International Journal of Current Research and Review
DOI: http://dx.doi.org/10.31782/IJCRR.2020.12071

Original Article

IJCRR
Section: Healthcare
Sci. Journal Impact Factor: 6.1 (2018)
ICV: 90.90 (2018)

Clinical Profile and Short - Term Mortality Predictors in Acute Stroke with Emphasis on Stress Hyperglycemia and THRIVE Score : An Observational Study

Virendra Atam[1], Avirup Majumdar[2], Kamal Kumar Sawlani[3], D. Himanshu[4]

[1]Professor & Head, Department of Medicine, King George's Medical University, Lucknow, UP, India; [2]Resident, Department of Medicine, King George's Medical University, Lucknow, UP, India; [3]Professor, Department of Medicine, King George's Medical University, Lucknow, UP, India; [4]Additional Professor, Department of Medicine, King George's Medical University, Lucknow, UP, India.

ABSTRACT

Objectives: Stress hyperglycemia, the acute and transient hyperglycemia has been studied in many critical illnesses like stroke and myocardial infarction. THRIVE score proved to be an impressive predictor of in-hospital mortality in previous studies but data on Indian population are lacking. This observational study was conducted to assess the different short term mortality predictors in acute stroke.

Materials & Methods: A total of 150 acute stroke patients presenting within 24 hours of onset, who had CT scan evidence and/or met minimum WHO criteria for diagnosis of stroke were included. Patients with TIA, recurrent stroke, secondary hyperglycemia, traumatic hematomas were excluded. Blood glucose and THRIVE score values were obtained on admission. Stroke severity assessed by NIHSS score, while mRS score was used for disability assessment.

Results: We divided our study cohort into 4 groups. A cut off blood glucose of 140mg/dl was set for defining hyperglycemia. Out of 71 patients in group C(non diabetics with stress hyperglycemia), 54 expired (76.1%). The burden of stress hyperglycemia was more in ischemic stroke(65.1%) as compared to hemorrhagic stroke (57.1%). In a multivariate model, where age, GCS, NIHSS score were kept as predictors of mortality, stress hyperglycemia had been found to be an independent predictor of in-hospital post stroke mortality. THRIVE score of 6 or above predicted mortality in majority of non survivors.

Conclusion: Stress hyperglycemia was found to be a significant poor prognostic determinant. While THRIVE score proves to be an impressive prognostic tool, its validation as independent mortality predictor in acute stroke needs further research.

Key Words: Stress hyperglycemia, Stroke, Admission hyperglycemia, Hyperglycemia stress, THRIVE score, Cerebrovascular accident

INTRODUCTION

'Stroke', a leading cause of significant mortality and morbidity, got its name from the Greek word " apoplexia" meaning "being struck with a deadly blow". [1, 2] Stroke was the second largest cause of global death (5.5 million) after ischemic heart disease in 2016.[3] Overall mortality was higher in hemorrhagic stroke as compared to ischemic stroke cases. The outcome of stroke is influenced by various factors including severity, type of stroke, predisposing factors and related complications. Stroke has many risk factors- some are modifiable like hypertension, dyslipidemia, smoking, alcohol consumption, sedentary lifestyle and some are non-modifiable factors like age, sex and ethnicity. One of the potentially modifiable risk factors of stroke is stress hyperglycemia or admission hyperglycemia. Various studies showed the adverse effects of admission hyperglycemia on the short term outcome in acute stroke.[4] This acute hyperglycemia in stroke is not always due to type 2 diabetes mellitus but instead may be due to stress response

Corresponding Author:
Dr. Avirup Majumdar, MD, Resident, Department of Medicine, Gandhi Ward, Department of Medicine, King George's Medical University, Lucknow, UP, India; Ph: 7318329401; Email: dr.a.majumdar99@gmail.com or majumdar.avirup99@gmail.com

ISSN: 2231-2196 (Print) **ISSN:** 0975-5241 (Online)
Received: 18.02.2020 **Revised:** 19.03.2020 **Accepted:** 30.03.2020

mediated partly by the release of cortisol and norepinephrine.[5] Hyperglycemia can lead to poor outcome in acute stroke by different mechanisms- direct tissue damage mediated by lactate and intracellular acidosis in ischemic brain, increased free fatty acid pool interfering with vasodilation, cerebral vasculopathy induced by hyperglycemia [6].

German stroke study in 2004, predicted that mortality in ischemic stroke increases with i) NIHSS score>25 ii) higher age iii) fever>38^{0}c [7]. Weimer et al [8] in 2006 proposed a new prognostic model of hemorrhagic stroke termed Essen ICH score in which he utilized variables like i) Age, ii) NIHSS Score, iii) Level of consciousness. Stress hyperglycemia or transient admission hyperglycemia has been studied in many critical illnesses including myocardial infarction and stroke.[9] The independent prognostic role of stress hyperglycemia in acute stroke is yet to be deciphered. Totaled Health Risks in Vascular Events (THRIVE) score (totaled health risks in vascular events) calculated with age, NIHSS, and the presence of hypertension, diabetes mellitus, and atrial fibrillation proved to be a significant mortality predictor in acute ischemic stroke in previous studies [10] but sufficient data are lacking. Thus, we planned our study to assess the different prognostic variables including stress hyperglycemia and THRIVE score and their impact on the outcome in acute stroke patients.

