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Mortality in ischemic stroke score: A predictive score of mortality for acute ischemic stroke

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Abstract:

OBJECTIVE: This prospective study was planned to formulate and evaluate a predictive score for in-hospital mortality in cases of acute ischemic stroke.

MATERIALS AND METHODS: In this study, 188 consecutive patients of ischemic stroke were included over 19 months. Only patients with renal failure and malignancy were excluded from the study. All patients were subjected to clinical evaluation along with Glasgow Coma Scale (GCS), National Institute of Health Science scale (NIHSS) score, and modified Rankin score (mRS). Investigations total leukocyte count (TLC), capillary blood sugar at admission, high-sensitivity C-reactive protein (HS-CRP), and troponin I, electrocardiogram, and neuroimaging were performed. The patients were followed up till their outcome in the hospital, and patients who expired were grouped as "mortality group" and the rest as "discharged group." One-way anova analysis was carried out among the significant parameters to identify independent predictors of mortality in cases of ischemic stroke.

RESULTS: After statistical analysis, it was found that late presentation to the hospital, pyrexia (temperature >99F), low diastolic blood pressure at the time of admission, hypoxia (saturation of oxygen <94%), NIHSS score >15, mRS >3, GCS <8, hyperglycemia (random blood sugar >200 mg/dL), raised TLC, and HS-CRP (>10 mg/L) are positive predictive factors of mortality in cases of ischemic stroke. Based on the above findings, a simple and easily applicable mortality in ischemic stroke (MIS) score is developed.

CONCLUSION: This MIS score system will help the clinicians in better management of the patient and improved counseling the relatives of patients with ischemic stroke.

Keywords:

Mortality in ischemic stroke score system, mortality in stroke, mortality score, stroke-related death, stroke severity

Introduction

Cerebral ischemia is caused by reduction in blood flow lasting longer than several seconds. Acute occlusion of an intracranial vessel causes reduction in blood flow to the brain region it supplies. The magnitude of flow reduction is a function of collateral blood flow, and this depends on individual vascular anatomy and the site of occlusion. Sudden death (i.e., within 1 h of onset of symptoms)

is very rarely due to cerebral infarction. Case fatality rate is about 20% at 1 month for stroke in general. In a study conducted in Greece, the most important factors that were found to affect the prognosis of a patient include severity of stroke, commonly measured by National Institute of Health Science scale (NIHSS), modified Rankin score (mRS), and Glasgow Coma Scale (GCS) scores.^[1,2]

Majority of acute stroke patients have disorders of glucose metabolism, and in

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most cases, this fact has been unrecognized. Diabetes worsens the outcome of acute stroke. Hyperglycemia at any time within the first 48 h from stroke onset is associated with poor outcome independently of stroke severity, infarct volume, diabetes, or age. Acute hyperglycemia predicts increased risk of in-hospital mortality after ischemic stroke in nondiabetic patients and increased risk of poor functional recovery in nondiabetic stroke survivors.^[3-5]

Inflammatory markers predict incident ischemic events, including myocardial infarction and stroke. Levels of high-sensitivity C-reactive protein (HS-CRP), an acute phase reactant, were strongly associated with stroke severity. Because stroke severity is also associated with mortality, it is not surprising that this marker is also associated with mortality after stroke.^[6]

Epidemiology

Cerebrovascular diseases include devastating disorders: ischemic stroke, hemorrhagic stroke, and cerebrovascular anomalies such as intracranial aneurysms and arteriovenous malformations.^[7]

Stroke burden in India has risen in the last few decades while it reached a plateau or decreased in developed countries. The average annual incidence of stroke in India is higher than Western nations at 145/100,000 populations. Up to 80% strokes in India are ischemic in nature.^[8,9] Mortality after stroke is high, with stroke ranked as the second most common single cause of death in the developed world.^[10] Of a total of 9.4 million deaths in India, 619,000 deaths are due to stroke. This gives stroke a mortality rate of 73/100,000 (estimated total population 849 million). Approximately 8%–12% of ischemic strokes are fatal (37%–38% hemorrhagic strokes are fatal). On the other hand, stroke declined from the third to the fourth leading cause of death in the United States recently.^[11]

Early prediction of severe disease and high mortality in cases of stroke is important for management and realistic prognostication of patient's relatives. For hemorrhagic stroke, intracerebral hemorrhage (ICH) scoring system has a good predictive value for mortality.^[12] This study was planned to find out various predictors of early death and if possible development of a scoring system to predict risk of in-hospital mortality. This scoring system, such as ICH score, will help clinicians in early prediction of in-hospital death in cases of ischemic stroke.

