intracranial pressure was an important predictor of mortality in acute stroke with mortality rate was 39%.

When it comes to the size of the lesion the volume of acute infarction was used to estimate stroke outcome using neuroimaging studies [28]. According to a study, which analysed the data from over 1800 patients who had CT or MRI within 72 hours of ischaemic stroke onset and found that age, NIHSS score, initial infarct volume and size of the lesion was an independent predictor of stroke outcome [29] but index study did not support this findings. As a consequence of brain stem damage or infratentorial mass effect, short-term mortality of patients with a posterior circulation stroke syndrome (grade 2 or 3 involving brainstem or cerebellum) was increased compared with anterior circulation stroke syndromes (grade1) [30]. But in present study, site of the lesion did not affect the short-term mortality significantly.

Hypertension [31,32], diabetes [33,34], dyslipidaemia [35,36] and carotid artery stenosis [37] have earlier been found to be more frequently associated with mortality in acute stroke. In this study, there was no correlation between risk factors and mortality.

Outcome after ischaemic stroke was most commonly influenced by medical complications. The rates of reported medical complications of stroke are high [38-41]. Around 95% of patients experienced one medical complication and 24% of the patients experienced at least one serious medical complication (defined as prolonged, immediately life threatening, or resulting in hospitalisation or death) in a prospective study that analysed the placebo group of the Randomised Trial of Tirilazad Mesylate in Acute Stroke (RANTTAS) database (n=279) [39]. The most common medical complications were pneumonia (22%), bedsores (21%), gastrointestinal bleeding (3%), congestive heart failure (3%), and cardiac arrest (2%). In this study, most common cause for mortality was aspirational pneumonia (61%), other complications which contribute to the mortality in acute stroke were AKI (36%), fever (42%), dysphagia (36%), bedsore (33%) and seizure (27%).

New onset cardiac complication did not affect the mortality significantly in present study. But a study conducted by Andersen KK et al., on 26,818 patients published in American heart association in 2011 found that age, stroke severity and AF was a significant predictor of 30-day mortality in acute stroke [42]. Another study by Collins TC et al., in Houston Centre for Quality Care & Utilisation Studies, 2002 (n=5,442 patients) found that in ischaemic stroke the mortality predictor are heart failure and cardiac arrhythmia. In haemorrhagic stroke it was age, liver disease, cardiac arrhythmias including atrial fibrillation, renal failure, chronic obstructive pulmonary disease, and chronic heart failure [43].

Co-morbid conditions like coronary artery disease [44], heart failure [45], atrial fibrillation [46], renal dysfunction or dialysis [47] are associated with increased risk of poor outcome following ischaemic stroke but in the present study previous handicap did not contribute to the mortality significantly.

Limitation(s)

The findings cannot be generalised, hence there is a need for multicentric studies.

CONCLUSION(S)

Most deaths in acute stroke were due to complication developed by the patients after the stroke. So, physiotherapy post stroke apart from acute care helps to prevent bedsore, better recovery from aspirational pneumonia and also in recovery of GCS, there by reduce the mortality. In developing countries like us improving the quality of care in hospitals and inclusion of specialised Stroke Unit for comprehensive stroke care under one roof in tertiary care centre is necessary to reduce mortality in acute stroke.