MATERIALS AND METHODS

The present study was a prospective observational study conducted in the department of Medicine, King George's Medical University, Lucknow in the Indian state of Uttar Pradesh. The study protocol was approved by the Institutional Ethical committee, King George's Medical University. A total of 150 consecutive acute stroke patients who presented to the outpatient department/emergency, within 24 hours of onset of deficit and who had CT scan evidence of stroke and/or who met minimum World Health Organisation criteria for the diagnosis of stroke(i.e. rapidly developing focal neurological deficit lasting 24 hours or more) were enrolled after taking formal informed written consent from legal guardians. Patients who presented after 24 hours, who had Transient Ischemic Attacks(TIA), recurrent stroke, secondary hyperglycemia, traumatic hematomas, vascular malformations, aneurysms and coagulopathies were excluded from the study.

All participants were evaluated by detailed history (including history of diabetes, hypertension and any other comorbidities), clinical examination and severity assessment by NIHSS(National Institute of Health Stroke Scale)score[11] and GCS (Glasgow coma scale) score. Ischemic stroke and hemorrhagic stroke were defined by neurological examination and CT brain (normal CT brain scan or recent infarct or evidence of haemorrhage in the clinically relevant area on scan done within 72 hours of onset).

A baseline Electrocardiogram was obtained from all patients. Fresh blood samples at the time of admission were drawn for complete blood counts, blood glucose, Glycosylated haemoglobin (HbA1c), C reactive protein (CRP) and lipid profile(Total cholesterol, LDL-cholesterol, HDL cholesterol).All blood investigations were carried out at the pathology and biochemistry laboratories of King George's Medical University using standard protocols.

Serial random venous blood glucose values were measured on day of admission and at 12 hours,48 hours, 72 hours post admission and on day of discharge. A meticulous drug history was taken (thiazides, betablockers, glucocorticoids, OCPs, cyclosporine) and patients taking such drugs were excluded from the study. Adequate care was taken not to take samples for RBS from sites with intravenous lines. Hyperglycemia in our study was defined as blood glucose > 140 mg/dl or 7.8 mmol/L.

We divided our study cohort on the basis of diabetic history or use of medications for diabetes, HbA1c and admission glucose values into four different groups:

1. **Group A - Diabetics with Hyperglycemia on Admission:** Patients with a history of diabetes or use of medications or HbA1c>6.5% and admission glucose > 140 mg/dl
2. **Group B - Diabetics without Hyperglycemia on Admission:** Patients with a history of diabetes or use of medications or HbA1c>6.5% and admission glucose <=140 mg/dl
3. **Group C - Non Diabetics with Hyperglycemia on Admission:** Patients without a history of diabetes or use of medications and HbA1c < 6.5% and admission glucose >140 mg/dl
4. **Group D - Non Diabetics without Hyperglycemia on Admission:** Patients without a history of diabetes or use of medications and HbA1c <6.5% and admission glucose <=140mg/dl

All patients were followed up during hospital stay for recovery (using regular GCS assessment), complications like Sepsis, co-morbidities, length of hospital stay and outcome that included mortality and discharge. Totaled Health Risks in Vascular Events (THRIVE) score was calculated for all patients participating in the study using parameters of age, NIHSS score and chronic disease scale that includes history of diabetes, hypertension, atrial fibrillation.Functional recovery on discharge was determined by Modified Rankin Scale(mRS).

Statistical Analysis: The statistical analysis was done using SPSS version 21.0 statistical analysis software. The values were represented in Number (%) and Mean $\pm$ Standard Deviation. To test the significance of two means, student's 't' test was used. Categorical variables were analysed with Chi square test. Cut-off levels of blood glucose values that predicted death was determined by ROC curve analysis. At

multivariate level, variables associated with mortality and poor functional outcome were determined using logistic regression analysis. Multivariate modeling included variables with $p < 0.05$ at uni-variate level. A p-value of <0.05 was considered significant.

RESULTS

A total of 150 patients were analysed in our study. Age of patients ranged from 18 to 98 years. Mean age of patients was 66.93±16.00 years. Majority of patients were males (70%). Male to female ratio was 2.33. Almost half (n=74; 49.3%) were hemorrhagic stroke cases whereas remaining (n=76; 50.7%) were ischemic stroke. Among the hemorrhagic stroke, combined basal ganglia and ventricles constituted the commonest site of involvement (75.7%) whereas middle cerebral artery(93.4%) was the commonest site involved in ischemic stroke cases.

Mean admission GCS and NIHSS were 8.03±2.64 and 26.09±6.66 respectively. Mean systolic and diastolic blood pressure values were 164.57±15.04 and 90.95±9.98 mmHg respectively. Mean admission blood glucose level was 178.53±70.45 mg/dl. Mean serum cholesterol, HDL, LDL and triglyceride levels were 141.54±45.56, 40.78±3.24, 86.14±14.18 and 138.46±24.57 mg/dl respectively which were not significant statistically. A total of 59 (39.4%) cases were discharged, however, a total of 91 (60.7%) expired. Thus, in-hospital mortality rate was 60.7%.