Materials and Methods

The prospective observational study was carried out over a period of 19 months after approval from the

Ethics Committee. All consecutive patients of acute ischemic stroke of age >18 years were included in this observational study. After inclusion, each patient was subjected to a detailed history and clinical evaluation. The time of onset of the stroke was defined as the time when the patient or observer first became aware of the symptoms. The patients were assessed as per the GCS, NIHSS score, and mRS. The patients were subjected to a computerized tomogram or magnetic resonance imaging and blood investigations hematological, biochemical, and high sensitive CRP (HS-CRP). Subsequently, the patients were treated according to the standard treatment protocols as per American Academy of Neurology guidelines, year 2007. The study in no way interfered with the treatment. Types of stroke were classified according to TOAST classification.^[13] All tests and examination were done at admission and within 12 h from the onset of stroke.

The patients were followed up till their outcome in the hospital, and patients who expired were grouped as "mortality group" and the rest as "discharged group." In-hospital mortality was defined as death within 30 days of admission, which is used both in Medicare Mortality Predictive System and in Medicare Hospital Mortality Information 1986.^[1]

Patients with renal failure and malignancy were excluded from the study.

Factors compared between two groups were duration of time between the onset of symptoms and presentation to the hospital, history of a previous stroke or transient ischemic attack, NIHSS, mRS, and GCS score at the time of admission, blood pressure at the time of admission, temperature at the time of admission, mean reading of oxygen saturation for 10 min at the time of admission, random blood sugar (RBS) at the time of admission, electrocardiogram at the time of admission, total leukocyte count at the time of admission, serum potassium at the time of admission, radiological imaging at the time of admission, HS-CRP levels at admission, and troponin I levels at the time of admission.

The findings of GCS, NIHSS, mRS, RBS, and HS-CRP at admission were divided into three scales, score of 1 for best and score of 3 for worst finding [Table 1]. Based on this system, each patient was given one mortality in ischemic stroke (MIS) score, and outcome was predicted and recorded.

Interpretation and analysis of the obtained results were carried out using one-way ANOVA statistical tests of significance using SPSS 11 (SPSS Inc. Chicago, USA), Chi-square test, and Pearson correlation coefficient.

Results

The study included 188 patients (126 male, mean age of 58.3 years \pm 13.3) over a period of 19 months. Among these, 47 (25%) patients expired whereas 141 (75%) patients survived up to 30 days of stroke. All patients in mortality group expired during the first admission, and none of the discharged patients expired within 1 months. Among all, 166 (88.2%) patients had TOAST type 1 stroke (large artery atherosclerotic). Different parameters among two groups are described in Table 1. The findings of one-way ANOVA test applied on the cohort are given in Table 2.

The average duration from the onset of symptoms of stroke to the presentation at the hospital was 47.510 \pm 39.727 h in mortality group compared to 22.553 \pm 43.067 h in discharged group ($P = 0.006$).

All of the 188 patients were assessed as per the NIHSS score at the time of admission. The mean NIHSS score in the mortality group was 32.659 \pm 0.938. The mean NIHSS score in the discharged group was 22.269 \pm 4.878 ($P = 0.0001$).

All of the 47 patients were admitted in the severe category as per the mRS system, and only 23 (16.3%) among discharged group presented with the severe score (score of 5). The mean mRS score in the mortality group is 5 \pm 0 while the mean mRS score in the patients that were discharged was 4.014 \pm 0.609 ($P = 0.0001$).

All of the 47 patients were in the severe category of GCS scores (3–8). On the other hand, in the discharged group,

twenty patients were in the severe category (3–8) at the time of admission, 84 patients were in the moderately severe category (9–12), and the remaining 37 patients were in the mild category (13–15) as per the GCS ($P = 0.0001$). Mean GCS in mortality group (3.787) was significantly low in comparison of other group (11.3) ($P = 0.0001$).

The RBS at the time of admission, irrespective to diabetic status, was found to higher in expired group. The mean RBS of the patients who expired was 184.53 \pm 83.66 mg/dl (10.26 mmol/L) compared to 149.29 \pm 71.38 mg/dl (8.26 mmol/L) in discharged patients ($P = 0.0001$).

Among patients who expired, forty of the 47 had a HS-CRP level of more than 10 mg/L and 7 had levels \leq 10 mg/L. In contrast, 25 patients of the 141 patients who were discharged had HS-CRP levels of more than 10 mg/L. One hundred and sixteen patients of the 144 patients that were discharged had HS-CRP levels of \leq 10 mg/L. The mean of HS-CRP levels of patients who expired was 13.82 \pm 4.18 mg/L, while that of the patients who were discharged was 4.76 \pm 4.36 mg/L ($P = 0.0001$). The above findings are summarized in Tables 1, 2, and 5.

None of our patients underwent craniectomy.