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APPENDIX: 1

At the Time of Admission				
	Variables	**Grade I**	**Grade II**	**Grade III**
1	Age in years	18-40	41-60	61-90
2	Clinical examination GCS level of consciousness	10-14	7-9	<7
3	Clinical severity of Neurodeficit	a) Motor deficits of one limb. Power<4/5 b) No facial palsy	a) One limb power <3/5 or two limb deficit b) Facial palsy ± speech/cognitive defect	a) Both limb power<3/5 b) Facial palsy c) Speech or cognitive defect±sensory deficit
4	Features of raised Intracranial Tension (ICT)	Headache or papilloedema	a) Headache b) Papilloedema	a) Headache b) Papilloedema c) Conjugate eye deviation and/or VI nerve palsy
5	Risk factor Hypertension	a) SBP=140-180 or DBP=90-110 (without drug) b) SBP/DBP< 150/90 (with drug)	a) SBP= 140-180 b) DBP=90-110 (with regular or irregular drug)	a) SBP> 180 or b) DBP>110 (with drug)
6	Diabetes mellitus (blood sugar without IV dextrose)	a) RBS>200 mg/dL without drug b) RBS<200 mg/dL (with drug)	RBS=200-300 mg/dL with drug or without drug in a known diabetic	RBS>300 mg/dL (known diabetic with or without drug)
7	Carotid artery stenosis	Asymptomatic	Symptomatic	
8	Hyperlipidaemia	Isolated TC*>250 mg/dL or isolated TGL† >200 mg/dL (without drug)	Isolated TC>250 mg/dL or isolated TGL>200 mg/dL (with drug)	a) TC>250 mg/dL b) TGL>200 mg/dL (with drug)
9	Complications Site of the lesion A) Ischaemic	a) Cortical or b) Subcortical halamus	a) Brainstem b) Cerebellum	Cortical+subcortical±infratentorial
	B) Haemorrhagic	a) Lobar b) Basal ganglia/Thalamus	a) Brainstem b) Cerebellum	Lobar+basal ganglia/ thalamus±infratentorial
10	Size of lesion A) Ischaemic	Lobar <1/2 lobe <20 ml (3cm diameter)	>1/2-1 lobe (3- 7.5 cm diameter) (20-200ml)	>1 lobe (200ml) (7.5 cm diameter)
	B) Haemorrhagic	Lobar <11mL <2cm diameter	a) Lobar(11-60 mL) (2-5 cm diameter) b) Cerebellum <8mL c) Pontine<1cm diameter	a) Lobar (>60 mL) (5 cm diameter) b) Cerebellum >8 mL c) Pontine >1 cm diameter
11	Mass effect	Sulci effacement of ventricular without shift	Midline shift 2-5cm	Midline shift > 5cm Compression
12	Delay in recovery of GCS	<3 days	3-7 days	>7 days
13	New onset Ischaemic heart disease	ST depression	Infarction complications	
14	New onset congestive cardiac failure	Congestive cardiac failure without shock/dyspnoea	Congestive cardiac failure dyspnoea or shock	
15	New onset cardiac arrhythmias	SVE/VE‡	SVT/VT/MAT/AF§	
16	Stress ulcers	Vomiting + epigastric tenderness	Hematemesis epigastric and/or melena	
17	Aspiration pneumonia	Crepitations in localised area	Crepts up to midzone/upper zone	
18	Electrolyte disturbance (repeated if required)	Na<130 mEq/L K < 3.5 mEq/L		
19	AKI	Increase in creatinine >0.3mg/dl or 50% in 48hr		
20	Fever	Axillary temperature >98.4o F		
21	Dysphagia	Needs nasogastric feeding		
22	Bedsore	Ulcer deep to dermis		

23	Seizure	New onset seizure (status epilepticus)		
24	Previous handicap: 1) Old CVA 2) Old AMI‖ 3) Old valvular defect 4) Old haemorrhagic diathesis 5) Old Atrial fibrillation 6) Old CKD			

*Total Cholesterol
†Triglyceride level
‡Supraventricular ectopic/ ventricular ectopic
§Supraventricular tachycardia/ ventricular tachycardia/ multifocal atrial tachycardia/atrial fibrillation
‖Acute myocardial infarction

APPENDIX: 2

At the End of Each Week for 4 Weeks				
1	Clinical examination GCS level of consciousness	10-14	7-9	<7
2	Clinical severity of Neurodeficit	a) Motor deficit of one limb. Power<4/5 b) No facial palsy	a) One limb power <3/5 or two limb deficit b) Facial palsy ± speech/cognitive defect	a) Both limb power<3/5 b) Facial palsy c) Speech or cognitive defect±sensory deficit
3	Features of raised ICT	Headache or papilloedema	a) Headache +Papilloedema	d) Headache e) Papilloedema +Conjugate eye deviation and/or VI nerve palsy
4	Risk factor Hypertension	a. SBP=140-180 or DBP=90-110 (without drug) b. SBP/DBP <150/90 (with drug)	a. SBP= 140-180 + DBP=90-110(with regular or irregular drug)	SBP >180 or DBP >110 (with drug)
5	Diabetes (BS without IV DNS)	RBS>200 without drug RBS <200 (with drug)	RBS=200-300 with drug or without drug in a known diabetic	RBS >300 (known diabetic with or without drug)
6	Delay in recovery of GCS	<3	3-7	>7
7	New onset IHD	ST depression	Infarction complications	
8	New onset CCF	CCF without shock/dyspnoea	CCF dyspnoea or shock	
9	New onset arrhythmias	SVE/VE	SVT/VT/MAT/AF	
10	Stress ulcer	Vomiting + epigastric tenderness	Haematemesis epigastric and/or melena	
11	Aspiration pneumonia	Crepts in localised area	Crepts up to midzone/upper zone	
12	Electrolyte imbalance	Na <130 mEq/L K < 3.5 mEq/L		
13	AKI	Increase in creatinine >0.3 mg/dL or 50% in 48hr		
14	Fever	Axillary temperature >98.4° F		
15	Dysphagia	Needs nasogastric feeding		
16	Bedsore	Ulcer deep to dermis		
17	Seizure	New onset seizure (status epilepticus)		