Mean RBS levels at baseline, 12 hrs, 48 hrs, 72 hrs and at discharge were 178.53±70.45, 145.69±44.30, 140.91±36.79, 132.56±32.70 and 117.76±15.26 mg/dl respectively. Proportion of cases with hyperglycemia as per baseline, 12 hrs, 48 hrs, 72 hrs and at discharge were 77.3%, 30.7%, 36.5%, 32.1% and 6.9% respectively.

Table 1: Association of Outcome with different clinico-pathological variables studied (n=150)

SN	Characteristic	Non-survivors (n=91)		Survivors(n=59)		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
1.	Mean Age±SD (Range) in years	69.60	14.91	62.80	16.86	2.59	0.010
2.	**Sex**						
	Male	64 (70.3%)		41 (69.5%)		χ^2=0.012; p=0.913	
	Female	27 (29.7%)		18 (30.5%)			
3.	**Diagnosis**						
	IC Bleed	50 (54.9%)		24 (40.7%)		χ^2=2.915; p=0.088	
	IC Infarct	41 (45.1%)		35 (59.3%)			
4.	**Time of admission**						
	<12 hrs	49 (53.8%)		26 (44.1%)		χ^2=1.369; p=0.242	
	>12 hrs	42 (46.2%)		33 (55.9%)			
5.	Mean GCS on admission±SD	7.56	2.77	8.75	2.27	-2.74	0.007
6.	Mean NIHSS±SD	27.11	6.40	24.51	6.80	2.37	0.019
7.	Mean SBP±SD	166.44	14.30	161.69	15.80	1.90	0.059
8.	Mean DBP±SD	91.75	11.32	89.71	7.39	1.22	0.224
9.	Mean RBS±SD	195.66	80.64	152.11	38.58	3.87	<0.001
10.	Mean Hb±SD	12.30	1.58	11.90	1.33	1.62	0.108
11.	Mean TLC±SD (per cumm^3)	10884.58	3773.22	10092.73	3956.14	1.23	0.220
12.	Mean INR±SD	1.32	0.31	1.35	0.24	-0.62	0.535
13.	Mean Cholesterol±SD	138.74	39.99	145.86	53.11	-0.94	0.351
14.	Mean HDL±SD	40.76	3.06	40.81	3.53	-0.10	0.919
15.	Mean LDL±SD	87.31	9.31	84.34	19.41	1.25	0.211
16.	Mean Triglycerides±SD	136.63	20.18	141.29	30.08	-1.14	0.258
17.	Mean HbA1C±SD	6.26	1.47	6.13	1.20	0.57	0.568

Table 2: Association of Outcome with RBS at different time intervals

SN	Characteristic	Non survivors		Survivors		Statistical significance	
		Mean	SD	Mean	SD	't'	'p'
1.	Baseline	195.66	80.64	152.11	38.58	3.867	<0.001
2.	12 hrs	153.12	53.25	134.22	20.53	2.601	0.010
3.	48 hrs	146.57	41.84	132.37	25.52	2.334	0.021
4.	72 hrs	135.92	42.13	127.88	30.23	1.221	0.224
5.	Mean	145.35	42.73	131.58	21.41	2.293	0.023

Above table shows that baseline or admission glucose has maximum correlation with outcome($p < 0.001$) as compared to 12 hour, 72 hours, 48 hours RBS readings.

Table 3: ROC Analysis for deriving Study specific cut-off value of baseline RBS to predict mortality under different study considerations

Consideration	Area under curve±SE (Significance)	Projected cut-off value	Projected sensitivity	Projected specificity
Overall study population	0.698±0.044*	>156.45	68.1%	64.4%
Diabetics	0.691±0.071*	>157	66.7%	64.0%
Non-diabetics	0.715±0.055*	>156.45	68.9%	64.7%

*p<0.001

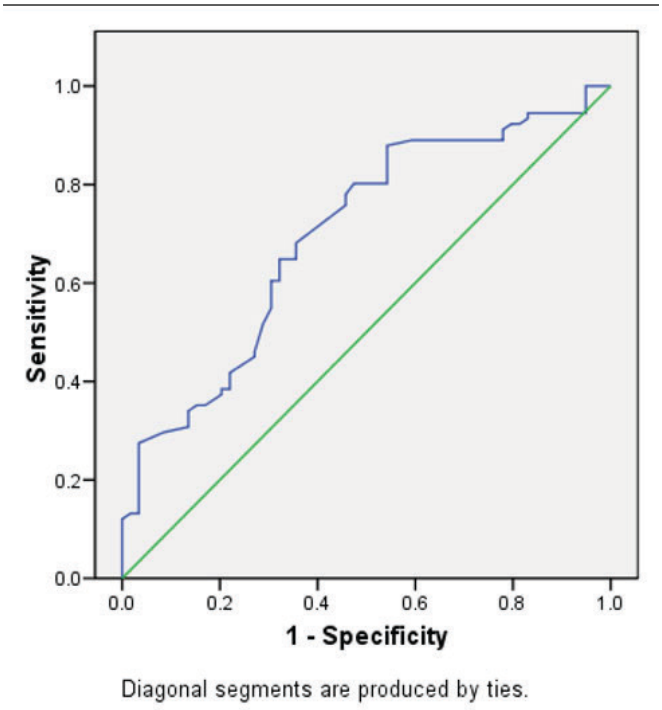

Figure 1(a): Overall study population.