Distribution of all 188 patients according to the different MIS scores [Table 3] is given in Table 4. Accordingly, we have 102 (54.3%) patients with score of <10 with no mortality, 63 (33.5%) patients with score 11–13 having 38% mortality rate, and 23 (12.2%) had score 14–15 with 100% mortality risk [Table 4 and Figure 1]. This was compared with the actual outcome of these patients, and the patients were found to have a comparable outcome as predicted by our scoring system ($P = 0.0001$, $r = 0.6176$, $P = 0.1$, by Pearson correlation coefficient).

Table 1: Comparison of basic parameters in two groups

Criteria	Mortality Group N=47		Morbidity group N=141	
	Mean	so	Mean	so
Demographic				
Age (yrs)	56.00	13.00	59.01	13.35
M/F	36/11		90/51	
Examination				
NIHSS	32.66	0.94	22.27	4.88
MRS	5.00	0.00	4.01	0.61
GCS	3.79	0.95	11.30	2.86
SBP(mm Hg)	130.21	42.86	135.60	24.06
(mm Hg)	75.53	29.18	82.06	14.32
Temp (F)	98.60	0.90	98.50	0.70
Investigation				
RBS (mg/dl)	184.53	83.66	149.29	71.38
SPo ₂ (%)	93.00	6.00	97.00	5.00
TLC (/cmm)	15258.51	6951.62	11475.12	4954.69
K (mEq/l)	4.42	0.70	4.12	0.63
HSCRP (mg/L)	13.82	4.18	4.76	4.36

Discussion

Soon after admission, following acute stabilization of patients, a primary goal of care of the treating physician is to discuss the status, overall prognosis, and end-of-life care preferences with family. Clinicians generally rely on their clinical experience when these discussions occur, and these predictions have been shown to be relatively accurate. Previous study on ischemic stroke patients showed that 90% of patients predicted to have poor prognosis were dead or dependent at 6 months, and only 65% of ischemic and hemorrhagic stroke patients predicted by clinicians to survive 1 year and be independent were actually independent (defined as mRS \leq 2).^[14]

A predictive model of stroke in-hospital mortality may be more useful for clinicians to improve communication with relatives and care of hospitalized patients. Here, we

Table 2: Anova test findings in two groups

	Sum of squares	df	Mean square	F	Significance (P)
RBS					
Between Groups	43444.149	1	43444.149	7.842	0.006
Within Groups	1030426.170	186	5539.926		
Total	1073870.319	187			
GCS					
Between Groups	1992.199	1	1992.192	312.499	0.0001
Within Groups	1185.759	186	6.375		
Total	3177.957	187			
NIHSS					
Between Groups	3794.980	1	3794.98	206.442	0.0001
With in Groups	3419.206	186	18.383		
Total	7214.196	187			
mRS					
Between Groups	34.257	134.257	34.257	122.602	0.0001
With in Groups	51.972	186	18.383		
Total	86.229	187			
HS CRP					
Between Groups	2896.347	1	2896.347	155.051	0.0001
Within Groups	3474.480	186	18.68		
Total	6370.827	187			
Age					
Between Groups	262.810	1	262.81	1.49	0.224
Within Groups	32815.716	186	176.429		
Total	33078.527	187			
Type					
Between Groups	0.028	1	0.028	0.04	0.842
With in Groups	131.716	186	0.708		
Total	131.745	187			
Time					
Between Groups	21956.314	1	21956.314	12.291	0.001
With in Groups	223370.596	186	1786.401		
Total	354226.910	187			
Temp					
Between Groups	1.512	1	1.512	2.87	0.092
Within Groups	97.975	186	0.527		
Total	99.486	187			
SP_O₂					
Between Groups	453.965	1	453.965	17.312	0.0001
Within Groups	4877.504	186	26.233		
Total	5331.468	187			
SBP					
Between Groups	42.598	1	42.598	0.06	0.807
With in Groups	132716.312	186	713.529		
Total	132758.910	187			
DBP					
Between Groups	181.560	1	181.560	0.715	0.399
With in Groups	47201.418	186	253.771		
Total	47382.979	187			
IHD					
Between Groups	0.064	1	0.064	2.067	0.152
Within Groups	5.745	186	0.031		
Total	5.809	187			
TLC					
Between Groups	504569925.114	1	504569925.114	16.582	0.0001
Within Groups	5659805424.696	186	30429061.42		
Total	6166375349.809	187			

Table 2: Contd...