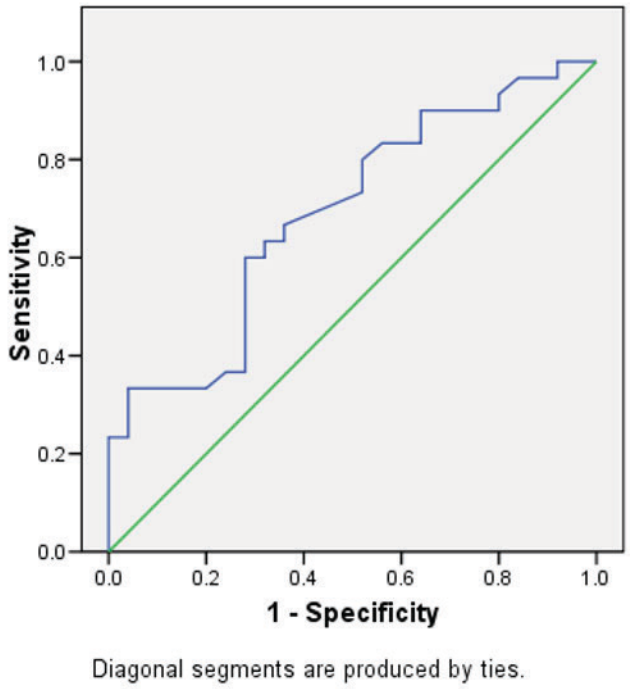

Figure 1(b): Diabetics

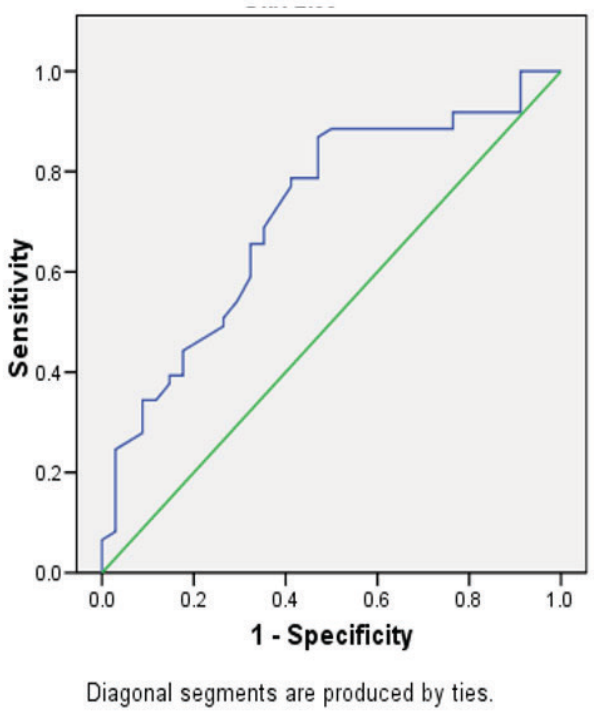

Figure 1(c): Non diabetics

The area under curve values for overall study population, diabetics and non-diabetics were 0.698, 0.691 and 0.715 respectively, thus indicating an average diagnostic efficacy of baseline random blood sugar levels. For entire study population and non-diabetics, same cut-off value (≥156.45 mg/dl or 8.68 mmol/L) was derived which was 68.1% sensitive and 64.4% specific for entire population and 68.9% sensitive and 64.7% specific for non-diabetics. For diabetics, the derived cut-off value was slightly higher at ≥157 mg/dl or 8.71 mmol/L and was projected to have 66.7% sensitivity and 64% specificity.

Table 4: Outcome of Stress hyperglycemics [Group C] (baseline RBS>140mg/dl and HbA1c<6.5% and no history of diabetes)as compared to other patients

SN	Characteristic	Non survivors	Survivors
1.	Diabetics with hyperglycemia at baseline (n=46) [Group A]	27 (58.7%)	19 (41.3%)
2.	Diabetics without hyperglycemia at baseline (n=9) [Group B]	3 (33.3%)	6 (66.7%)
3.	Non-diabetics with hyperglycemia at baseline (n=71)[Group C]	54 (76.1%)	17 (23.9%)
4.	Non-diabetics without hyperglycemia (n=24) [Group D]	7 (29.2%)	17 (70.8%)

χ^2=19.92; p<0.001

Mortality rate was maximum among non-diabetics with hyperglycemia at baseline(stress hyperglycemics) (76.1%) (**Group C**) followed by diabetics with hyperglycemia at baseline (58.7%)(Group A), diabetics without hyperglycemia at baseline (33.3%)(Group B) and was minimum among non-diabetics without hyperglycemia at baseline (29.2%) (Group D). Statistically, this intergroup difference was significant (p<0.001).

Table 5: Comparison of demographic factors and clinical predictors among different study groups

SN	Variable	Group A (n=46)		Group B (n=9)		Group C (n=71)		Group D (n=24)		Statistical significance (ANOVA)	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	F	p
1.	Age	71.00	13.55	63.56	22.74	67.23	15.40	59.50	17.39	2.972	0.034
2.	SBP	165.09	14.87	165.56	17.40	164.82	14.81	162.50	15.95	0.186	0.906
3.	DBP	88.46	13.33	91.11	6.01	92.52	6.92	91.00	10.92	1.563	0.201
4.	GCS	8.72	2.57	8.56	2.30	7.32	2.83	8.58	1.82	3.343	0.021
5.	NIHSS	26.28	6.41	22.22	6.18	27.34	7.15	23.46	4.53	3.244	0.024
6.	THRIVE score	6.33	1.45	5.89	1.54	5.25	1.37	5.00	1.44	7.007	<0.001
7.	Baseline RBS	207.29	94.26	123.67	6.87	187.09	50.41	118.65	14.83	13.05	<0.001

Table 5 shows that the mean NIHSS score in group A, group B, group C and group D were 26.28 ± 6.41,22.22 ± 6.18,27.34 ± 7.15 and 23.46± 4.53 respectively Mean Baseline RBS values in different groups were respectively 207 .29±94.26,123.67±6.87,187.09±50.41 and 118.65±14.83 respectively. Mean THRIVE score among different groups were 6.33±1.45,5.89±1.54,5.25±1.37 and 5±1.44 in groups A,B,C and D respectively. All of these three parameters show statistically significant intergroup differences (p<0.05) with baseline RBS showing maximum significance(p<0.001). This also shows that patients with stress hyperglycemia have maximum stroke severity as compared to other groups.

Table 6: Stress hyperglycemia in IC Bleed and IC infarct patients separately and correlation with outcome

SN	Group	Total No. of cases	No. expired	% Expired
1.	IC Bleed (n=74)			
	With stress hyperglycemia	23	16	69.6
	No stress hyperglycemia	51	34	66.7
	χ^2=0.061; p=0.805			
2.	IC Infarct			
	With stress hyperglycemia	33	28	78.8
	No stress hyperglycemia	43	15	34.9
	χ^2=14.47; p<0.001			

Table 7: THRIVE Score and its association with mortality

SN	THRIVE Score	Non survivors	Survivors
1.	6 or above (n=79)	55 (69.6%)	24 (30.4%)
2.	<6 (n=71)	36 (50.7%)	35 (49.3%)

χ^2=5.607; p=0.018

Above table shows that patients with THRIVE score 6 or above have maximum mortality (p=0.018).

Table 8: Association of mortality with THRIVE score and stress hyperglycemia

SN	Condition	Non survivors	Survivors
1.	Stress hyperglycemia with THRIVE score >6 (n=25)	22 (88.0%)	3 (12.0%)
2.	Others (n=125)	69 (55.2%)	56 (44.8%)

χ^2=9.393; p=0.002

Patients having stress hyperglycemia with THRIVE score ≥6 had a significantly higher mortality rate (88%) as compared to others (55.2%) (p=0.002).

Proportion of those with mRS≥4(poor functional recovery) was maximum among diabetics with hyperglycemia at baseline (47.4%)(Group A) followed by non-diabetics with hyperglycemia at baseline (31.3%)(stress hyperglycemics)(Group C), non-diabetics without hyperglycemia (17.6%)(Group D) and diabetics without hyperglycemia at baseline(Group B) (16.7%). However, these differences were not significant statistically (p=0.224).

Table 9: Association of Diabetes and stress hyperglycemic status with mRS on discharge

SN	Status	Total No.	No. of patients with mRS>4 (Poor functional recovery)	%
1.	Diabetics with hyperglycemia at baseline [Group A]	19	9	47.4
2.	Diabetics without hyperglycemia at baseline [Group B]	6	1	16.7
3.	Non-diabetics with hyperglycemia at baseline (stress hyperglycemics)[Group C]	16	5	31.3
4.	Non-diabetics without hyperglycemia [Group D]	17	3	17.6

χ^2=4.371; p=0.224

Table 10: Multivariate analysis (Binary logistic regression)

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1(a)	Stress Hyperglycemia	-1.078	.429	6.298	1	.012	.340
	Age	.017	.016	1.141	1	.285	1.017
	GCS	-.116	.107	1.193	1	.275	.890
	NIHSS	-.007	.045	.021	1	.885	.993
	Baseline RBS	.012	.004	8.146	1	.004	1.012
	THRIVE Score	.119	.196	.366	1	.545	1.126
	Constant	3.774	3.885	.943	1	.331	43.542

In a multivariate model where age, GCS, NIHSS, baseline RBS, THRIVE score and stress hyperglycemia were kept as predictors of mortality, only stress hyperglycemia and baseline RBS levels were found to be significant independent predictors of in-hospital mortality.