	Sum of squares	df	Mean square	F	Significance (P)
K					
Between Groups	3.001	1	3.001	7.115	0.008
With in Groups	78.014	185	0.422		
Total	81.015	186			

Table 3: Parameters selected for scoring system

SN	Parameters	Score 1 for each	Score 2 for each	Score 3 for each
1	NIHSS	0-5	6-14	>15
2	mRS	0-2	3-4	5
3	GCS	13-15	9-12	3-8
4	Random glucose at admission	<120	121-199	>200
5	HS-CRP	<10	10-15	>15
Minimum to Maximum score		5	10	15

Table 4: Distribution of all patients according to various scales

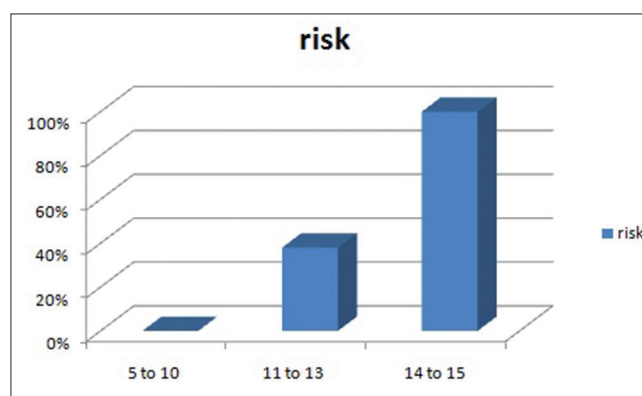
Score	Number of patients	Deaths
5-6	0	0
7-8	20	0
9-10	82	0
11-12	37	5 (13.5%)
13	26	19 (73%)
14	18	18 (100%)
15	5	5 (100%)

Table 5: P values of significant findings

Factor	P
Onset to Presentat on Duration	0.006
NIHSS score at Admission	0.0001
MRS score at Admission	0.0001
GCS score at Admission	0.0001
RBS at Admission	0.0001
HS CRP at Admission	0.0001

propose a new system for predicting in-hospital mortality of patients suffering from ischemic stroke, titled as Mortality in Ischemic Stroke "MIS" score. A score of <10 was found to be associated with best outcome and score of >14 with worst in ischemic stroke.^[15,16]

In our study, 25% patients expired during hospital admission after acute ischemic stroke that was higher as compared to Western data (Northern Manhattan Stroke Study, 2001, found a mortality of 5% at 1 month) but similar to another Indian study. In-hospital mortality is related to stroke severity and related complications.^[10,11] That is why three of our parameters in scoring system were related to clinical severity - NIHSS, mRS, and GCS - that are directly linked to early deaths in ischemic stroke. NIHSS more than 15, mRS more than 3, and GCS <8 were significantly associated with high mortality [Table 5] similar to previous studies.^[17-20]

**Figure 1: Distribution of the patient outcome as per our scale**

In most of the prior studies, predictive factors of mortality included atrial fibrillation, ischemic heart disease, and diabetes, history of stroke, ex-smoker status, older age, and more severe stroke. More than half of in-hospital mortality was attributed to secondary complications, especially increased intracranial pressure and pneumonia.^[17-21] Proportion of atrial fibrillation and ischemic heart disease was very less in our sample and age. History of stroke was not found significant. History of diabetes was not significantly associated with high mortality. However, higher blood sugar level at the time of admission was directly associated with high mortality. It is known that hyperglycemia increases growth of the infarct core in patients with surrounding hypoperfusion, suggesting that hyperglycemic blood is toxic to ischemic brain.^[22]

The last parameter included is the level of HS-CRP. HS-CRP an acute phase reactant was also strongly associated with stroke severity. Since stroke severity is strongly associated with mortality after stroke, HS-CRP is also associated with mortality.^[4,23]

One other and most recent scoring system for predicting stroke-related death is "IScore" developed by Canadian

stroke society. Multivariable predictors of 30-day and 1-year mortality included older age, male sex, severe stroke, nonlacunar stroke subtype, glucose ≥ 7.5 mmol/L (135 mg/dL), history of atrial fibrillation, coronary artery disease, congestive heart failure, cancer, dementia, kidney disease on dialysis, and dependency before the stroke. Based on these factors, a risk score index stratified the risk of death at 30 days and 1 year and identified low- and high-risk individuals.^[24] This system includes all parameters for short as well as long-term mortality, so it is more extensive and therefore little lengthy for bedside utility and is more useful for long-term mortality.

The mortality in ischemic stroke score (MISS) system is applicable for prediction of in-hospital mortality in stroke patients at presentation. It is short, simple, and easy to apply as it uses bedside clinical scales and simple investigations whose results are quickly available. The selected parameters for MISS are related to clinical severity of stroke and are helpful for early prediction of MIS. The radiological assessment of brain parenchyma involvement is not relied upon since different recoveries with similar parenchyma involvement have been noted. Besides size of the infarct may not accurately define, the severity as a small-sized infarct in a crucial area may do more harm than a large infarct in a relatively less critical area.

Conclusion

Our MIS system can effectively predict the mortality in patients with ischemic stroke at the time of presentation and thereby help physicians and neurologists predict the outcome of patients at the presentation to the hospital.

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Conflicts of interest

There are no conflicts of interest.

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