DISCUSSION

Cerebro-vascular accident or stroke is a major debilitating neurological disease contributing for an ever increasing burden of global mortality and morbidity. Diabetes and hyperglycemia are established risk factors for ischemic stroke. [12-15] While there are a number of studies based on ischemic stroke that showed worse outcomes with hyperglycemia [16], few others have shown that hyperglycemia can be protective in small vessel disease.[17]

A strong association is seen between hyperglycemia and increased mortality and morbidity, irrespective of the diabetes status in multiple cohorts [18-24] while contrasting reports are seen in some others. [25-26] Literature shows two meta-analysis which concluded that high blood glucose values increase both short term and long term mortality in hemorrhagic stroke. [27,28] However subarachnoid hemorrhage cases had also been included in these studies. There are many factors through which hyperglycemia could increase cerebral damage in ischemic stroke.[29] A high blood glucose on admission impaired recanalisation in patients with acute ischemic stroke. When brain is exposed to excessive levels of glucose, blood brain barrier gets disrupted and events like anaerobic glycolysis, lactate accumulation, acidosis, generation of free radicals, excitatory neurotransmitters release and calcium influx into the cell ensue. Poorly controlled hyperglycemia interferes with perfusion to the brain, tissue oxygenation and raises intracranial pressure thereby resulting in neuronal death. These mechanisms are responsible for hyperglycemia induced damage in hemorrhagic stroke.

There is no clear cut off values of admission glucose which can predict outcome in acute stroke patients. We tried to find a definite cut off for admission glucose in our study that could signify poor prognosis in stroke patients by using ROC analysis.[Fig 1] For entire study population and non diabetics, same cut off value (≥ 156.45mg/dl or 8.68 mmol/L) was derived which was 68.1% sensitive and 64.4% specific for the entire population[Fig 1 a] and 68.9% sensitive and 64.7% specific for non-diabetics.[Fig 1c] For diabetics, the derived cut off value was slightly higher at ≥ 157mg/dl or 8.71mmol/L with 66.7% sensitivity and 64% specificity.[Fig 1b] The almost same cut off values for both diabetics and non diabetics could be due to the well controlled diabetics being included in our cohort.

The in-hospital mortality in our study was 60.7% which is quite higher than previous studies. [30-32]This can be attributed to the greater stroke severity (mean NIHSS score 26.09+_6.66), inability to perform thrombolysis or surgical interventions and lack of a well equipped stroke unit in our hospital.

Group C or the stress hyperglycemia group had the maximum mortality(76.1%) followed by Group A (58.7%).[Table 4] Group C also had a higher mean NIHSS (27.34+ 7.15) which signifies greater stroke severity among them.[Table 5] Admission hyperglycemia is related to greater stroke severity which is evident in previous studies. [33]

Most of the available studies related to stress hyperglycemia are on ischemic stroke patients [34-40] with limited data on hemorrhagic stroke. [41,42] Our study cohort consisted of both ischemic and hemorrhagic stroke cases. Stress hyperglycemia proved to be a poor prognostic marker for both types but the effect on the outcome of ischemic stroke is more deleterious than on hemorrhagic type (78% vs 69.6% mortality).[Table 6]

Totaled Health Risks in Vascular Events (THRIVE) score (totaled health risks in vascular events) is calculated with age, NIHSS, and the presence of hypertension, diabetes mellitus, and atrial fibrillation and was validated to predicting clinical outcome and hemorrhagic transformation in patients receiving tissue Plasminogen Activator, showed to be a simple score to help clinicians to estimate outcome and death after acute ischemic Stroke [43]. The performance of THRIVE score in predicting short term mortality had been established in a Brazilian study [9]. In our study, a THRIVE score of 6 or above was present in majority of non survivors (69.6%) (p=0.018). A greater proportion of non survivors (88%) with a high THRIVE score (≥ 6) had a stress response (stress hyperglycemia) (p=0.002).

Our study failed to delineate the impact of stress hyperglycemia on functional recovery after stroke. [Table 9] A poor functional recovery (mRS≥ 4) was more evident among diabetics with admission hyperglycemia (Group A) as compared to stress hyperglycemics (Group C) which is in contrast to the previous studies. [32,34] This discrepancy may be due to a shorter follow up period of patients in our study.

The Glycemia in Acute Stroke (GLIAS) study was a large, multicentre cohort study of 476 patients. The study showed that a capillary glucose value ≥155 mg/dL(8.5 mmol/L) at any time within the first 48 hours, independent of age, stroke severity, or infarct volume, is associated with a higher mortality risk in ischemic stroke patients. [44]

In univariate analysis, in our study, except for age, on admission GCS, NIHSS score, stress hyperglycemia and THRIVE score, none of the other clinical or laboratory parameters showed a significant association with outcome (p <0.05). Sepsis showed a non significant association with mortality (p=0.34), thus excluded from multivariate model.

In multivariate analysis, our study demonstrates stress hyperglycemia to be an independent predictor of mortality. [Table 10] THRIVE score failed to show significance in multivariate model.

However, our study had a few limitations. Being a tertiary care centre, patients often got their pre-referral treatment like dextrose containing drips at primary centres that might have affected the admission glucose values in our study. Post discharge glycemic status and its relation with mortality had not been taken into account which forms another major limitation. Besides, limited sample size and inability to evaluate hematoma/infarct volume which has independent prognostic effect on outcome were the drawbacks of our study. The impact of glucose lowering on the outcome of stroke couldn't be determined.

CONCLUSION

In this observational study, stress hyperglycemia was found to be an independent predictor of short term mortality in acute stroke patients when adjusted with age, GCS and NIHSS score. A baseline blood glucose more than 156.45mg/dl or 8.68 mmol/L was found to be significantly associated with mortality. Though THRIVE score was not found to be an independent mortality predictor, a score of 6 or above could predict mortality in majority of non survivors. In conclusion, our study raises two vital queries –

1. Do we need to treat stress hyperglycemia in acute stroke patients?
2. Do we need to include acute glucose in THRIVE prognostic model to better predict post stroke outcome?

Large multicentric studies need to be conducted to address the above mentioned issues.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the technical support provided by the Department of Neurology and Department of Pathology, King George's Medical University, Lucknow, India. Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

Conflicts of Interest: None stated

Funding: No funding source

Ethical Approval: Ethical clearance for the study was obtained from Institutional ethical committee, King George's Medical University.

Informed Consent: Written informed consent was obtained from legal guardians of all study patients.

ABBREVIATIONS:

GCS- Glasgow Coma Scale

NIHSS- National Institutes of Health Stroke Scale

THRIVE score- Totaled Health Risks in Vascular Events

WHO- World Health Organisation

mRS- Modified Rankin Score

REFERENCES

1. Pound P, Bury M, Ebrahim S,From Apoplexy to Stroke, Age Ageing 1997;26:331-337.
2. Clarke E, Apoplexy in Hippocratic writings. *Bull Hist Med* 1963;37:301-314.
3. Gorelick PB. The global burden of stroke: Persistent and disabling. The Lancet Neurology. 2019 May 1;18(5):417-8.
4. Gentile, NT, Seftchick, MW, Huynh, T. Decreased mortality by normalizing blood glucose after acute ischemic stroke. Acad Emerg Med 2006; 13: 174–180.
5. Mi D, Wang P, Yang B, Pu Y, Yang Z, Liu L. Correlation of hyperglycemia with mortality after acute ischemic stroke. Therapeutic advances in neurological disorders. 2018 Jan 10;11:1756285617731686
6. Mehta KC. Stress hyperglycemia. Med Update. 2005;62:300
7. German Stroke study Collaboration Predicting outcome after acute ischemic stroke: An external validation of prognostic model. Neurology. 2004 Feb;vol 62(4):208–216.
8. Weimar C, Mieck T, Buchthal J et al. for the German Stroke Study Collaboration. Neurologic worsening during the acute phase of ischemic stroke. Arch Neuroly. 2005;62:393–397.
9. DiNardo MM, Korytkowski MT, Siminerio LS. The importance of normoglycemia in critically ill patients. Crit Care Nurs Q 2004;27:126-34.
10. Kuster GW, Dutra LA, Brasil IP, Pacheco EP, Arruda MJ, Volcov C, Domingues RB. Performance of four ischemic stroke prognostic scores in a Brazilian population. Arquivos de neuro-psiquiatria. 2016 Feb;74(2):133-7.
11. Scale NS. The Internet Stroke Center, cited at http://www.strokecenter.org/professionals/stroke-diagnosis/stroke-assessment-scales/
12. Mankovsky BN, Metzger BE, Molitch ME, Biller J. Cerebrovascular disordersin patients with diabetes mellitus. J Diabetes Complicat. (1996) 10:228–42.
13. Sacco RL. Identifying patient populations at high risk for stroke. Neurology(1998) 51:S27–30.
14. Mankovsky BN, Ziegler D. Stroke in patients with diabetes mellitus. Diabetes Metab Res Rev. (2004) 20:268–87.
15. Mandava P, Martini SR, Munoz M, Dalmeida W, Sarma AK, Anderson JA, et al. Hyperglycemia worsens outcome after rt-PA primarily in the large-vessel occlusive stroke subtype. Transl Stroke Res. (2014) 5:519–25.
16. Bruno A, Levine SR, Frankel MR, Brott TG, Lin Y, Tilley BC, et al. Admission glucose level and clinical outcomes in the NINDS rt-PA Stroke Trial. Neurology (2002) 59:669−74.
17. Uyttenboogaart M, Koch MW, Stewart RE, Vroomen PC, Luijckx GJ, De Keyser J. Moderate hyperglycaemia is associated with favourable outcome in acute lacunar stroke. Brain (2007)
18. Tapia-Pérez JH, Gehring S, Zilke R, Schneider T. Effect of increased glucose levels on short-term outcome in hypertensive spontaneous intracerebral hemorrhage. Clin Neurol Neurosurg. (2014) 118:37–43.
19. Stöllberger C, Exner I, Finsterer J, Slany J, Steger C. Stroke in diabetic and nondiabetic patients: course and prognostic value of admission serum glucose. Ann Med. (2005) 37:357–64.
20. Tan X, He J, Li L, Yang G, Liu H, Tang S, et al. Early hyperglycaemia and the early-term death in patients with spontaneous intracerebral haemorrhage: A meta-analysis. Intern Med J. (2014) 44:254.
21. Sun S, Pan Y, Zhao X, Liu L, Li H, He Y, et al. Prognostic value of admission blood glucose in diabetic and non-diabetic patients with intracerebral hemorrhage. Sci Rep. (2016) 6:32342.
22. Namani G, Rampure D M, Murali M. Clinical profile and mortality in patients presenting with intra-cerebral hemorrhage in a tertiary care centre. Schol J Appl Med Sci. (2014) 2:3005–6.
23. Xi G, Fewel ME, Hua Y, Thompson BG, Hoff JT, Keep RF. Intracerebral hemorrhage: pathophysiology and therapy. Neurocrit Care (2004) 1:5–18.
24. Capes SE, Hunt D, Malmberg K, Pathak P, Gerstein HC. Stress hyperglycemia and prognosis of stroke in non-diabetic

and diabetic patients: A systematic overview. Stroke (2001) 32:2426–32.
25. Lee SH, Kim BJ, Bae HJ, Lee JS, Lee J, Park BJ, et al. Effects of glucose level on early and long-term mortality after intracerebral haemorrhage: the acute brain bleeding analysis study. Diabetologia (2010) 53:429–34.
26. Tetri S, Juvela S, Saloheimo P, Pyhtinen J, Hillbom M. Hypertension and diabetes as predictors of early death after spontaneous intracerebral hemorrhage. J Neurosurg. (2009) 110:411–7.
27. Tan X, He J, Li L, Yang G, Liu H, Tang S, et al. Early hyperglycaemia and the early-term death in patients with spontaneous intracerebral haemorrhage: A meta-analysis. Intern Med J. (2014) 44:254–60.
28. Guo X, Li H, Zhang Z, Li S, Zhang L, Zhang J, et al. Hyperglycemia and mortality risk in patients with primary intracerebral hemorrhage: A meta-analysis. Mol Neurobiol. (2016) 53:2269–75.
29. Ribo M, Molina C, Montaner J, Rubiera M, Delgado-Mederos R, Arenillas JF, Quintana M, Alvarez-Sabín J. Acute hyperglycemia state is associated with lower tPA-induced recanalization rates in stroke patients. Stroke. 2005 Aug 1;36(8):1705-9.
30. Kongwad LI, Hegde A, Menon G, Nair R. Influence of admission blood glucose in predicting outcome in patients with Spontaneous intracerebral hemorrhage. Frontiers in neurology. 2018;9:725.
31. Zhao Y, Yang J, Zhao H, Ding Y, Zhou J, Zhang Y. The association between hyperglycemia and the prognosis of acute spontaneous intracerebral hemorrhage. Neurological research. 2017 Feb 1;39(2):152-7.
32. Snarska KK, Bachórzewska-Gajewska H, Kapica-Topczewska K, Drozdowski W, Chorąży M, Kułakowska A, Małyszko J. Hyperglycemia and diabetes have different impacts on outcome of ischemic and hemorrhagic stroke. Archives of medical science: AMS. 2017 Feb 1;13(1):100.
33. Green SR, Lokesh S, Mathew TK, Jayasingh K, Ragupathy S. A study of stress hyperglycemia and its relationship with the neurological outcome in patients presenting with acute ischemic stroke. International Journal of Advances in Medicine. 2016 Jul;3(3):546.
34. Gofir A, Mulyono B, Sutarni S. Hyperglycemia as a prognosis predictor of length of stay and functional outcomes in patients with acute ischemic stroke. International Journal of Neuroscience. 2017 Oct 3;127(10):923-9.
35. Raghavendra Prasad B. N. , Dr. Sandeep Reddy A. , Dr. Prabhakar et al. Stress hyperglycemia as a prognostic marker in acute ischaemic stroke. EJPMR, 2016,3(3), 247-256.
36. Levetan CS. Effect of hyperglycemia on stroke outcomes. Endocr Pract 2004;10(Supplement 2):34–9. doi:10.4158/EP.10.S2.34.
37. Chang KC, Tseng MC, Weng HH et al, Prediction of length of stay of first-ever ischemic stroke. Stroke 2002;33:2670–4.
38. Nakao S, Takata S, Uemura H, et al. Relationship between Barthel index scores during the acute phase of rehabilitation and subsequent ADL in stroke patients. J Med Invest 2010;57:81–8.
39. Williams LS, Rotich J, Qi R, et al. Effects of admission hyperglycemia on mortality and costs in acute ischemic stroke. Neurology 2002;59(1):67–71.
40. Parsons MW, Barber PA, Desmond PM, et al. Acute hyperglycemia adversely affects stroke outcome: a magnetic resonance imaging and spectroscopy study. Ann Neurol 2002;52(1):20–8.
41. Kongwad LI, Hegde A, Menon G, Nair R. Influence of admission blood glucose in predicting outcome in patients with Spontaneous intracerebral hemorrhage. Frontiers in neurology. 2018;9:725.
42. Zhao Y, Yang J, Zhao H, Ding Y, Zhou J, Zhang Y. The association between hyperglycemia and the prognosis of acute spontaneous intracerebral hemorrhage. Neurological research. 2017 Feb 1;39(2):152-7.
43. Lei C, Wu B, Liu M, Chen Y, Yang H, Wang D et al. Totaled health risks in vascular events score predicts clinical outcomes in patients with cardioembolic and other subtypes of ischemic stroke. Stroke. 2014;45(6):1689-94.
44. Fuentes B, Castillo J, San José B, Leira R, Serena J, Vivancos J, Dávalos A, Nuñez AG, Egido J, Díez-Tejedor E. The prognostic value of capillary glucose levels in acute stroke: The Glycemia in Acute Stroke (GLIAS) study. Stroke. 2009 Feb 1;40(2):562-8.